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ORIGINAL ARTICLE

Kaiser model-based hazard vulnerability analysis in event risk assessment and emergency management of operating room in a hospital in China

Análisis de vulnerabilidad ante peligros basado en el modelo de Kaiser en la evaluación de riesgos de sucesos y la gestión de emergencias en el quirófano de un hospital de China

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Abstract

Objective: *This study aimed to identify the high-risk events in the operating room so as to provide a decision-making basis for emergency management.* **Method:** *The Kaiser model-based Hazard vulnerability analysis (HVA) was used to determine the risk matrix. The Delphi method was used to create the risk assessment form. The potential risk events were quantitatively evaluated. The relative risk percentages of the risk events were calculated to identify the top high-risk events.* **Results:** *A risk matrix containing 4 components (natural disasters; technological hazards; human hazards; and hazardous materials) was determined, and a risk assessment form was created using the Delphi method. The top three high-risk events are as follows: internal radiation exposure (41%), infectious disease outbreaks (38%), and internal fires (33%). The emergency management measures for high-risk events were developed.* **Conclusions:** *The Kaiser model-based HVA in event risk assessment of operating room can effectively identify potential high-risk events, determine emergency priorities, and optimize resource allocation, thereby ensuring the quality and safety of surgical treatment.*

Keywords: *Operating rooms. Risk assessment. Hospital administration. Safety management. Disasters.*

Resumen

Objetivo: *Este estudio busca identificar eventos de alto riesgo en quirófano con el fin de proporcionar una base para la toma de decisiones en la gestión de emergencias.* **Método:** *Para determinar la matriz de riesgos se utilizó el análisis de vulnerabilidad de peligros (HVA) basado en el modelo de Kaiser. Se utilizó el método Delphi para crear el formulario de evaluación de riesgos. Se evaluaron posibles eventos de riesgo cuantitativamente. Se calcularon porcentajes de riesgo relativo de los sucesos de riesgo para identificar sucesos de mayor riesgo.* **Resultados:** *Se determinó una matriz de riesgos que contenía cuatro componentes (desastres naturales, peligros tecnológicos, peligros humanos y materiales peligrosos) y se creó un formulario de evaluación de riesgos utilizando el método Delphi. Los tres principales sucesos de alto riesgo son exposición a radiaciones internas (41%), brotes de enfermedades infecciosas (38%) e incendios internos (33%). Se elaboraron medidas de gestión de emergencias para los sucesos de alto riesgo.* **Conclusiones:** *El HVA basado en el modelo de Kaiser en la evaluación del riesgo de eventos en quirófano puede identificar eficazmente posibles eventos de alto riesgo, determinar prioridades de emergencia y optimizar la asignación de recursos, garantizando así la calidad y seguridad del tratamiento quirúrgico.*

Palabras clave: *Quirófanos. Evaluación de riesgos. Administración hospitalaria. Gestión de la seguridad. Catástrofes.*

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Introduction

Our hospital is one of the first batch of national tertiary Grade A women's and children's hospitals in China. As an important clinical department in our hospital, our operating room undertakes surgical procedures for the departments of gynecology, reproduction and internal secretion, obstetrics, pediatric surgery, and andrology. Our hospital's surgical volume is more than 60,000 cases/year and many of them have high complexity. In our hospital, 80% of the surgeries are at levels 3 and 4, while minimally invasive surgeries account for 83% of the total. In response to our hospital's development policy, the operating room has carried out pediatric orthopedic surgeries, urological surgeries, and da Vinci robotic surgical procedures. As the surgical teams from the plastic surgery and otorhinolaryngology departments will use the operating room, new devices will be required for surgeries, and surgical volume will increase sharply. The operating room working environment is enclosed, as exposing large quantities of blood and body fluids from surgical patients could easily cause the breeding and transmission of various pathogens. Repeated long-term usage of various apparatus and equipment makes the operating room a high-risk department when dealing with sudden hazards, while the management and clinical work of the operating room become increasingly risky and challenging.

Hazard vulnerability analysis (HVA) is an important method used to stratify the risk of potential hazardous events, measure the probability of potential hazardous events, and guide hazard preparedness and prevention[1]. HVA is an internationally recognized excellent method that can systematically evaluate the vulnerability of urban facilities (such as hospitals and schools) as well as the population, while comprehensively evaluating the ability of emergency medical treatment, disease prevention and treatment, and health security for injuries caused by hazard events[2,3].Therefore, HVA has become an important part of emergency management in operating rooms. HVA provides scientific guidance for managers to effectively identify weaknesses in work and risk exposure in the operating room, allowing for clear focus and direction in emergency management, formulation of corresponding management strategies, enhancement of communication and cooperation between the operating room and relevant departments within the hospital, and effectively improving the response level of operating room staff in handling high-risk events.

Method

Ethics approval

This study was conducted in accordance with the Declaration of Helsinki. All research methods were carried out in accordance with the relevant guidelines and regulations. This study was approved by the medical ethics committee of the first author's institution. Verbal informed consent to participate in this study was obtained from all participants. The medical ethics committee of the first author's committee approved the procedure of verbal informed consent of this study.

Research team

The research team was composed of 7 members. Of them, 1 possessed a doctoral degree, 4 possessed a Master's degree, and 2 possessed an undergraduate qualification; with 1 being a chief physician, 3 co-chief nurses, and 3 supervising nurses amongst the team. Their range of employment history spanned from 12 to 30 years.

Kaiser model-based operating room risk assessment form

Indicator selection

The Joint Commission International Accreditation Standards for Hospitals defines hospital HVA as the scientific identification of potential emergency situations and their possible direct and indirect impacts on a healthcare facility's running and services. The Kaiser model, developed by Kaiser Permanente Medical Group, is a tool for HVA and evaluation, with scientific and reliable results[4,5]. The indicator selection of risk assessment form for operating room HVA was based on the Kaiser model. Our hospital's operating room staff (including doctors, anesthetists, nurses, and nursing workers) functioned as the object of our research. A 12-month self-inspection of hidden hazards was carried out during the period of June 2021-June 2022. The risk event register was truthfully filled in, after which the research team created a summary of the data. According to the concept and connotation of hospital hazard vulnerability, the main contents of the

Kaiser model, and the actual situation of our hospital and operating room, 4 components of the operating room risk matrix were determined: namely, natural disasters, technological hazards, human hazards, and hazardous materials. Based on these 4 components, the operating room risk event register was created. Indicators of the operating room risk assessment form (including 4 level 1 indicators, and 26 level 2 indicators) were determined, and the Delphi method was used for expert consultation.

Expert consultation questionnaire

The expert consultation questionnaire contains three parts:

- Consultation description; including the research goals and significance, the description of filling in the questionnaire, and the time of expert feedback
- Consultation questions were used to evaluate the importance of each indicator according to the 5-point Likert scale: 5 points means "very important", 4 points means "important", 3 points means "fairly important", 2 points means "low importance", and 1 point means "not at all important". An open-ended feedback column was included for the respondents to explain the added or deleted indicators
- Basic information about the experts, including a profile of them, as well as the experts' familiarity with the research, and their self-evaluation of the basis of judgment.

Expert selection

The expert inclusion criteria, determined according to the research objective, were as follows:

- Gave informed consent to voluntarily participate in this study
- Engaged in emergency medicine and nursing, operating room nursing, operating room management, or medical education
- Working years $\geq$ 10 years
- Possessed solid theoretical knowledge and rich clinical experience, or management experience
- Possessed an undergraduate qualification or above
- Possessed a professional title at the intermediate level or above.

A total of 27 experts from 6 hospitals in Chengdu, Xi'an, and Yunnan participated in this study. The numbers of tertiary Grade A and tertiary Grade B hospitals were 4 and 2, respectively. In terms of the experts' professional titles: 7 possessed senior professional titles, 11 possessed deputy senior professional titles, and 9 possessed intermediate professional titles. For educational background, 7 possessed doctoral degrees, 10 possessed Master' degrees (including 3 nurses who majored in disaster nursing), and 10 possessed undergraduate qualifications. For job content, 14 engaged in clinical work, 9 engaged in management work, and 4 engaged in education and training.

Implementation of expert consultation

The research team conducted two rounds of expert consultation through email, from February 7 to February 9, 2022. After the first round of expert consultation questionnaires were returned, the research team summarized the experts' opinions on scores, and modifications concerning indicators. Then they added, deleted, and modified the indicators to form the second round of expert consultation questionnaire for the subsequent survey. After the second round of expert consultation, opinions reached by the experts had converged, so no other expert consultation was required. The research team modified and perfected the indicators to form the final operation room risk assessment indicators, featuring 4 level 1 indicators and 19 level 2 indicators (Table 1).

HVA scoring criteria

The scoring criteria of the Kaiser model risk assessment matrix[6,7] was used. It contains 7 components: likelihood of occurrence, human impact, property impact, business impact, emergency preparedness, internal response, and external response. Each indicator was set with 4 levels, demonstrated through scores ranging from 0 to 3. For likelihood of occurrence, human impact, property impact, and business impact, the highest score "3" was assigned to level 3. For emergency preparedness, internal response, and external response, the lowest score "0" was assigned to level 3.

Calculate the relative risk percentage and assess the degree of hazard

The operating room staff included in the study filled in the online operating room risk assessment form.

Table 1. Operating room risk assessment indicators

Level 1 indicators	Level 2 indicators
Natural disasters	Earthquake
Technological hazards	Power outages
	Water supply suspension
	Information system failure
	Internal flood
	Internal fires
	Fire alarm failure
	Medical gas failure
	Medical material supply shortage
	Explosion
Human hazards	Drunk or armed intruder
	Infectious disease outbreaks
	Medical disputes
	Fall down/fall out of bed
	Foreign object was left in the patient's body
	Patient fainting
	Cardiac respiratory arrest occurred in the surgical patient
	Occupational exposure to human immunodeficiency virus during surgery
Hazardous materials	Internal radiation exposure

After the forms were returned, the researchers summarized and sorted the answers. A relative risk percentage was calculated using the following formula:

Relative risk % = (likelihood of occurrence/3) × {(personal impact + property impact + business impact + emergency preparedness + internal response + external response)/18} %

The relative risk value of each high-risk event was ranked. A relative risk percentage of 0-30% is considered low risk; a relative risk percentage of 30-60% is considered medium risk; and a relative risk percentage of 60-100% is considered high risk. Fragile reinforcement should be implemented for high-risk events.

Statistical methods

SPSS 26.0 was used for data analysis. Descriptive analysis was represented by mean, standard deviation, coefficient of variation, and component ratio. Expert enthusiasm was expressed by the questionnaire recovery rate. A questionnaire recovery rate of > 70% was considered good enthusiasm. The degree of concentration in expert opinions was described with the mean of the importance assigned to the indicators. The degree of expert authority was expressed by the expert authority coefficient (Cr). Agreement among experts' opinions was described with Kendall's coefficient of concordance (W).

Results

Expert enthusiasm

Two rounds of expert consultation were carried out in this study. A total of 27 questionnaires were distributed in each round. Twenty-six and twenty-five questionnaires were returned in round 1 and round 2, respectively. All the returned questionnaires were valid, with recovery rates of 96% in round 1 and 92% in round 2. As both figures were higher than 70%, this indicates that the experts had great interest in this study, and the validity of these consulting results was high.

Degree of expert authority (Cr)

The coefficient of expert authority is determined by two factors: the judgment coefficient (Ca) and the degree of familiarity (Cs)[8]. The basis of experts' judgment contains 4 aspects: work experience; theoretical analysis; reference to domestic and foreign data; and intuitive feeling. The degree of influence judged by the experts is divided into three levels: high, medium, and low, concerning frequency and relative frequency[9]. For experts' familiarity with the items, 0.9 indicates very familiar, 0.7 indicates somewhat familiar, 0.5 indicates neutral, 0.3 indicates a little unfamiliar, and 0.1 indicates unfamiliar.

The formula for calculating the degree of expert authority (Cr) is as follows: Cr = (Ca+Cs)/2. Cr ≥ 0.7 is considered good reliability[10]. In the first round of expert consultation, the familiarity coefficient was 0.742, the judgment coefficient was 0.900, and the authority coefficient was 0.820. In the second round of expert consultation, the familiarity coefficient was 0.820, the judgment coefficient was 0.923, and the authority coefficient was 0.825. Both of the authority coefficients in the two rounds were > 0.8, showing that

the experts had a high level of theoretical knowledge and clinical work experience on the content of the study. Therefore, this study has a high level of authority and the consulting results are reliable and effective.

Agreement among experts' opinions

The agreement among experts' opinions reflects the concentration of them and shows the consistency of experts' judgment of various indicators. Therefore, Kendall's coefficient of concordance (W) is an important indicator. Statistically significant differences were identified in Kendall's coefficients of concordance in the two rounds of expert consultation ($p < 0.01$), indicating a high degree of concordance of experts' opinions (Table 2).

Table 2. Agreement among expert opinions

Round of consultation	Level of indicators	Kendall's coefficient of concordance (W)	χ^2	p
Round 1	Level 1	0.012	0.533	< 0.001
	Level 2	0.276	96.350	< 0.001
Round 2	Level 1	0.059	3.953	< 0.001
	Level 2	0.184	63.022	< 0.001

HVA evaluation results and operating room risk assessment forms

The research team distributed the online operating room risk assessment forms to 360 operating room staff included in the study. A total of 356 valid forms were returned, meaning a recovery rate of 98%. After relative risk percentages were calculated, the HVA evaluation results were obtained (Table 3). The top three high-risk events ranked by the HVA in the operating room are as follows: internal radiation exposure (41%), infectious disease outbreaks (38%), and internal fires (33%) (Fig. 1).

Discussion

Significance of HVA based on Kaiser model for risk event assessment in operating room

There is a lack of scientific tools to provide guidance for risk event assessment in the operating room, leading to managers primarily relying on their experience to conduct the assessments independently. They are more inclined to analyze the causes of the events that have occurred during work, deal with these events, and then look for corresponding improvements, but lack an understanding of prevention through assessing vulnerability. The Kaiser model can provide a scientific and efficient management tool for risk event assessment in the operating room. It integrates disaster medicine, vulnerability analysis, and nursing emergency management organically through the risk assessment matrix, to guide managers toward identifying vulnerabilities in the system. This method, (through assessing, ranking, and identifying various potential risks in the operating room), can help distinguish the varying levels of vulnerability to different risks in the system[11]. Moreover, it can also enable managers to assess which are the most risky, most likely, and most serious events in the operating room emergency system. This in turn, will allow managers to take measures to prioritize solutions, strengthen emergency drills for these risk events, improve response efficiency, and ensure the supply of materials.

Significance of HVA using Kaiser model for emergency management in operating room

HVA can be divided into pre-assessment and post-assessment. Pre-assessment emphasizes feed-forward control of events, effective prediction and objective evaluation of risk events, and carrying out emergency drills to reduce the incidence. The Ministry of Health of China[12] clearly proposed in the hospital grade evaluation that HVA should be incorporated into the establishment and improvement of hospital emergency management systems. The Kaiser model is widely used in hospital management, especially in quantitative risk assessment. In 2017, the California Hospital Association updated the Kaiser model[13] by adding content relating to early warning events, and the number of effective actions, so as to present the emergency management of the organization in a more comprehensive way.

Using the Kaiser model-based HVA to assess risk events is to identify the most significant problems of vulnerability in the entire operating room system, so as to guide managers toward analyzing and preventing

Table 3. Hazard vulnerability analysis in the operation room

Hazardous events	Probability	Severity						Relative risk	Rank
Assessment criteria	Likelihood of occurrence	Human impact	Property impact	Business impact	Emergency preparedness	Internal response	External response		
		Injury or death in medical staff	Property losses and damages	Interruption of healthcare services	Emergency pre-planning and drills	Time, effectiveness, and resources	Social support to the hospital		
	0 = None / Not applicable 1 = Low 2 = Medium 3 = High	0 = None / Not applicable 1 = Low 2 = Medium 3 = High	0 = None / Not applicable 1 = Low 2 = Medium 3 = High	0 = None / Not applicable 1 = Low 2 = Medium 3 = High	0 = None / Not applicable 1 = High 2 = Medium 3 = Low/None	0 = None / Not applicable 1 = High 2 = Medium 3 = Low/None	0 = None / Not applicable 1 = High 2 = Medium 3 = Low / None		
Natural disasters									
Earthquake	1.09	1.42	1.45	1.74	2.73	2.24	1.48	0.22	16
Technological hazards									
Power outages	1.50	1.09	0.80	1.94	0.97	1.80	3.14	0.27	9
Water supply suspension	1.62	1.09	0.80	1.67	1.29	2.11	3.14	0.30	7
Information system failure	1.92	0.73	0.95	1.68	1.94	1.03	2.26	0.31	4
Internal flood	1.26	2.42	2.70	2.88	1.47	1.41	2.45	0.31	4
Internal fires	1.56	1.76	2.59	2.39	1.24	1.18	2.42	0.33	3
Fire alarm failure	1.11	2.65	2.97	2.42	1.55	2.35	2.98	0.31	4
Medical gas failure	1.30	1.39	1.98	1.59	1.38	1.77	2.82	0.26	11
Medical material supply shortage	1.18	0.59	1.15	2.55	1.56	2.45	2.39	0.23	13
Explosion	1.17	1.89	1.89	2.38	1.68	1.85	1.32	0.24	12
Human hazards									
Drunk or armed intruders	0.42	1.55	1.65	1.68	0.73	0.73	0.85	0.06	19
Infectious disease outbreaks	1.71	2.74	2.36	2.17	1.09	1.56	2.08	0.38	2
Medical disputes	1.41	1.67	1.82	1.74	1.97	1.97	2.08	0.29	8
Fall down/fall out of bed	1.21	0.00	1.73	1.88	1.68	1.86	3.20	0.23	13
Foreign object was left in the patient's body	1.17	0.95	1.85	2.83	1.21	1.35	2.27	0.23	13
Patient fainting	1.50	0.41	0.98	2.21	1.73	1.62	2.82	0.27	9
Cardiac respiratory arrest occurred in the surgical patient	1.17	0.11	0.94	2.53	0.88	1.09	2.39	0.17	18
Occupational exposure to human immunodeficiency virus during surgery	0.83	2.98	2.08	2.42	1.29	1.06	1.97	0.18	17
Hazardous materials									
Internal radiation exposure	1.88	2.83	2.05	2.21	1.20	1.30	2.27	0.41	1

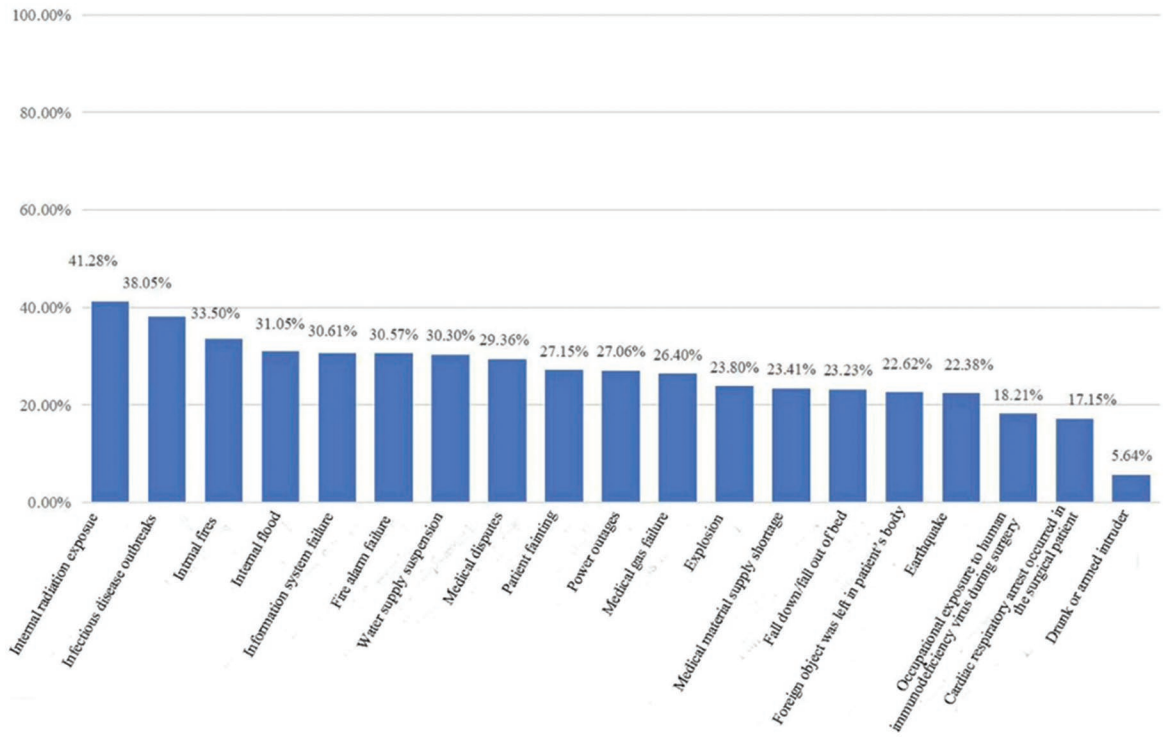

Figure 1. *Rank of relative risk percentages of events in the operation room.*

risk events, while clarifying the emergency management's direction for continuous improvement. Through the 19 listed risk events in the operating room, the managers can analyze the reasons and formulate countermeasures for the top three high-risk events, avoiding the blindness of emergency management.

Risk of internal radiation exposure

Our hospital is a specialized hospital for women and children, thus the majority of the surgeries carried out before our study were limited to gynecology, obstetrics, and reproductive endocrinology. With the integration of the medical market and the broadening of our hospital's development ideas and directions, surgical specialties have expanded to pediatric orthopedic surgeries and interventional surgeries carried out by radiation equipment. However, the original operating room facilities cannot meet the protection requirements of these surgeries, and the operating room staff lacks the relevant protection awareness, knowledge, and skills. In addition, due to the special environment in the operating room and the long working hours of operating room staff, management mistakes or protection loopholes when dealing with radioactive substances may lead to negative health impacts on operating room staff, and cause certain public hazards[14]. Therefore, due to the imperfect protection management and the great harm of radioactive material exposure, internal radiation exposure became the highest risk event in the operating room.

Risk of infectious disease outbreaks

As an important place for disease diagnosis, treatment, and first aid, the operating room also takes on important responsibilities during the outbreak of infectious diseases. Due to the enclosed surgical environment and the particularity of surgical methods, infected persons can become infection sources. Exposed blood, body fluids, and respiratory tracts become the main transmission medium, while aerosol transmission also exists in the enclosed environment. Epidemic outbreaks are sudden, urgent, and uncertain, making operating room work more risky and difficult to respond to.

Risk of internal fires

There are 62 operating rooms in our hospital, covering an area of more than 5,000 square meters, and the

annual operation volume reaches more than 20,000 cases. Every operating room is equipped with an endoscopic surgery system, various kinds of electrosurgical equipment, an information management system, an intelligent material management system, etc. A large number of electrical instruments and equipment run for extensive periods of time, and the daily average flow rate of nearly 1,000 people brings great challenges to operating room fire safety management. Once a fire occurs, the safety of patients and staff, along with the protection of large valuable assets of the hospital, becomes at risk.

Improve the operating room risk emergency management mechanism

It is necessary to establish an operating room risk management team composed of the director of anesthesia, the head nurse, the surgical team leader, and the person in charge of operation management. The management team shall formulate detailed work plans and contents, clarify the job responsibilities of each member, prepare the quality and evaluation criteria of clinical work, get familiar with the risk management process, monitor all steps in surgeries, and start all necessary emergency preparedness plans at times when vulnerable links are found.

Improve the risk management system and optimize the risk management process

The risk management team regularly revises and improves the management and working systems in the operating room, and annually formulates risk management plans, emergency preparedness plans, specialized training plans, assessment plans, emergency drill plans, etc., based on vulnerability analysis and risk event assessment. It is advisable to optimize workflows, smooth the reporting channels of risk and defect events, smooth the communication and coordination channels between the operating room and other departments, and facilitate the timely collection of feedback on the treatment and effect of risk events.

Raise our awareness of risk management and strengthen our ability to cope with risks

It is advisable to strengthen the relevant training of risk management for operating room staff and improve the risk management awareness of each staff member so that they can have a sharpened insight into potential risks. Through specialized training and emergency drills, the staff can learn to strictly abide by the rules and regulations, strictly implement work procedures, and gain relevant coping abilities for facing potential risk events.

Conclusions

The Kaiser model is a concise, applicable, scientific and effective HVA tool, and has strong applicability to the assessment of risk events in the operating room. Medical institutions, especially operating rooms, have dynamic changes in operating room risks due to the severity of surgical treatment, complexity of instruments and equipment, diversity of personnel, and their enclosed environment. Only by using scientific management tools and regularly identifying and evaluating risks, we can effectively control the vulnerable links in operating room management. This should mean: constantly implementing fragile reinforcement, strengthening emergency management abilities, improving medical quality, and guaranteeing the safety of operating room staff and patients.

Ethics approval

All procedures of this study were performed in compliance with relevant laws and institutional guidelines and have been approved by the Medical Ethics Committee of West China Second University Hospital, Sichuan University (2023 Medical Scientific Research for Ethical Approval No. [054]).

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Funding

The authors declare that they have not received funding.

Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of human and animal subjects. The authors declare that the procedures followed complied with the ethical standards of the responsible human

experimentation committee and adhered to the World Medical Association and the Declaration of Helsinki. The procedures were approved by the institutional Ethics Committee.

Confidentiality, informed consent, and ethical approval. The study does not involve patient personal data nor requires ethical approval. The SAGER guidelines do not apply.

Use of artificial intelligence for generating text. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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ARTÍCULO ORIGINAL

Carcinoma hepatocelular en un centro público de alta complejidad en Argentina: características epidemiológicas y resultados terapéuticos

Hepatocellular carcinoma in a high-complexity public center in Argentina: epidemiological characteristics and therapeutic outcomes

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Resumen

Objetivo: *El carcinoma hepatocelular (CHC) es la tercera causa mundial de muerte relacionada con el cáncer. En nuestro medio existen pocos estudios sobre su epidemiología y tratamiento. Nuestro objetivo fue caracterizar una cohorte de pacientes con CHC en un centro público de alta complejidad en Argentina durante 10 años.* **Método:** *Estudio retrospectivo de cohorte observacional y analítico. Se incluyeron todos los pacientes mayores de 18 años con diagnóstico de CHC entre enero de 2013 y diciembre del 2022 en el Hospital El Cruce.* **Resultados:** *Se incluyeron 380 pacientes, el 75% eran hombres; edad promedio 57 ± 10.14 años. El 94% de los casos se asentaron sobre hígado cirrótico. Se empleó cirugía en 182 pacientes (138 trasplantes hepáticos, 44 resecciones quirúrgicas), terapias locorregionales en 121 (104 quimioembolización transarterial como terapia única y 17 asociadas) y una ablación por radiofrecuencia. Se administró tratamiento sistémico a 34 pacientes (en 17 de ellos como única terapia). La mortalidad de la serie según la Barcelona Clinic Liver Cancer Classification (BCLC) fue como sigue: 0, 1/2 (50%); A, 92/220 (41.8%); B, 60/98 (61.2%); C, 21/23 (91.3%) y D, 37/37 (100%).* **Conclusiones:** *El CHC es un tumor complejo con mal pronóstico, por lo que la prevención y detección temprana son claves para mejorar los resultados.*

Palabras clave: *Carcinoma hepatocelular. Epidemiología. Trasplante hepático. Resección hepática.*

Abstract

Objective: *Hepatocellular carcinoma (HCC) is the third leading cause of cancer-related mortality globally. In our region, there is a scarcity of studies addressing its epidemiology and treatment. The aim was to characterize a cohort of HCC patients in a high-complexity public center in Argentina over a span of 10 years.* **Method:** *This study employed a retrospective observational and analytical cohort design. All patients aged 18 and above, diagnosed with HCC between January 2013 and December 2022 at Hospital El Cruce, were included.* **Results:** *The cohort comprised 380 patients, 75% being male, average age of 57 ± 10.14 years. Cirrhotic liver was evident in 94% of cases. Surgery was employed in 182 (138 hepatic transplants, 44 surgical resections), locoregional therapies in 121 (104 sole transarterial chemoembolization, and 17 in combination), and one radiofrequency ablation. Systemic treatment was administered to 34 patients, 17 of whom received it as monotherapy. Mortal-*

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ity within the series according to the Barcelona Clinic Liver Cancer (BCLC) staging: 0, 1/2 (50%); A, 92/220 (41.8%); B, 60/98 (61.2%); C, 21/23 (91.3%); D, 37/37 (100%). **Conclusions:** *HCC emerges as a complex tumor with an unfavorable prognosis, underscoring the pivotal role of prevention and early detection in improving outcomes.*

Keywords: *Hepatocellular carcinoma. Epidemiology. Liver transplant. Hepatic resection.*

Introducción

El carcinoma hepatocelular (CHC) es la tercera causa mundial de muerte relacionada con el cáncer, la quinta en hombres y la octava en mujeres en los EE.UU., con una tasa de supervivencia a los cinco años de aproximadamente el 18%. Se espera que para 2030 fallezcan aproximadamente 41,120 personas por esta enfermedad[1]. La similitud entre la incidencia y la mortalidad (830,000 muertes por año) subraya el sombrío pronóstico asociado con esta enfermedad[2]. Las tasas de prevalencia e incidencia más altas del mundo se encuentran en los continentes asiático y africano. En Argentina representa la novena causa de muerte por cáncer en hombres y la décima en mujeres, con una tasa de mortalidad ajustada entre 2007-2011 de 4.3 y 2.3 respectivamente[2].

El diagnóstico de CHC alcanza su máximo en personas entre 60 y 70 años, y afecta predominantemente a hombres[3,4]. La incidencia varía según la región geográfica y etnia, lo que se atribuye en gran medida a la prevalencia (y al grado y tiempo de exposición) de los principales factores de riesgo. La mayoría de los pacientes con CHC tienen antecedentes de enfermedad hepática crónica como consecuencia de infecciones crónicas asociadas al virus de la hepatitis B (VHB) o C (VHC), el abuso de alcohol o la esteatohepatitis alcohólica (EHA), y la enfermedad del hígado graso no alcohólico (EHGNA) o la esteatohepatitis no alcohólica (EHNA). La obesidad, la diabetes *mellitus* y el consumo de nicotina también se han asociado al aumento en la incidencia de CHC, al igual que otras enfermedades menos frecuentes como la hemocromatosis o la tirosinemia hereditaria tipo 1.

La prevalencia de los factores de riesgo varía a nivel mundial, con una predominancia de VHB en Asia, VHC en Japón, y EHGNA, EHNA y alcohol en Europa y América del Norte. En la mayoría de los casos, el riesgo de desarrollar CHC es multifactorial e incluye factores demográficos (edad, sexo y etnia), gravedad y actividad de la enfermedad hepática subyacente (etapa y grado de fibrosis, actividad inflamatoria y tratamiento), metabólicos (diabetes y obesidad) y relacionados con el consumo de exotóxicos (alcohol, tabaco y otras drogas). La incidencia global de CHC relacionado con las hepatitis virales ha disminuido desde la década del 2000 debido a la implementación de programas de vacunación neonatal contra el VHB y la disponibilidad de tratamientos antivirales altamente efectivos para el VHB y el VHC[5,6].

Está bien establecido que la enfermedad hepática crónica predispone a la formación del CHC, por lo tanto, su prevención reduce la población en riesgo. El efecto de esta estrategia se ha demostrado claramente en Taiwán, donde la introducción de un programa nacional de vacunación contra el VHB para recién nacidos en 1984 resultó en una reducción del 35.9% en la incidencia de CHC en menores de 30 años[7-9]. Aunque no hay una vacuna equivalente para el VHC, la creación de antivirales de acción directa ofrece la posibilidad de erradicar el VHC[10,11]. Mientras tanto, las enfermedades hepáticas no alcohólicas asociadas a la obesidad están emergiendo como factores de riesgo dominantes, haciendo urgente la implementación de políticas de salud pública para enfrentar esta transición epidemiológica. Actualmente existen pocos datos que respalden la eficacia de programas de vigilancia del CHC en este subgrupo de pacientes.

A diferencia de muchos otros tipos de tumores comunes, las opciones terapéuticas para el CHC se limitan, en su mayoría, a estudios de cohortes. Los abordajes quirúrgicos, como el trasplante hepático, la resección hepática y la ablación por radiofrecuencia (ARF), han demostrado los mejores resultados en términos de supervivencia a largo plazo[12-14]. En cuanto a los tratamientos no curativos, la quimioembolización transarterial y el tratamiento sistémico son los únicos que han demostrado mejorar la supervivencia[15,16]. La investigación epidemiológica en relación con el CHC resulta crucial para comprender la distribución, causas y factores de riesgo de esta patología en nuestra población. En Latinoamérica, la información sobre la prevalencia, incidencia y factores de riesgo del CHC sigue siendo limitada debido a la ausencia de bases de datos nacionales o regionales. Este enfoque es vital para establecer medidas preventivas y generar estrategias de control y vigilancia.

El objetivo de este estudio fue caracterizar una cohorte de pacientes diagnosticados con CHC en un centro público de alta complejidad en Argentina durante un periodo de 10 años. Los objetivos secundarios fueron describir las características demográficas, etiológicas y clínicas de la población, modalidades diagnósticas y terapéuticas implementadas, sobrevida y mortalidad relacionada con el CHC.

Método

Se realizó un estudio retrospectivo sobre una base de datos de carga prospectiva de cohorte observacional y analítico. Se incluyeron todos los pacientes mayores de 18 años con diagnóstico de CHC entre enero de 2013 y diciembre del 2022 en el Hospital de Alta Complejidad en Red El Cruce en Argentina. Se excluyeron los casos con historias clínicas incompletas o con datos faltantes que hicieron imposible el diagnóstico de CHC. Los datos del estudio fueron cargados y procesados bajo estricta confidencialidad, según lo establecido por las leyes 25.326 de Protección de Datos Personales y 26.529 de Derechos del Paciente en su Relación con los Profesionales e Instituciones de la Salud del Código Civil Argentino. Se obtuvo la aprobación del Comité de Docencia e Investigación de nuestra institución. Se seleccionaron aquellos casos con CHC confirmado y con seguimiento o tratamiento en la institución.

Los datos utilizados se obtuvieron a partir del Sistema de Gestión Hospitalaria (SIGEHOS®) desarrollado por la Dirección General de Sistemas Informáticos del Ministerio de Salud de la Ciudad Autónoma de Buenos Aires y el sistema de historia clínica electrónica de internación Galileo (NOEMALIFE®). Se revisaron manualmente las historias clínicas electrónicas para la recolección, carga y validación de los datos.

Para el diagnóstico de CHC se utilizaron estudios por imagen o análisis anatomopatológicos. Se utilizó el sistema *Liver Imaging Reporting and Data System* (LI-RADS)[17] para los estudios por imágenes de corte transversal de alta calidad (tomografía computarizada [TC] multicorte abdominopélvica trifásica o resonancia magnética nuclear abdominal contrastada con gadolinio) en pacientes con hepatopatía de base. La estadificación se completó con TC de tórax y centellograma óseo en caso de fuerte sospecha clínica. Se diagnosticó cirrosis hepática según análisis de biopsias de tejido hepático o a partir de las manifestaciones clínicas de su descompensación. Se empleó la clasificación de Child-Pugh y MELD (*Model for End Stage Liver Disease*) para establecer el pronóstico de la cirrosis hepática.

Se emplearon los criterios de Milán[18] para la selección de candidatos a trasplante hepático y los estadios de la *Barcelona Clinic Liver Cancer* (BCLC)[19] para clasificar a los pacientes y orientar el abordaje terapéutico.

Todos los pacientes fueron discutidos en ateneo interdisciplinario. Siguiendo los lineamientos establecidos por la guía de la BCLC se aplicaron las diferentes estrategias terapéuticas según estadios de la enfermedad, hepatopatía de base y condiciones generales de los pacientes (intención curativa, no curativa o paliativa). Se calculó supervivencia global según estadios BCLC.

Se analizaron distintas variables demográficas, etiológicas y clínicas relacionadas con el CHC. La recolección y tabulación de los datos se realizaron en Microsoft Excel 2019 (Microsoft Corporation, Redmond, Washington®). El análisis estadístico se realizó utilizando la plataforma MedCalc Versión 20.218 (MedCalc Software Ltd, Ostende, Bélgica®).

Se estimaron las tasas de mortalidad relacionadas con el CHC según el método de Kaplan-Meier para los diferentes estadios, calculando la prueba de Mantel-Cox para contraste de las diferentes curvas. Se utilizó según necesidad la prueba de chi-cuadrado para explorar variables categóricas (intervalo de confianza del 95% [IC95%]; grado de significación [p] $\leq$ 0.05).

Resultados

Se analizaron en total 572 historias clínicas electrónicas (HCE), de las cuales el 71.7% presentaron CHC. Luego de eliminar aquellas HCE duplicadas y con datos insuficientes o incompletos para ser incluidas en la muestra final, se obtuvieron 380 pacientes.

El 75% de nuestra población era de sexo masculino, con una edad promedio de 57 ± 10.14 años (rango: 16-86, moda y mediana: 57). El 97.4% de los pacientes eran argentinos. El 94% de los casos se asentaron sobre hígado cirrótico. Los datos demográficos y características de los pacientes se muestran en la tabla 1. La infección crónica por el VHC y el VHB y el abuso de alcohol fueron las causas más frecuentes de enfermedad hepática (46.5 y 32.2%, respectivamente). La categoría «criptogénica» (correspondiente a la tercera causa en nuestra serie) se aplicó a los casos sin antecedentes significativos de consumo de alcohol, marcadores negativos de hepatitis viral y sin estudios que confirmen otros posibles factores

Tabla 1. Características demográficas y epidemiológicas de los pacientes diagnosticados con CHC entre 2013 y 2022 (n = 380)

Características	n = 380	%
M/F	286/94	75.3/24.7
Edad promedio (años)	56.7 ± 10.1	
Nacional/extranjero	370/10	97.4/2.6
Hepatopatía subyacente	357	93.9
Etiología de la hepatopatía		
VHC	157	44
Alcohol	115	32.2
Criptogénica	27	7.6
EHNA	18	5
Hepatitis autoinmune	14	3.9
Cirrosis biliar primaria	10	2.8
VHB	9	2.5
Síndrome de Alagille	2	0.6
Cirrosis biliar secundaria	2	0.6
Hemocromatosis	2	0.6
Colangitis esclerosante primaria	1	0.3
Genotipo VHC		
No determinado	92	58.6
1A	23	14.6
1B	16	10.2
1C	1	0.6
2A	3	1.9
3A	19	12.1
4A	3	1.9
Comorbilidades mayores	242	63.7
Tamaño tumoral		
< 5 cm	139	
≥ 5 cm	53	
Alfafetoproteína		
< 8 ng/ml	158	41.6
≥ 8 ng/ml	222	58.4

EHNA: esteatohepatitis no alcohólica; VHB: virus de la hepatitis B; VHC: virus de la hepatitis C.

etiológicos. En 18 pacientes (5%) se identificó a la EHGNA/EHNA como causa de la cirrosis. Ciento cuarenta y dos (40.3%) de los 353 pacientes con enfermedad hepática subyacente fueron seguidos bajo un programa de vigilancia y diagnosticados bajo esa estrategia. Los pacientes restantes fueron diagnosticados a partir de la clínica y/o hallazgos imagenológicos asociados con el tumor o patología hepática de base (muchos de ellos derivados desde otros centros a nuestra institución).

Al momento del diagnóstico, 203 (53.4%) fueron clasificados como Child-Pugh en estadio A, 116 (30.5%) en estadio B y 61 (16.1%) en estadio C (Tabla 2). Estadios BCLC al momento del diagnóstico: 0, 2 (0.5%) casos; A, 220 (58.2%) casos; C, 23 (5.8%) casos y D, 37 (9.7%) casos.

Tabla 2. Estadio BCLC al momento del diagnóstico (n = 380)

Child-Pugh	BCLC
A: 53.4 (n = 203)	0: 0.5 (n = 2)
B: 30.5 (n = 116)	A: 58.2 (n = 220)
C: 16.1 (n = 61)	B: 25.8 (n = 98)
	C: 5.8 (n = 23)
	D: 9.7 (n = 37)

BCLC: *Barcelona Clinic Liver Cancer Classification.*

De los 23 pacientes que no presentaban hepatopatía de base, se destacan casos como: paciente de sexo masculino de 30 años con polineuropatía amiloide familiar (amiloidosis hereditaria autosómica dominante caracterizada por el depósito sistémico de material amiloide en tejidos, especialmente en nervios periféricos, ocasionada por una variante mutada de la transtirretina, cuyo único tratamiento efectivo es el trasplante hepático, órgano de síntesis de esta) en cuyo explante se halló un CHC bien diferenciado de 1 cm; otro paciente de sexo masculino de 34 años portador de adenomatosis hepática en quien se realizó una segmentectomía VI videolaparoscópica, cuya anatomía patológica reveló un CHC bien diferenciado de 2 cm y que se negó a ser inscripto en lista de espera para potencial trasplante hepático, y 2 pacientes con CHC variante fibrolamelar (dos mujeres, una de 18 años en estadio avanzado que realizó tratamiento sistémico y otra de 16 años sometida a hepatectomía derecha por un gran tumor de 10 x 12 cm).

En la tabla 3 se exponen todos los tratamientos instaurados. Se realizó tratamiento quirúrgico en 182 pacientes (incluyendo 138 trasplantes hepáticos y 44 resecciones quirúrgicas). Se instauraron terapias locorregionales en 121 casos (104 bajo quimioembolización transarterial como terapia única y 17 asociadas a diferentes tratamientos sistémicos) y una ARF. Se administró tratamiento sistémico a 34 pacientes (17 de ellos como única terapia).

De las 44 resecciones quirúrgicas, 36 (81.8%) se realizaron por vía convencional. Treinta y un procedimientos (70.5%) fueron resecciones menores (≤ 2 segmentos hepáticos)[108]. Las hepatectomías mayores siempre se realizaron sobre pacientes sin hepatopatía de base. Se utilizó el abordaje laparoscópico en 19 casos, con una tasa de conversión del 52%, siendo el control hemostático y la invasión vascular las causas principales. Hubo una preferencia de este

Tabla 3. Tratamientos instaurados

Tratamiento	n = 380	%
Trasplante hepático	138	36.3
TAE/TACE	104	27.4
Resección	44	11.6
Sistémico	17	4.5
ARF	1	0.3
Otros	76	20
Paliación	37	9.7
Pérdida de seguimiento	22	5.8
TACE + sorafenib	14	3.7
TACE + sunitib	1	0.3
TACE + levantinib	1	0.3
TACE + docetaxel + 5-FU	1	0.3

5-FU: 5-fluorouracilo; ARF: ablación por radiofrecuencia; TACE: *transarterial chemoembolization* (quimioembolización transarterial); TAE: *transarterial embolization* (embolización transarterial).

abordaje en pacientes cirróticos con una aplicabilidad del 55.2% (p = 0.026). La modalidad de diagnóstico más utilizada fue la TC multicorte (70.5%). El valor de alfafetoproteína (AFP) promedio al momento de la resección fue de 424 ± 1,126.2 ng/ml (rango: 1.3-5,404.6 ng/ml). El 84% presentaban un solo nódulo con un tamaño promedio de 47.3 mm (diámetro transversal máximo, rango: 12-200 mm). Se realizó en solo un paciente resección multivisceral: se extirpó el segmento VI junto al colon derecho por invasión por contigüidad (el examen histopatológico reveló un CHC pobremente diferenciado grado histológico 3). Casi la totalidad de los pacientes (97.7%) eran Child-Pugh A, con un MELD promedio de 11.6 ± 4.7 (rango: 5-11). La mitad de los pacientes resecados presentó recurrencia de la enfermedad, el 86.4% (19/22) en hígado. El promedio de sobrevida libre de enfermedad fue de 16 ± 16.6 meses (rango: 2.3-74 meses). La mortalidad global del subgrupo fue del 38.6%. La supervivencia global a 1, 3 y 5 años fue del 77.2, 47.7 y 13.6%, respectivamente. La recurrencia temprana estuvo relacionada con menor diferenciación celular, compromiso vascular por invasión o trombosis tumoral y mayor grado nuclear (p = 0.05). Según la clasificación de Dindo-Clavien, la morbilidad de la serie fue del 47.7%, siendo mayoritariamente complicaciones menores (88%). La mortalidad a 90 días fue del 6.8%. En el grupo de pacientes cirróticos, dos pacientes fallecieron debido a falla multiorgánica, y un paciente no cirrótico falleció debido a neumonía intrahospitalaria.

En cuanto a los pacientes sometidos a trasplante hepático, 113 (81.9%) cumplieron con los criterios de Milán, habiéndose otorgado puntaje suplementario en lista de espera. El 59.4% (82) de los pacientes presentaba función hepática conservada (Child-Pugh A), el 27.5% era Child-Pugh B y el 13.1% Child-Pugh C. El puntaje MELD promedio al trasplante para aquellos pacientes en quienes fueron otorgados puntos suplementarios fue de 23.6 contra 25 puntos para aquellos que no cumplían los criterios de Milán. La modalidad diagnóstica más empleada para el diagnóstico de CHC fue la TC (68%). El valor de AFP promedio al momento del trasplante fue de 62.4 ± 158.4 ng/ml (rango: 0.8-1,100 ng/ml). El 61.6% presentaban un solo nódulo con un tamaño promedio de 30.6 mm (diámetro transversal máximo, rango: 15-52 mm). El tiempo de espera promedio al trasplante fue de 10.1 ± 11 meses (rango: 1.1-58.4 meses). Discriminados por subgrupos, el tiempo de espera para aquellos con puntos suplementarios fue de 10.6 ± 11.9 vs. 8.1 ± 4.8 meses para aquellos que no los recibieron. La mortalidad del grupo fue del 30.4% (42). El 8.7% (12) de los pacientes presentaron recurrencia (4 en hígado, 4 en pulmón y 4 en huesos). El promedio de sobrevida libre de enfermedad fue de 24.7 ± 20.3 meses. Se realizó en 49 pacientes (35.5%) quimioembolización transarterial (TACE, *transarterial chemoembolization*) como terapia puente al trasplante, con un promedio de 1.2 sesiones. La supervivencia global a 1, 3 y 5 años fue del 76.8, 53.6 y 23.18% respectivamente. Se logró *downsizing* o *downstaging* en el 71.4% de los pacientes. De estos, el 54.2% pudieron acceder definitivamente al trasplante hepático.

En cuanto a los 104 pacientes en que se realizó TACE como único tratamiento, la AFP promedio previo al inicio del tratamiento fue de 2,508.3 ± 13,249.7 ng/ml (rango: 1.3-116,903 ng/ml). El 73.5% presentaba función hepática conservada (Child-Pugh A). Ninguno de los pacientes del subgrupo presentaba función hepática gravemente deteriorada (Child-Pugh C). El puntaje MELD promedio fue de 11 ± 3.6. La modalidad diagnóstica preferida fue la TC en el 72.5% de los casos. El promedio de nódulos LI-RADS V por paciente fue de 2.2, con un diámetro promedio del nódulo dominante de 53.5 mm y con un promedio de la suma de todos los diámetros de las lesiones de 77.2 mm. El seguimiento morfológico tumoral y la evaluación de la respuesta al tratamiento de todos los pacientes se realizó con TC. El promedio de sesiones terapéuticas fue de 1.7 (rango: 1-7). La

mortalidad de los pacientes tratados con TACE alcanzó el 85.6%. El promedio de sobrevida fue de 11.2 ± 10.7 meses.

Por último, de los 17 pacientes sometidos a tratamiento sistémico exclusivamente, el 64.7% (11) presentaban metástasis extrahepáticas al momento del diagnóstico (principalmente en huesos y pulmones). El tratamiento de elección en la mayoría de los casos fue sorafenib (76.5%, 12). En los demás casos se empleó regorafenib o lenvatinib. La totalidad de los pacientes fallecieron, con un promedio de sobrevida de 4.4 ± 4.9 meses. Según la clasificación BCLC (y analizando caso por caso de manera estricta), el 84.5% de los pacientes (321 en total) recibieron el tratamiento recomendado, mientras que el 15.5% recibió otra opción de tratamiento. La tabla 4 muestra el protocolo de tratamiento administrado de acuerdo con el estadio BCLC.

La mortalidad de la serie según la clasificación BCLC fue la siguiente: 0, 1/2 (50%); A, 92/220 (41.8%); B, 60/98 (61.2%); C, 21/23 (91.3%), y D, 37/37 (100%).

La sobrevida promedio en meses según la clasificación BCLC y sin tener en cuenta el tratamiento recibido fue de: 0, 40 meses; A, 32.9 meses; B, 15.6 meses; C, 5.9 meses, y D, 1.7 meses. En la figura 1 se observan las diferentes curvas de sobrevida según los estadios BCLC que complementa a la tabla 5. Se excluye el estadio 0 debido a que solo fueron dos pacientes, por lo cual no puede extrapolarse al gráfico. Se observaron diferencias significativas en la supervivencia según los estadios ($p < 0.0001$).

En la figura 2 se observan las diferentes curvas de sobrevida según el tratamiento instaurado. Se excluye la ARF debido a que solo fue un paciente, por lo cual no puede extrapolarse al gráfico. Se observaron asimismo diferencias significativas en la supervivencia según el tratamiento instaurado ($p < 0.0001$).

Tabla 4. Terapéutica instaurada según las guías de la BCLC

BCLC	Tipo de tratamiento
0 (n = 2)	1 ARF, 1 TH
A (n = 220)	128 TH, 40 TAE/TACE, 38 resección, 12 pérdida de seguimiento, 1 TACE + sorafenib, 1 sistémico
B (n = 98)	9 TH, 58 TAE/TACE, 1 sistémico, 5 resección, 14 TACE + sistémico, 11 pérdida de seguimiento
C (n = 23)	3 TAE/TACE, 15 sistémico, 1 resección, 1 TAE/TACE + sorafenib, 3 paliación
D (n = 37)	34 paliación, 3 TAE/TACE

5-FU: 5-fluorouracilo; ARF: ablación por radiofrecuencia; BCLC: Barcelona Clinic Liver Cancer Classification; TACE: transarterial chemoembolization (quimioembolización transarterial); TAE: transarterial embolisation (embolización transarterial); TH: transplante hepático.

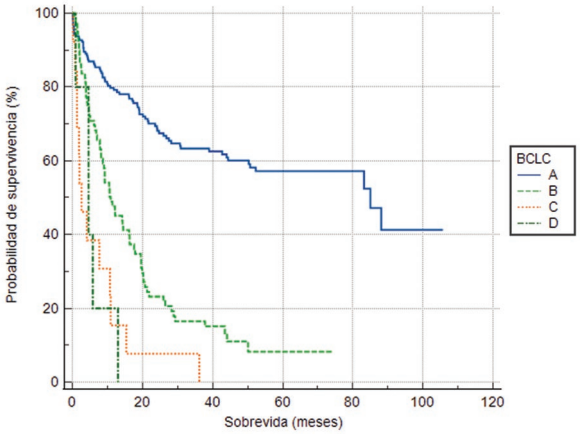

Figura 1. *Supervivencia de los diferentes grupos según estadio de la* Barcelona Clinic Liver Cancer Classification (BCLC).

Discusión

En la presente serie de 380 casos de CHC el sexo masculino fue el más afectado (75%), lo que coincide con lo reportado por Fassio[20] y Calderon Novoa[21] en sus dos series nacionales (72 y 71.4%, respectivamente). La edad al diagnóstico fue de 57 años, en contraste con los 62 y 64.7 años publicados por los autores anteriores. El principal factor de riesgo para el desarrollo de CHC continúa siendo la enfermedad hepática subyacente, presente en el 93.9% de los casos (muy similar a lo publicado por Fassio, del 93%). Debido a ello, y según lo explicado previamente, los consensos actuales recomiendan el tamizaje de CHC mediante ecografía cada dos años en pacientes con cirrosis, portadores de VHC con fibrosis avanzada (F3-F4 de la escala METAVIR) y en aquellos portadores de VHB.

Los principales factores etiológicos en nuestra cohorte fueron las hepatitis virales y el abuso de alcohol, coincidiendo con las principales causas de cirrosis reportadas en Argentina. El porcentaje correspondiente a la cirrosis criptogénica/incierta se sitúa entre medio de lo publicado por la bibliografía (5.2%[20] y 9.2%[21]). En 18 pacientes (5%) se identificó a la EHGNA/EHNA como causa de la cirrosis. Este porcentaje es llamativo, ya que es muy dispar con aquellos publicados en la literatura (cercanas al 30%)[22].

La resección quirúrgica representa la principal opción de tratamiento curativo para pacientes con CHC.

Tabla 5. Sobrevida global según los diferentes estadios BCLC

BCLC	1 año	3 años	5 años
0 (n = 2)	100%	50%	50%
A (n = 220)	67.7%	44.1%	20%
B (n = 98)	46.9%	21.4%	11.2%
C (n = 23)	21.7%	12.3%	5.2%
D (n = 37)	5.4%	0%	0%

BCLC: *Barcelona Clinic Liver Cancer Classification.*

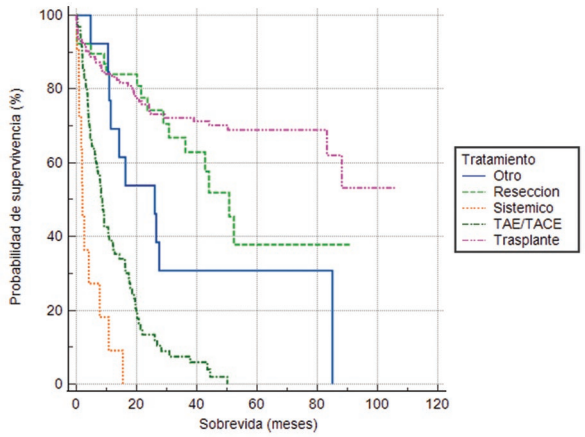

Figura 2. *Supervivencia de los diferentes grupos según tratamiento instaurado.*
TACE: transarterial- chemoembolization (quimioembolización transarterial); TAE: transarterial embolisation (embolización transarterial).

El manejo quirúrgico de pacientes con CHC que presentan cirrosis es complejo (debido a la alteración de la función hepática y las múltiples comorbilidades que generalmente estos presentan). El CHC en un hígado no cirrótico es menos común que su contraparte que asienta sobre hígado enfermo. En esta población, la resección hepática debería ser la primera opción de tratamiento si el tumor es técnicamente resecable[23,24]. El objetivo de la resección hepática es extirpar completamente la lesión con márgenes adecuados (R_0)[25-27]. Casi la totalidad de los pacientes resecados (97.7%) presentaban función hepática conservada al momento de la cirugía. En nuestra serie, 29 pacientes resecados eran cirróticos. Los 15 restantes no presentaban cirrosis, no obstante tres de ellos poseían algún grado de fibrosis hepática asociada a infección crónica por VHC. La desventaja principal de la resección es la alta incidencia de recurrencia tumoral en el hígado, que ocurre en hasta el 80% de los pacientes[28]. En nuestra serie reportamos una recurrencia del 50% de los pacientes resecados, casi todos ellos (19 de 22, 86.4%) en hígado. El promedio de sobrevida libre de enfermedad fue de 16 ± 16.6 meses (rango: 2.3-74 meses), similar en lo reportado en la literatura[28]. Por otra parte, en pacientes con CHC sometidos a trasplante hepático se puede lograr una tasa de supervivencia a cinco años del 75-80% con un bajo riesgo de recurrencia (aproximadamente del 15%). Desde la introducción de los criterios de Milán en la práctica diaria, las tasas de sobrevida después del trasplante hepático para el CHC han mejorado significativamente. Actualmente, la sobrevida global a cinco años de los pacientes dentro de los criterios de Milán alcanza tasas similares a las de las indicaciones no tumorales (65-70%)[29]. La razón detrás de estos resultados superiores es que el trasplante hepático trata tanto al CHC con márgenes quirúrgicos más amplios, como a la cirrosis hepática subyacente (factor de riesgo clave para la recurrencia tumoral). La principal limitación de esta terapéutica es la escasez de órganos disponibles para todos los pacientes que lo necesitan, por lo que se han realizado esfuerzos para seleccionar a los pacientes con los mejores resultados esperables luego del trasplante hepático. Por otra parte, los resultados de supervivencia de nuestra serie resultan muy dispares con las medianas estimativas realizadas por los estadios de la BCLC: BCLC 0-A, 3.3 y 2.7 años (en contrapartida con lo publicado [más de cinco años]); BCLC B, 15.6 meses (vs. aproximadamente 20-30 meses); BCLC C, 5.9 meses (vs. aproximadamente 8-10 meses), y BCLC D, 1.7 (vs. aproximadamente 3 meses)[28-30].

Consideramos que esto puede deberse a diversos factores: en su gran mayoría, los pacientes que son evaluados por nuestra unidad son derivados, lo que puede demorar su ingreso efectivo al sistema hospitalario. En consonancia con lo anteriormente expuesto, los pacientes iniciaron su tratamiento de manera más tardía, lo que impactó directamente en la sobrevida. Y debido a la pandemia que sufrimos a partir del año 2020, el seguimiento de los pacientes se vio gravemente afectado.

Para evitar la progresión tumoral, los pacientes reciben tratamiento mientras permanecen en lista de espera, lo que se conoce como «terapia puente». Los pacientes también pueden recibir tratamientos específicos para reducir la masa tumoral y cumplir un criterio particular para el trasplante, lo que se conoce como *downsizing* o *downstaging* (no existe traducción literal en nuestra lengua, podría ser interpretado como

«reducción de tamaño» o «reducción de estadio»)[31]. Se realizó en 49 pacientes (35.5%) TACE como terapia puente al trasplante, con un promedio de 1.2 sesiones. La supervivencia global a 1, 3 y 5 años fue del 76.8, 53.6 y 23.18%, respectivamente. Se logró *downsizing* o *downstaging* en el 71.4% de los pacientes sometidos a esta estrategia (49), de los cuales la mitad pudo acceder definitivamente al trasplante hepático. Esto demuestra la utilidad e importancia de este concepto para permitir a estos pacientes fuera de los criterios clásicos de trasplante una posibilidad de curación. La modalidad más comúnmente utilizada como terapia puente es la quimioembolización transarterial (la única empleada hasta el momento por nuestro equipo), aunque también puede utilizarse la ablación o la terapia radiante.

Por último, la terapia sistémica es la modalidad de tratamiento preferida para pacientes con CHC en estadio avanzado, así como para pacientes con CHC en estadio intermedio que no califican para terapias locales. La supervivencia de los pacientes tratados con agentes sistémicos ha mejorado significativamente desde el año 2017 con la introducción de nuevos agentes.

Para garantizar que los pacientes sean tratados con la terapia óptima, la toma de decisiones clínicas requiere un equipo multidisciplinario que evalúe y adapte las estrategias terapéuticas. Aunque las terapias locales siguen siendo el pilar de tratamiento en las etapas tempranas de la enfermedad, ha habido un cambio de paradigma en los pacientes con CHC intermedio. Como resultado del progreso sustancial en los tratamientos sistémicos, es obligatorio hacer una revisión crítica de la indicación de las terapias locorregionales. Los estudios han proporcionado evidencia de que la sobrevida global media con TACE es significativamente peor en poblaciones de pacientes no seleccionados (sobrevida global media < 20 meses) en comparación con pacientes seleccionados con función hepática mantenida y tumores pequeños (30-45 meses)[31]. Por lo tanto, las directrices recomiendan TACE en pacientes con enfermedad limitada al hígado, tamaño tumoral < 7 cm, sin infiltración macrovascular, función hepática preservada y un buen estado funcional según la escala ECOG (*Eastern Cooperative Oncology Group*). Además de identificar los candidatos óptimos para las terapias locales, no se debe perder de vista la oportunidad y momento adecuado para pasar de las terapias locales a las sistémicas.

Consideramos que este estudio tiene varias fortalezas. Cuenta con un alto número de pacientes, considerando que se trata de un solo centro con pocos años de existencia (desde el comienzo). Al ser un centro de referencia y derivación a nivel nacional, se ha concentrado la atención de estos pacientes por un equipo especializado (teniendo en cuenta la baja prevalencia del CHC en nuestra región). Desde su concepción como unidad de alta complejidad, se contó con el trabajo multidisciplinario e interdisciplinario de varias especialidades con la fortuna de disponer de una amplia gama de opciones terapéuticas. Por otra parte, su naturaleza retrospectiva entorpece la recolección de datos, lo que podría generar errores sistemáticos como sesgos de información o clasificación. Debido a esto, varios pacientes fueron excluidos por no cumplir con los datos necesarios para la muestra o por haber sido perdidos durante el seguimiento.

Conclusiones

El CHC es un tumor complejo y agresivo que presenta mal pronóstico debido a la cirrosis donde generalmente asienta, lo que limita las opciones terapéuticas y aumenta las posibilidades de recaída. A pesar de numerosos estudios, aún presenta bajas posibilidades de curación, por lo que la prevención primaria de la cirrosis y la detección precoz del CHC son clave para mejorar los resultados.

Este estudio aborda de manera integral todas las esferas del CHC, desde su etiología hasta su tratamiento y seguimiento, y destaca tanto aspectos positivos como áreas que necesitan mejoras. Es necesario crear bases de datos prospectivas, así como políticas sanitarias para reducir la incidencia de cirrosis y CHC.

La evolución de los factores de riesgo no virales requiere estrategias innovadoras de prevención y vigilancia, y a pesar de los desafíos en el tratamiento, se están desarrollando terapias más efectivas y biomarcadores predictivos más precisos para un tratamiento personalizado. La investigación sobre el CHC sigue avanzando y hay razones para ser optimistas sobre el mejoramiento de los resultados del tratamiento en el futuro.

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Conflicto de intereses

Los autores declaran no tener conflicto de intereses.

Consideraciones éticas

Protección de personas y animales. Los autores declaran que para esta investigación no se han realizado experimentos en seres humanos ni en animales.

Confidencialidad, consentimiento informado y aprobación ética. Los autores han seguido los protocolos de confidencialidad de su institución, han obtenido el consentimiento informado de los pacientes, y cuentan con la aprobación del Comité de Ética. Se han seguido las recomendaciones de las guías SAGER, según la naturaleza del estudio.

Declaración sobre el uso de inteligencia artificial. Los autores declaran que no utilizaron ningún tipo de inteligencia artificial generativa para la redacción de este manuscrito.

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ORIGINAL ARTICLE

Sleeve gastrectomy improves HDL function examined by Apo-A1 and atherogenic indices in non-diabetic obese patients

La gastrectomía en manga mejora la función HDL examinada por Apo-A1 e índices aterogénicos en pacientes obesos no diabéticos

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Abstract

Objective: *Dysregulation of lipid metabolism can be one of the pathophysiological mechanisms linking high-density lipoprotein cholesterol (HDL-C) dysfunction to obesity. The aim of the study is to show possible changes in lipid metabolism with atherogenic indices in obese patients after sleeve gastrectomy (SG) surgery.* **Method:** *Thirty patients who had SG surgery for obesity were included in the prospective study. The atherogenic risk indices were calculated pre-operatively, at 3 and 6 months post-operatively. Furthermore, serum paraoxonase-1 (PON-1), apolipoprotein-A1 (Apo-A1), and platelet-activating factor acetylhydrolase (PAF-AH) levels, amount of oxidized low-density lipoprotein (Ox-LDL) was measured.* **Results:** *We observed improvement in atherogenic risk indices and improved HDL-C functionality after SG. Increases were observed in HDL-C and HDL-C-related Apo-A1 levels 6 months after obesity surgery. Besides, the amount of serum triglycerides (TGs), PON-1 activity, and atherogenic risk indices decreased significantly within 6 months.* **Conclusion:** *As far as we know, there is no study in the literature examining the dynamic changes in SG and PON-1, PAF-AH, Apo-A1, and Ox-LDL parameters. This preliminary study dynamically detected improvement in HDL-C function and reduction in atherogenic risk indices after SG.*

Keywords: *Obesity. High-density lipoprotein cholesterol. Apo-A1. Atherogenic risk indices.*

Resumen

Objetivo: *La desregulación del metabolismo de los lípidos puede ser uno de los mecanismos fisiopatológicos que relacionan la disfunción del colesterol vinculado a lipoproteínas de alta densidad (c-HDL) con la obesidad. El objetivo del estudio es mostrar posibles cambios en el metabolismo de los lípidos con índices aterogénicos en pacientes obesos después de la cirugía de gastrectomía en manga (SG).* **Método:** *Los índices de riesgo aterogénico se calcularon en el pre-operatorio, y a los tres y seis meses del post-operatorio. Además, se midieron los niveles séricos de PON-1, apolipoproteína A1 (Apo-A1) y factor activador de acetilhidrolasa (PAF-AH), y la cantidad de lipoproteína de baja densidad oxidada (Ox-LDL).* **Resultados:** *Observamos una mejora en los índices de riesgo aterogénico y en la funcionalidad del c-HDL después de la SG, así como aumentos en los niveles de c-HDL y Apo-A1 relacionados con el c-HDL seis meses después de la cirugía de obesidad. Además, la cantidad de triglicéridos séricos, la actividad de PON-1 y los índices de riesgo aterogénico disminuyeron significativamente en seis meses.* **Conclusión:** *Hasta donde sabemos, no hay ningún estudio en la literatura que examine los cambios dinámicos en los parámetros SG y PON-1, PAF-AH, Apo-A1 y Ox-LDL. Este estudio preliminar detectó dinámicamente una mejora en la función del c-HDL y una reducción en los índices de riesgo aterogénico después de SG.*

Palabras clave: *Obesidad. Colesterol vinculado a lipoproteínas de alta densidad. Apo-A1. Índices de riesgo aterogénico.*

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Introduction

Obesity has serious comorbidities that impair the quality of life and shorten the life span[1]. Today, obesity is accepted as a multifactorial chronic disease characterized by inflammation and dyslipidemia[2]. Obesity, which has become an epidemic today, can actually be positively affected by even small changes in body weight and living habits[3]. Sleeve gastrectomy (SG) surgery can reduce the incidence of obesity-related cardiovascular events in addition to weight loss in patients[4,5]. Some recent studies have demonstrated the effects of SG on atherosclerosis and vascular endothelial functions[5,6]. The functionality of high-density lipoprotein cholesterol (HDL-C) rather than its amount that can be measured in blood is very important in understanding the mechanism of recovery of patients with obesity and bariatric surgery. Numerous studies in the literature have shown that HDL-C functions are impaired by obesity[7,8].

HDL-C is a highly heterogeneous particle. Most of the more than 200 proteins in the HDL-C structure can be associated with obesity. HDL-C is a lipoprotein with antiatherogenic properties as well as anti-inflammatory and many other properties. The main function of HDL-C is to remove excess cholesterol from peripheral tissues and transport it to the liver for metabolism and excretion. In fact, HDL-C functions as an anti-infective, athero-protective, anti-apoptotic and anti-thrombotic agent, and reverses cholesterol flow[9,10]. Normal functional HDL-C has a high level of antioxidant activity, enzymes, and anti-inflammatory activity. Atherosclerotic lesions begin with the accumulation of oxidized low-density lipoprotein (Ox-LDL) in macrophages in the artery wall. Antioxidant molecules in the HDL-C structure, mainly paraoxonase-1 (PON-1), can prevent Ox-LDL oxidation in the arterial wall. Apolipoprotein A-1 (Apo-A1) is the main structural protein of HDL-C and makes up 70% of its proteins. Numerous studies have also shown that Apo-A1 is a powerful antioxidant and anti-inflammatory molecule[9-11].

Today, predictive index calculations such as the atherogenic index of plasma (AIP), atherogenic index (AI), and lipoprotein combined index (LPCI) have been developed to predict the risk of future cardiovascular disease (CVD). However, studies using the CVD risk predictive index in obese patients undergoing SG are few in the literature. In one study, a significantly higher AIP was reported in subjects with abdominal obesity than in subjects without abdominal obesity[12]. In another study, a higher AIP level was positively and strongly associated with obesity. In addition, the AIP index can decrease rapidly and significantly with obesity surgery[13,14].

However, there is no study yet showing the effect of SG surgery on functional molecules in the HDL-C structure, such as platelet-activating factor acetylhydrolase (PAF-AH), PON-1, or Apo-A1, which can show antiatherogenic activity. In addition, the possible relationship between the calculated atherogenic risk indices (AIP, AI, and LPCI) and SG surgery is not yet known. This preliminary study may contribute to the improvement of HDL-C functionality and understanding the possible antiatherogenic effects of SG surgery.

Method

Patients

Thirty consecutive patients aged 18-65 years, without diabetes or lipid disorders and diagnosed with morbid obesity were included in this study. All patients were evaluated by a multidisciplinary team (general surgeon, anesthesiologist, psychiatrist, and endocrinologist) for obesity-related comorbidities such as body mass index (BMI) $\geq$ 40 or BMI $\geq$ 35 and type II diabetes mellitus and hypertension.

Method

Blood samples from patients included in the study group were taken into vacuum-sealed, yellow-capped, gel biochemistry tubes between 08:00 and 09:30, following a 12-h night fast just before surgery. The blood samples were centrifuged at 4000 rpm for 10 min within half an hour, and their serum was separated. Hemolyzed serum samples were excluded from the study. Routine biochemistry measurements, glucose, triglycerides (TGs), total cholesterol (TC), HDL-C, and low-density lipoprotein cholesterol (LDL-C) were made without waiting. Serum samples were transferred to plastic-capped Eppendorf tubes and stored at −80°C until the day they were analyzed. The same procedures were repeated in post-operative patients at 3 and 6 months after surgery. Apo-A1, Ox-LDL, PON-1, and PAF-AH were analyzed from the stored samples. Beckman AU 5800® (Beckman Coulter Diagnostics, California, USA) for glucose, TG, TC, HDL-C, LDL-C parameters biochemistry auto analyzer and

commercial diagnostic reagent kits (Beckman Coulter Inc, California, USA) of the same brand were used.

Quantitative enzyme-linked immunosorbent assay (ELISA) for Apo-A1, Ox-LDL, PON-1, and PAF-AH (Lp-PLA2) measurements YL Biont® (Shangai YL Biotech Co., Ltd., Shanghai, China) brand manual diagnostic reagent kits were used with the immunoanalytical method, ELISA. At the end of the experiment, optical density measurement was performed with an ELX 800 BioTek (BioTek®, ELX 800, San Francisco, USA) ELISA reader.

The following non-traditional atherogenic indices were calculated in the present study: AIP, AI, and LPCI. The AIP is calculated as the logarithmic transformation of the ratio of the TG level to HDL-C level and the formula is AIP = log10 (TG/HDL-C). The AIP indicates the risk of atherosclerosis according to the values obtained: an AIP of −0.3-0.1 indicates low risk, an AIP of 0.1-0.24 indicates medium risk, and > 0.24 indicates high risk[15,16]. AI is defined as the ratio of non-HDL-C level to HDL-C level and calculated using the formula AI = non-HDL-C/HDL-C. LPCI is calculated using the formula LPCI = (TC × TG × LDL)/HDL-C.

Statistical analysis

Statistical analysis of the data was performed using the MedCalc® Version 19.3 software. The compliance of the data to a normal distribution was evaluated with the Kolmogorov-Smirnov test. Data conforming to a normal distribution were expressed as median and interquartile range (IR), and data not conforming to a normal distribution were expressed as median and IR values. Since the number of subjects in both groups was < 30, a non-parametric test was used. The Wilcoxon test was used for countable data. Pearson's correlation test and regression analysis were used for correlation analysis. The value of $p < 0.05$ was considered statistically significant.

Results

The demographic characteristics of the patients are shown in table 1. The mean blood TG levels of the patients were 151 mg/dL pre-operatively (IR: 104.25-199) and 120 mg/dL (IR: 102.25-160.5) post-operatively (3th month) ($p = 0.034$). The blood TG values of the patients at the 6th post-operative month were 99 mg/dL (IR: 84.2-129.75) and were significantly lower than the pre-operative values ($p < 0.001$). As a result, the blood TG levels of the patients after SG showed a statistically significant decrease from the 3rd month, as shown in table 2.

Table 1. General characteristics of the patients and comorbidities

General characteristics	Median, range
Age (in years)	37.05 (32.42-41.08)*
Sex (Female/Male) (%, n)	83.33% (25) / 16.67% (5)
Weight before surgery (kg)	121.52 (110.9-124.2)*
BMI (kg/m^2)	44.27 (41-45.8)*
Comorbidities	**(%) n**
Type 2 diabetes	23.33%, 7
Hypertension	16.67%, 5
Asthma	13.33%, 4
Migraine	6.67%, 2
Sleep apnea syndrome	3.33%, 1

Median and interquartile range. BMI: body mass index.

The pre-operative TC levels of the patients were within normal limits (188 mg/dL, IR: 159.5-212.5). Unlike TG values, TC values were 203 mg/dL (IR: 168.25-223.25) and 204 mg/dL (IR: 175.5-241.5) at the 3rd and 6th months post-operatively, respectively, yet this slight increase was not statistically significant. The blood HDL-C level of the patients increased from 40 mg/dL pre-operatively (IR: 36.5-47.25) to 44 mg/dL (IR: 39.75-48) at the 3rd post-operative month ($p = 0.091$). The increase in HDL-C continued 6 months post-operatively, and HDL-C levels were 48 mg/dL (IR: 45.75-51.5, $p < 0.001$ and $p = 0.004$) (Table 2).

Contrary to what was expected in pre-operative patients, the serum LDL-C level increased from 121 mg/dL (IR: 97.56-137) to 133 mg/dL (IR: 118.28-143) at the 3rd post-operative month. Moreover, this increase in LDL-C was statistically significant at 3 months ($p = 0.008$). At 6 months post-operatively, LDL-C increased to 134 mg/dL (IR: 118-163.25) and significantly increased compared to pre-operative values ($p = 0.02$). Although there was no statistically significant difference between the 3rd and 6th months ($p = 0.1$) (Table 2), the slight increase continued. Apo-A1 blood values, which are abundant in the HDL-C structure in pre-operative patients, averaged 2.28 mg/mL (IR: 1.97-3.47). This increase in Apo-A1 level was not statistically significant at 2.59 mg/mL (IR: 2.08-3.07) at the 3rd post-operative month ($p = 0.47$). However, the mean blood Apo-A1 level was found to be 2.61 mg/mL at 6 months after SG (IR: 2.31-3.04).

Table 2. Pre- and post-operative 3rd and 6th months statistical data of TG, TC, HDL-C, and LDL-C

Parameter (mg/dL)	Pre-operative			Post-operative 3rd month			Post-operative 6th month			p*		
	n	Median	IR	n	Median	IR	n	Median	IR	Pre-operative-post-operative 3rd month	Pre-operative-post-operative 6th month	Between post-operative 3rd and 6th months
TG	24	151	104.25-199	27	120	102.25-160.5	22	99	84.2-129.75	0.034	0.00046	0.027
TC	21	188	159.5-212.5	21	203	168.25-223.25	21	204	175.5-241.5	0.082	0.14	0.11
HDL-C	24	40	36.5-47.25	27	44	39.75-48	22	48	45.75-51.5	0.091	0.0007	0.0042
LDL-C	24	121	97.56-137	27	133	118.28-143	22	134	118-163.25	0.0083	0.02	0.1

*Wilcoxon test. TG: triglycerides; TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; IR: interquartile range.

As a result, Apo-A1 levels increased at 6 months post-operatively compared to pre- and post-operative levels at 3 months (p = 0.028 and p = 0.05).

Apo-A1, Ox-LDL, PON-1, and PAF-AH values are shown in table 3. However, as shown in figure. 1, the Ox-LDL levels that we used as an oxidative stress (OS) marker in the blood at the 3rd post-operative month were 440.48 ng/L (IR: 400-659) in pre-operative patients, while the Ox-LDL level was 432.77 ng/L at the 3rd month. (IR: 382-517). This minimal decrease was not statistically significant (p = 0.46). However, the mean Ox-LDL level decreased to 426.98 ng/L (IR: 377-618) at 6 months post-operatively, but this decrease in Ox-LDL was not statistically significant compared to pre- and post-operative 3 months (Table 3 and Fig. 2).

The PON-1 enzyme level in the HDL-C structure showed a significant decrease compared to pre-operative levels at the 3rd and 6th months. For example, at the 3rd post-operative month, its level was 23.64 ng/mL (IR: 17.98-35.38) (p = 0.038). The decrease continued, and the mean PON-1 values decreased to 20.88 ng/mL (IR: 17.33-27.17) in the 6th post-operative month, and a significant decrease was found according to the pre-operative values (p = 0.05). According to the results, the blood PON-1 enzyme level decreased in pre-operative patients in the 3rd month, and the decrease slowed down in the 6th month and maintained the same level. Statistically, the amount of PON-1 did not show a significant change between the 3rd and 6th months post-operatively (p = 0.85). There was a strong statistically significant correlation between PON1, Ox-LDL, and Apo-A1. The amount of Ox-LDL and PON-1 enzyme in the correlation calculations is shown in table 4. The reduction in PON-1 is compensatory, perhaps due to the reduced need for Ox-LDL. As a result, the distribution of Ox-LDL and PON-1 values can be seen in figures 2 and 3. However, there was no statistically significant change in the antioxidant enzyme PAF-AH levels in the blood HDL-C structure after SG in the 6th month (p = 0.5).

One of the most important findings is the atherogenic risk indices that decreased with SG. As a result, the calculated atherogenic risk index values continued to decrease in pre-operative patients from the 3rd month and reached their lowest levels at the 6th month. In particular, AIP dropped from a high-risk level to a low-risk level.

Similarly, AI (p = 0.012) and LPCI (p = 0.042) levels decreased significantly post-operatively (Table 5).

Table 3. Changes in Apo-A1, Ox-LDL, PON-1, and PAF-AH pre-operative and 3rd and 6th months post-operative

Parameter	Pre-operative			Post-operative 3rd month			Post-operative 6th month			p*		
	n	Median	IR	n	Median	IR	n	Median	IR	Pre-operative-Post-operative 3rd month	Pre-operative-Post-operative 6th month	Between post-operative 3rd and 6th months
Apo-A1 (mg/mL)	30	2.28	1.97-3.47	30	2.59	2.08-3.07	30	2.61	2.31-3.04	0.47	0.028	0.05
Ox-LDL (ng/L)	30	440.48	400-659	30	432.77	382-517	29	426.98	377-618	0.46	0.13	0.58
PON-1 (ng/mL)	29	23.64	17.98-35.38	29	21.69	19.09-27.59	30	20.88	17.33-27.17	0.038	0.05	0.85
PAF-AH (ng/mL)	30	5.25	3.78-7.42	30	5.06	3.29-6.25	30	5.19	3.1-6.89	0.092	0.5	0.87

*Wilcoxon test. Ox-LDL: oxidized low-density lipoprotein; PON-1: Paraoxonase-1, PAF-AH: Platelet-activating factor acetylhydrolase, IR: interquartile range; Apo-A1: Apolipoprotein A-1.

Figure 1. *Apolipoprotein A-1 distribution by pre- and post-operative 3rd and 6th months. In the box-and-whisker plot, the central box represents the values from the lower to upper quartile (25-75 percentile). The middle line represents the median. The horizontal line extends from the minimum to the maximum value, excluding outside and far-out values, which are displayed as separate points.*

Figure 2. *Oxidized low-density lipoprotein distribution by pre- and post-operative 3rd and 6th month. In the box and whisker plot, the central box represents the values from the lower to upper quartile (25-75 percentile). The middle line represents the median. The horizontal line extends from the minimum to the maximum value, excluding outside and far-out values, which are displayed as separate points.*

Discussion

The main findings of this study were that HDL-C and Apo A1, which are indicators of HDL-C function, increased significantly after SG, and patients had a better lipid profile than pre-operative values. Furthermore, there was a strong correlation between Ox LDL and PON-1 as a result of reduced OS. Furthermore, new atherogenic risk indices AIP, AI, and LPCI, which were not included in the literature for SG and were shown comprehensively for the 1st time in the current study,

Table 4. Correlation of Ox-LDL and the amount of PON-1 enzyme

n	Ox-LDL pre-operative	Ox-LDL post-operative 3rd month	Ox-LDL post-operative 6th month
PON-1 pre-operative			
Correlation coefficient	0.932		
Significance level (p)	< 0.0001		
n	29		
PON-1 Post-operative 3rd month			
Correlation coefficient		0.895	
Significance level (p)		< 0.0001	
n		29	
PON-1 Post-operative 6th month			
Correlation coefficient			0.925
Significance level (p)			< 0.0001
n			29

Ox-LDL: oxidized low-density lipoprotein; PON-1: paraoxonase-1.

Table 5. Statistical improvement of AIP, AI, and LPCI

Parameters	Pre-operative	Post-operative 3rd month	Post-operative 6th month
non-HDL	3.86	4.66	4.17
AIP	0.22 (High risk)	0.1 (Low risk)	< 0.1 (Low risk)
AI	3.64	3.68	3.31*
LCPI	25.42	21.01	19.20**

*p = 0.012. **p = 0.042. AIP: atherogenic index of plasma (low risk < 0.1, intermediate risk 0.1-0.21, high risk > 0.21); AI: atherogenic index; LPCI: lipoprotein combined index. All values calculated mmoL/L.

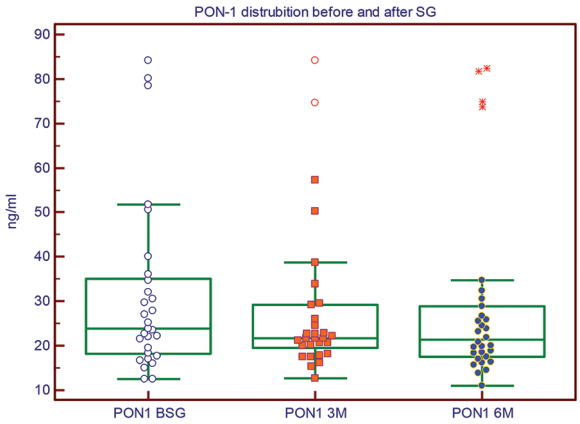

Figure 3. *Paraoxonase-1 enzyme distribution by pre- and post-operative 3rd and 6th months. In the box-and-whisker plot, the central box represents the values from the lower to upper quartile (25-75 percentile). The middle line represents the median. The horizontal line extends from the minimum to the maximum value, excluding outside and far-out values, which are displayed as separate points.*

decreased after SG surgery. Thus, the significant improvement in atherogenic risk indices after SG surgery may demonstrate the strong corrective effect of SG on lipid metabolism in patients with obesity. In the 6th month after SG, the AIP value of the patients decreased from the risk level to the lower risk level. The patients in the pre-operative group had a high risk of AIP, such as 0.22. In addition, the AI value and especially the LPCI values decreased significantly at the end of the 6th month. This decrease in atherogenic risk indices is actually an indication that HDL-C functions have improved significantly.

Today, every patient with morbid obesity should be examined for lipid metabolism. Increased TGs, mixed dyslipidemia associated with LDL-C and Ox-LDL, and increased atherogenic risk should be expected in obesity[15]. Increased adipose tissue in obese individuals contributes to low-grade inflammation and OS[3,16]. Significantly decreased TG levels and increased HDL-C and Apo-A1 levels after SG surgery determined in this study are perhaps the most important reasons for the decrease in atherogenic risk indices. In this study, the most important contribution to HDL-C functions after SG was the significant increase in the amount of Apo-A1 after 6 months.

Conversely, SG surgery can cause a clear reduction in chronic inflammation and atherogenic risk indices by decreasing plasma oxidative markers, including Ox-LDL and PAF-AH enzyme activity, as shown in this study. Our results show that the proatherogenic lipid profile and increased atherogenic risk indices (AIP, AI, and LCPI) characteristic of morbid obesity patients improve after SG[12-14].

In general, an increase in HDL-C was observed in the 3rd month after SG. There was also a significant decrease in TG levels, which reduced dyslipidemia. However, there was no statistically significant change

in TC and Ox-LDL after SG surgery. Increasing systemic bile acid levels and changing bile acid composition after SG can affect lipid absorption, but the molecular mechanism is not understood. In addition to the surfactant role of bile after SG, bile acids also function as signaling molecules for a number of cellular nuclear receptors and plasma membrane receptors[17]. SG is a bariatric surgery technique that preserves the small intestine (especially the jejunum), so it may cause a significant increase in HDL-C[4,18].

In our study, we did not find any statistically significant changes in Ox-LDL and PAH enzyme levels in the blood for up to the 6th month. However, the Ox-LDL levels in the blood of patients with SG did not change significantly. In fact, this result should be expected, since the enzyme PAF-AH in the blood is mainly contained in LDL-C content of more than 80%, but < 20% is associated with HDL-C. Decreased chronic inflammation and decreased production of OS in the blood after SG can contribute to the stabilization of the levels of Ox-LDL and PAF-AH in the blood[19].

According to the literature, HDL-C levels increase by 47% compared to pre-operative SG values 10 years after SG surgery. In our study, the follow-up period after SG was up to 6 months, but even in this short time, the HDL-C ratio increased by 29% compared to pre-operative values. Therefore, an increase in HDL-C values indicates a statistically significant improvement in patients with obesity[20,21]. PON-1, which falls in the blood after SG, is actually a multifunctional enzyme associated with HDL-C, contrary to what we expected. PON-1 exerts antiatherogenic effects by increasing cholesterol influx from macrophages to HDL with ATP binding cassette transporter 1. Studies have shown that increased PON-1 activity is associated with a reduction in the incidence of major cardiovascular events[9,22]. HDL-C's most important antiatherogenic effect is thought to occur through macrophage-cholesterol flow and the reverse cholesterol transport system[10]. In addition, HDL-C improves endothelial function by increasing nitric oxide production and acts as a protective agent against oxidation and inflammation with Apo-A1- activity[10,22]. The main antiatherogenic property of functional HDL-C is inhibition of LDL-C oxidation[9]. Apo-A1, lecithin-cholesterol acyltransferase,and PON-1 enzymes functionally inhibit LDL oxidation in the HDL-C structure[9,10,22]. In this study, the amount of PON-1 enzyme found in the blood of patients after SG decreased after the 3rd month. This enzyme, which acts as an antioxidant in the structure of HDL-C, can mainly function in preventing the formation of Ox-LDL in patients after SG, and there may be a compensatory decrease in the need for PON-1. In fact, a lower level of chronic inflammation, low atherogenic activity, and much less oxidant molecule production should be expected as a result of the reduction in active adipose tissue in patients after bariatric surgery[23,24]. The PON-1 enzyme, which acts as an antioxidant in the structure of HDL-C, mainly prevents the formation of Ox-LDL in patients after SG. Finally, the decrease in PON-1 needs after SG surgery may be due to the decrease in radicals of OS synthesis[25,26].

The response of each bariatric surgical procedure to obesity-related dyslipidemia is different. Previous studies have reported a significant decrease in TG and a significant increase in HDL-C and Apo-A1 in patients undergoing SG[26-29]. The improvement in insulin sensitivity and the effect of this improvement on lipoprotein lipase activity may be explained by the meaningful and effective decrease in TG levels after SG[26-29]. Another finding in our study is that although TC did not change significantly, LDL-C increased significantly from the early post-operative period to the 3rd month. Fortunately, SG surgery can balance the increase in LDL-C inflammation and OS by reducing oxidative and microvascular function markers in adipose tissue[30,31]. Finally, in this study, Ox-LDL levels did not change significantly immediately after surgery and remained without a significant increase at the 6-month follow-up. In one study, a significant increase in HDL-C and Apo-A1 and a decrease in LDL-C and Ox-LDL were observed after the other SG[30-32].

Conclusion

According to our study results, HDL-C levels were increased in patients who had undergone SG surgery. In addition to this numerical increase, the increase in Apo-A1, which is part of the HDL-C function, may be very significant. In addition, the decrease in atherogenic risk indices due to the decrease in Ox-LDL and adipose tissue and the improvement of HDL-C functions after SG may be significant for the anti-atherosclerotic effect of SG surgery and reduce the risk of stroke and cardiovascular events in patients over time. The insufficient number of studies showing the relationship of atherogenic risk indices with SG makes this study a preliminary study, being the first study to report a decrease in atherogenic risk indices after SG surgery and an increase in HDL-C and Apo-A1 serum levels at 3 and 6 months. It is also a preliminary study showing that patients' HDL-C function improved after SG and

significantly reduced TGs and Ox-LDL in the blood. However, it has some limitations; it has a limited number of subjects and longer patient follow-up is not possible.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of human and animal. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have obtained approval from the Ethics Committee for the analysis of routinely obtained and anonymized clinical data, so informed consent was not necessary. Relevant guidelines were followed.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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ORIGINAL ARTICLE

Survival analysis in a high-altitude lung transplant program: insights from a real-life observational study

Análisis de la supervivencia en un programa de trasplante pulmonar en alta altitud: conocimientos de un estudio observacional de la vida real

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Abstract

Objective: *Survival in lung transplantation (LT) may be influenced by recipient-related variables, donor factors, donor-recipient interaction, surgical approach, and medical center expertise. The objective of this study was to describe the sociodemographic, clinical characteristics, and survival of patients who have undergone LT.* **Method:** *We conducted an observational analysis between 2014 and 2022. Survival was calculated using the Kaplan-Meier method at the 1st, 3rd, and 5th years of follow-up post-transplantation.* **Results:** *We analyzed data from 50 subjects, of whom 56% (28/50) were men, with a median age of 54 years (interquartile range: 39-59). The unadjusted survival rates post lung transplantation were 81.4% at 12-months, 65.8% at 3-years, and 53.6% at 5-years. Excluding mortality attributed to COVID-19, survival rates were 78.2% at 12-months, 68.8% at 3-years, and 63.5% at 5-years. The survival of pulmonary fibrosis with a non-usual interstitial pneumonia (N-UIP) pattern was 85% at 1 year and 54% at 5 years, while pulmonary fibrosis with a usual interstitial pneumonia (UIP) pattern demonstrated a solid survival rate of 80% at 1 year and 60% at 5 years.* **Conclusions:** *Patients with pulmonary fibrosis with a N-UIP pattern demonstrated superior survival after 1 year of follow-up, while those with pulmonary fibrosis with a UIP pattern described the highest survival at the 5th year. COVID-19 decreased long-term survival in transplant patients.*

Keywords: *Lung transplantation. High altitude. Survival.*

Resumen

Objetivo: *La supervivencia en el trasplante de pulmón (TP) puede verse afectada por variables relacionadas con el receptor, el donante, la interacción de donante y receptor, el enfoque quirúrgico y la experiencia del centro médico. El objetivo de este estudio fue describir las características sociodemográficas y clínicas, y la sobrevida, de pacientes sometidos a TP.* **Método:** *Realizamos un análisis observacional entre 2014 y 2022. La supervivencia se calculó utilizando el método de Kaplan-Meier al primer, tercer y quinto años de seguimiento posterior al trasplante.* **Resultados:** *Analizamos datos de 50 pacientes, de los cuales el 56% (28/50) eran hombres, con una edad mediana de 54 años (RIQ: 39-59). Las tasas de supervivencia no ajustadas después del trasplante pulmonar fueron del 81.4% a los 12 meses, del 65.8% a los 3 años y del 53.6% a los 5 años. Excluyendo la mortalidad atribuida a COVID-19, las tasas de supervivencia fueron del 78.2% a los 12 meses, del 68.8% a los 3 años y del 63.5% a los 5 años. La supervivencia de los pacientes con fibrosis pulmonar con un patrón de neumonía*

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intersticial no usual fue del 85% al año y del 54% a los 5 años, mientras que aquellos con fibrosis pulmonar con un patrón de neumonía intersticial usual mostraron una sólida tasa de supervivencia del 80% al año y del 60% a los 5 años. **Conclusiones:** *Los pacientes con fibrosis pulmonar con un patrón de neumonía intersticial no usual tuvieron una mayor supervivencia después de 1 año de seguimiento, mientras que aquellos con fibrosis pulmonar con un patrón de neumonía intersticial usual tuvieron la mayor supervivencia en el quinto año. La COVID-19 disminuyó la supervivencia a largo plazo en los pacientes receptores de trasplante.*

Palabras clave: *Trasplante pulmonar. Alta altitud. Supervivencia.*

Introduction

Lung transplantation (LT) serves as a therapeutic recourse for individuals grappling with advanced lung diseases of diverse origins[1]. The global prevalence of chronic respiratory diseases has surged, encompassing over 540 million people, marking a substantial 39.8% increase since 1990[2]. Concurrently with this surge, there has been a documented increase in the establishment of specialized LT centers and a corresponding enhancement in the availability of organs for transplantation[2,3]. Despite its efficacy, LT outcomes, particularly in terms of survival, exhibit variability contingent on the underlying disease and generally manifest at lower rates compared to the transplantation of other solid organs such as the heart, liver, and kidney[4].

At present, our understanding of the physiological changes during lung transplants in high-altitude cities is limited[5]. Altitude-induced physiologic alterations become prominent at elevations beyond 1,500 m above sea level (masl) and intensify with increasing altitudes. Exposure to hypoxia at high altitudes induces physiological changes, including hyperventilation spurred by the hypoxic ventilatory response, leading to an increase in oxygen partial pressure and a decrease in carbon dioxide partial pressure[5,6]. This is accompanied by heightened heart rate and cardiac output due to sympathetic activation, as well as hemoconcentration[6,7]. In addition, hypoxia enhances the response to carbon dioxide by lowering the ventilatory recruitment threshold and increasing ventilatory sensitivity to this gas[8]. At the pulmonary level, non-cardiogenic pulmonary edema may arise due to excessive hypoxic pulmonary vasoconstriction, resulting in an exaggerated increase in capillary pressure and pulmonary arterial pressure[6,7].

Given these physiological nuances, it is imperative to compare the results of LT in high-altitude cities with those below 1,500 masl, particularly considering the potential impact of altitude-induced changes on patient outcomes[6-8]. This study aims to elucidate the survival rates at 1 and 5 years post-transplantation and the clinical characteristics of patients within a high-altitude lung transplant program in Latin America. Furthermore, we seek to juxtapose our clinical findings with the latest publications from the International Society for Heart and LT (ISHLT) and other global groups, thereby contributing to a comprehensive understanding of the unique challenges and outcomes associated with LT in high-altitude settings[5,6,8].

Method

This observational analytical single-center study was conducted using data from the institutional registry of patients undergoing LT at La Cardio-Fundación Neumológica Colombiana in Bogota, Colombia, spanning the years 2014 to 2022.

Criteria for eligibility

The eligibility criteria encompassed consecutive patients who underwent LT and had available clinical data during a 5-year follow-up period. Exclusion criteria comprised individuals with incomplete medical history data and those who succumbed within 30 days of hospital admission.

Variables studied

Key variables included age, sex, and clinical characteristics of patients, encompassing the pathology necessitating transplantation, the type of transplant, and short-term complications. Transplant etiologies covered pulmonary fibrosis with a non-usual interstitial pneumonia (N-UIP) pattern, chronic obstructive lung disease (COPD), pulmonary fibrosis with a usual interstitial pneumonia (UIP) pattern, lymphangioleiomyomatosis, bronchiolitis, bronchiectasis non-cystic fibrosis, cystic fibrosis, and others. Survival analysis was conducted, involving patients with a minimum 5-year follow-up post-transplantation.

Sample size

All subjects meeting the selection criteria were included, with consecutive admissions until the study concluded. To minimize biases, an experienced researcher undertook evaluation, transcription, and double verification of the obtained values.

Statistical analysis

Statistical analysis was performed using STATA version 17 software (STATA Corp., Texas, USA). Quantitative variables were summarized by measures of central tendency and dispersion, using means and standard deviations (SD) for normal distributions, medians, and interquartile ranges (IQR), for non-normal distributions. The Shapiro-Wilk test was used to assess normality, considering a value of $p < 0.05$ as significant. The qualitative variables were summarized in frequencies and percentages. To compare quantitative variables, the Student's T and Mann-Whitney U-tests were used. According to the distribution of the data, and for the qualitative variables, the Fisher exact test was used. Survival at 1 and 5 years was evaluated through tables, and it was plotted with the Kaplan-Meier method, and the Log-Rank test was used to evaluate the statistical differences in the survival curves, according to the independent variables.

Ethical considerations

The study adhered to international ethical guidelines (Helsinki Declaration, Belmont Report) and national standards (Resolution 8430 of 1993, Colombian Ministry of Health). Patient data confidentiality was maintained in compliance with habeas data law 1266 of 2008, and the research protocol received prior approval from the Ethics and Research Committee (2017-203441) of La Cardio - Fundación Neumológica Colombiana.

Results

Demographic characteristics and key results

Fifty individuals who underwent LT were enrolled, with 56% (28/50) being male, possessing a median age of 54 years (IQR: 39-59 years), and a mean body mass index of 24 kg/m^2 (SD: 4.0), as detailed in table 1. Notably, 90% (45/50) of the patients underwent two-LT. The primary indication for LT was pulmonary fibrosis with a N-UIP pattern, accounting for 42% (21/50), followed by COPD at 12% (6/50), and pulmonary fibrosis with a UIP pattern at 10% (5/50). Within the cohort, 20% (10/50) experienced chronic rejection, defined as rejection following two courses of steroid treatment. Throughout the follow-up period, 28% of patients (14/50) were diagnosed with SARS-CoV-2 infection.

Overall survival analysis

A total of 40% (20/50) of patients succumbed during the follow-up period, with severe COVID-19 identified as the cause of death in 35% (7/20) of cases. The unadjusted survival rates post LT were 81.4% at 12 months, 65.8% at 3 years, and 53.6% at 5 years. On excluding mortality attributed to COVID-19, survival rates remained substantial at 78.2% at 12 months, 68.8% at 3 years, and 63.5% at 5 years (Figs. 1 and 2).

Survival analysis by disease group

An in-depth survival analysis by disease group revealed that pulmonary fibrosis with a N-UIP pattern exhibited a robust survival of 85% at 1 year and 54% at 5 years, while pulmonary fibrosis with a UIP pattern demonstrated a solid survival rate of 80% at 1 year and 60% at 5 years (Fig. 3).

Furthermore, within the study cohort, 20% (10/50) of patients developed chronic rejection during follow-up, experiencing a survival rate of 75% at 1 year, with a subsequent decline to 50% at the 5-year mark.

Discussion

In this publication, we share insights from a lung transplant reference center situated in a high-altitude city. Our findings reveal an elevated survival rate among patients with pulmonary fibrosis featuring a N-UIP pattern after 1 year of follow-up. Interestingly, at the 5-year mark, those with pulmonary fibrosis featuring a UIP pattern exhibited the highest survival. When excluding patients who succumbed to COVID-19, survival increased to 68.8% at 3 years and 63.5% at 5 years of follow-up. Furthermore, patients experiencing chronic rejection during follow-up demonstrated lower survival rates compared to those without chronic graft rejection.

Table 1. General characteristics

Number of patients, n (%)	50 (100)
Male, n (%)	28 (56)
Age, median (IQR)	54.0 (39-59)
Body mass index, mean (SD)	24 (4.0)
Bipulmonar transplant, n (%)	45 (90)
Transplant etiology, n (%)	
Pulmonary fibrosis non-UIP	21 (42)
Chronic obstructive lung disease	6 (12)
Pulmonary fibrosis – UIP	5 (10)
Lymphangioleiomyomatosis	5 (10)
Bronchiolitis	4 (8)
Bronchiectasis non-CF	3 (6)
CF	2 (4)
Others causes	4 (8)
mPAP, median (IQR)	29.5 (24-36)
Chronic rejection, n (%)	10 (20)
COVID-19 infection, n (%)	14 (28)
Cause of death, n (%)	
COVID-19 infection	7 (14)
Others causes	13 (26)

SD: standard deviation; IQR: interquartile range; UIP: usual interstitial pneumonia; CF: cystic fibrosis; mPAP: mean pulmonary arterial pressure.

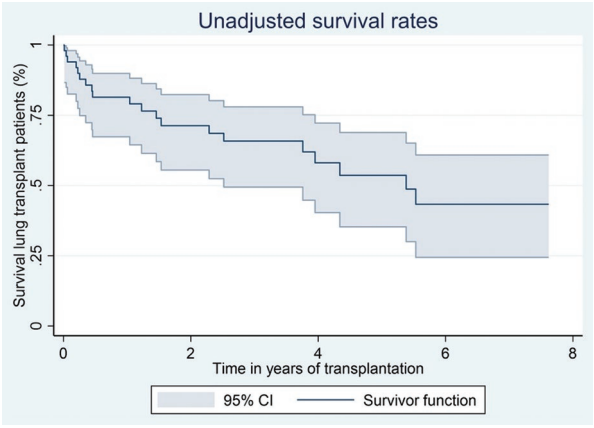

Figure 1. *Unadjusted survival rates after lung transplantation, Kaplan-Meier curve.*

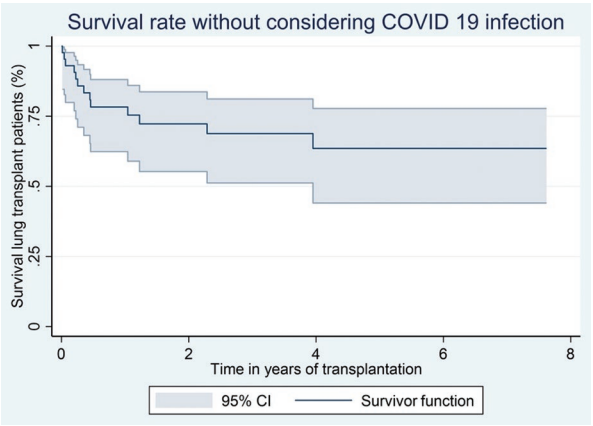

Figure 2. *Survival rates after lung transplantation excluding COVID-19, Kaplan-Meier curve.*

Post-transplant survival has demonstrated improvement over time, although it remains inferior to that reported for other solid organs. This discrepancy may stem from diverse factors, including recipient and donor characteristics, the dynamics of donor-recipient interaction, surgical methodologies, and the expertise of the transplant center[9-12]. Yet, limited research has delved into the impact of high altitude, with no available publications on high-altitude centers. Our resident population at a high altitude (2,640 meters above sea level) exhibits physiological adaptations to hypoxia, such as hyperventilation, hemoconcentration, pulmonary vasoconstriction, increased intracellular oxidative enzymes, and heightened muscle capillary density[13,14]. These altitude-induced adaptations may prompt distinct physiological responses in patients undergoing LT, potentially influencing outcomes.

Our patients' overall survival in the 1st year of follow-up was 81.4%, and when severe COVID-19 was excluded as a cause of death, it was 78.2%. These figures closely align with the ISHLT report, reflecting survival rates near 80% at 1 year[5]. Comparative analyses with other cohorts, such as the Balsara group, reveal similar values[11]. Survival rates for patients with N-UIP pulmonary fibrosis in our study were 85% at 1 year and 54% at 5 years, surpassing those reported by the Balsara et al. (78.5% and 51.6%, respectively)[11].

For residents at high altitude, chronic physiological adaptations to the local conditions seem to have no discernible impact on transplantation outcomes[9-14]. Conversely, patients referred from lower altitudes undergo pulmonary rehabilitation processes before transplantation, potentially facilitating their adaptation to high altitude – a phenomenon documented in individuals engaging in sports activities at elevated altitudes[6].

Examining our study population, the median age was 54 years, aligning with the ISHLT registry data indicating a median age of 55 years for lung transplants as of 20,103. Comparisons with other cohorts

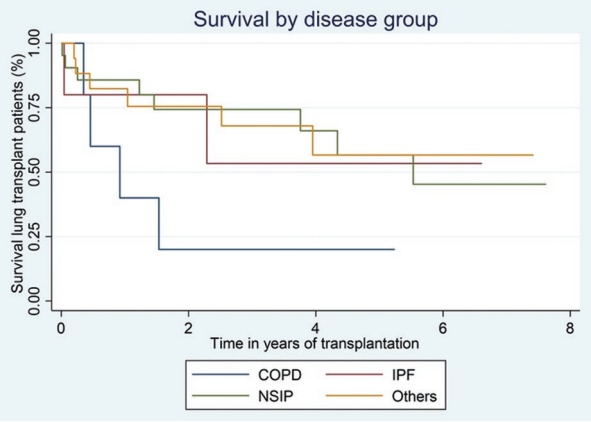

Figure 3. *Survival rates after lung transplantation by indication of lung transplant, Kaplan-Meier curve.*
COPD: chronic obstructive lung disease; IPF: pulmonary fibrosis with a usual interstitial pneumonia; NSIP: pulmonary fibrosis with a non-usual interstitial pneumonia.

often reveal median ages close to 50 years[3,11]. Notably, our center predominantly performs lung transplants for pulmonary fibrosis with a N-UIP pattern, diverging from other populations where chronic obstructive pulmonary disease and cystic fibrosis are more prevalent indications[3,15]. This divergence can be attributed to our center's role as a national reference, resulting in fewer adult patients with cystic fibrosis compared to those with progressive fibrosing pathologies.

Critical to post-transplant success is adherence to immunosuppressive treatment. In our center, the immunosuppression protocol involves tacrolimus as a calcineurin inhibitor, mycophenolate as a cell cycle inhibitor, and prednisolone as a corticosteroid – an approach in accordance with international recommendations for lung transplant patient management[16,17].

Limitations

Strengths of this study include the assurance of complete follow-up for all 50 included patients, marking the inaugural publication from a reference center situated at high altitude. Nevertheless, limitations arise from the modest sample size inherent to compiling the experience of a single reference center dedicated to LT at high altitude. In addition, the 14% mortality rate due to severe COVID-19 during follow-up introduces a potential constraint on the interpretability of our study results. Despite being a observational study based on medical records, measures were implemented to minimize information bias, such as the training of the personnel in charge of collecting medical data and the construction of the manuscript based on the checklist of items that should be included in cohort study reports (Table 1). Our results align closely with publications from the ISHLT and low-altitude lung transplant centers[5].

Conclusions

In our investigation, patients with pulmonary fibrosis with a N-UIP pattern demonstrated superior survival after 1 year of follow-up, while those with pulmonary fibrosis with a UIP pattern exhibited the highest survival at the 5-year mark. Significantly, the exclusion of patients who succumbed to COVID-19 resulted in improved survival rates at both the 2-year and 5-year follow-up intervals.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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ORIGINAL ARTICLE

Evaluating the role of pre-operative hemoglobin, albumin, lymphocyte, and platelet scores in predicting perioperative morbidity in rectal cancer patients

Evaluando el rol de los puntajes preoperatorios hemoglobina, albúmina, linfocitos y plaquetas en la predicción de la morbilidad perioperatoria en pacientes con cáncer rectal

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Abstract

Objective: *Our study aims to explore the predictive value of the hemoglobin, albumin, lymphocyte, and platelet (HALP) score, calculated from routine blood tests measuring HALP levels, for perioperative morbidity in rectal cancer surgery patients.* **Method:** *We conducted a retrospective study focusing on patients who underwent elective rectal cancer surgery from January 2017 to September 2023. The study analyzed demographic, clinical, and laboratory data, including the HALP score, to assess its correlation with perioperative morbidity using logistic and linear regression analyses.* **Results:** *Univariate analysis showed no correlation between the HALP score and perioperative morbidity. Intriguingly, an increase of each centimeter in tumor size was associated with a significant reduction in the HALP score ($p = 0.042$), and operation time exhibited an inverse relationship with HALP scores ($p < 0.001$). Further, our study identified sex (male, $p = 0.017$) and age (> 65, $p = 0.016$) as significant predictors of perioperative morbidity.* **Conclusions:** *Our study found that pre-operative HALP scores did not significantly predict perioperative morbidity or local recurrence in rectal cancer surgery, challenging their presumed prognostic value. However, a notable association was observed between higher HALP scores, reduced tumor size, and shorter operative times, suggesting a potential indirect relationship of HALP in surgical outcomes.*

Keywords: *Rectum cancer. Perioperative morbidity. Immunonutritional status.*

Resumen

Objetivo: *Explorar el valor predictivo del puntaje HALP, calculado a partir de análisis de sangre sistemáticos que miden los niveles de hemoglobina, albúmina, linfocitos y plaquetas, para la morbilidad perioperatoria en pacientes de cirugía de cáncer rectal.* **Método:** *Estudio retrospectivo de pacientes sometidos a cirugía electiva de cáncer rectal desde enero de 2017 hasta septiembre de 2023, analizando datos demográficos, clínicos y de laboratorio para evaluar la correlación del puntaje HALP con la morbilidad perioperatoria mediante análisis de regresión logística y lineal.* **Resultados:** *No se encontró correlación entre el puntaje HALP y la morbilidad perioperatoria. El aumento por cada centímetro en el tamaño del tumor redujo significativamente el puntaje HALP ($p = 0.042$), y el tiempo de operación se relacionó inversamente con los puntajes HALP ($p < 0.001$). El sexo (masculino, $p = 0.017$) y la edad (> 65 años, $p = 0.016$) fueron predictores significativos de morbilidad perioperatoria.* **Conclusiones:** *Los puntajes HALP preoperatorios no predijeron significativamente la morbilidad perioperatoria ni la recurrencia local en la cirugía de cáncer rectal, cuestionando su valor pronóstico. Sin embargo, se observó una notable asociación*

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entre los puntajes HALP más altos, el menor tamaño del tumor y los tiempos quirúrgicos más cortos, sugiriendo una relación indirecta potencial del puntaje HALP en los resultados quirúrgicos.

Palabras clave: *Cáncer rectal. Morbilidad perioperatoria. Estado inmunitario y nutricional.*

Introduction

Rectal cancer is a prevalent type of cancer and a significant health concern[1,2]. Despite the development of additional modalities, surgery remains the primary treatment element[3]. Rectal cancer surgery is associated with high morbidity rates. Neoadjuvant and adjuvant treatments, according to the stage of cancer, can have a negative impact on the patient's physiological reserve and physical condition[4,5]. It can be tough to minimize surgical complications and achieve excellent oncological outcomes in rectal cancer surgery[6]. Identifying situations with a high potential for perioperative morbidity during surgical planning is crucial for achieving successful outcomes[7].

The literature highlights that assessing the inflammatory response induced by tumors in colorectal cancer can be beneficial for predicting prognosis[8,9]. Furthermore, the literature has examined the impact of nutritional status on the disease prognosis and perioperative morbidity[10]. At that point, the hemoglobin, albumin, lymphocyte, and platelet (HALP) score is a combined parameter utilized to evaluate the patient's inflammatory and nutritional status. The HALP score is calculated from the values of hemoglobin, albumin, lymphocytes, and platelets, which are available in routine blood tests, and its implications for prognosis and survival have been studied in many types of cancer[11-13].

Colorectal cancers exhibit heterogeneity due to their tumor localization, structure, and genetic characteristics[14,15]. Therefore, diverging from existing literature, we specifically investigated the relationship between the HALP score and perioperative morbidity in patients undergoing surgery for rectal cancer.

Method

We obtained approval from the Bursak Yüksek İhtisas Training and Research Hospital Ethics Committee for our study, decision number 2011-KAEK-25 2023/11-17.

The patient, who was diagnosed with rectal cancer as a result of elective procedures at the clinic, underwent assessment and received treatment from a multidisciplinary tumor council. The surgical procedure of total mesorectal excision can be conducted either openly or laparoscopically, depending on the predilection of the surgeon and the specific clinical requirements of the patient.

We included patients who were 18 years or older and had undergone surgery for rectal cancer between January 2017 and September 2023. Patients who underwent emergency surgery, abdominopelvic resection, adjacent organ invasion, metastatic disease, liver failure, and those with insufficient medical records, including operation time and pathological records, were excluded (Fig. 1).

Data on patient' characteristics, including age, sex, American Society of Anesthesiologists (ASA) score, and body mass index (BMI), as well as information on pathological factors, such as tumor size, lymphovascular invasion status, T stage, and pathological stage, were collected. Surgical data, including operation time, perioperative morbidity, number of dissected lymph nodes, and mortality, were also compiled. In addition, clinical data such as duration of stay, local recurrence, and readmission, as well as laboratory data including hemoglobin, albumin, lymphocyte count, platelet count, and HALP score, were included in the study. Due to the limited duration of our study and the low mortality rate, we did not analyze the survival data.

The HALP score is an immunonutritional marker and is calculated as hemoglobin x albumin x lymphocyte count/platelet count[16-18]. Our hypothesis suggests a correlation between the immunonutritional status of patients and the occurrence of perioperative morbidity and surgical outcomes in individuals undergo elective rectal cancer surgery. We assessed the patients' immunonutritional status using the HALP score as a numerical metric and examined its correlation with variables such as operation time, length of hospital stay, readmission rate, perioperative morbidity, mortality, and local recurrence. Perioperative morbidity was defined as the occurrence of a complication that required treatment within 1 month after the operation. It was assessed using the Clavien–Dindo score.

Within the scope of the statistical analysis, categorical variables were presented as numbers and percentages. Continuous variables are expressed as mean±standard deviation (SD), and median values. The effects of the patients' clinical and surgical characteristics on morbidity

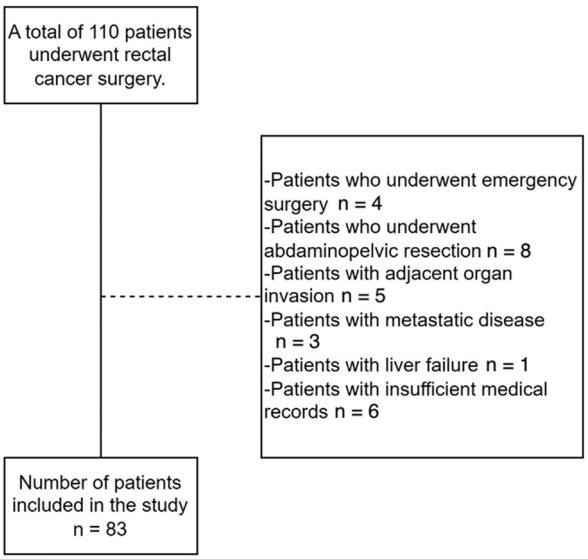

Figure 1. *Flow chart of patients included in the study.*

and recurrence development were examined using logistic regression models. Age, sex, certain clinical features, and laboratory results on morbidity and recurrence were analyzed using the univariate logistic regression (LR) method, followed by the analysis of significant variables with stepwise multivariable LR (Enter method). The median values of the quantitative variables were determined as the cutoff point and added to the logistic regression model. The relationship between the dependent variable, HALP score, and patient characteristics was investigated using univariable and multivariable linear regression models. Multivariable linear regression variables were included in the analysis using the enter method. Moreover, multicollinearity was examined for factors with variance inflation factor (VIF) of < 5 and included in the model. All statistical calculations were performed using SPSS software (version 29.0; SPSS Inc., Chicago, IL, USA). All reported p-values were calculated based on two-tailed hypotheses, and statistical significance was set at $p < 0.05$.

Results

When the socio-demographic and clinical characteristics of the cases were examined (Table 1), it was determined that 69.9% were male, the average age was 66.75 ± 12, and the average BMI was 26.16 ± 3.74. It was observed that 43.9% of the patient had an ASA score of 2, laparoscopic surgery was performed in 57.8%, and the tumor was located in the upper rectum

Table 1. General characteristics of the patients

Parametres	n (%) or mean ± SD (M)
Gender	
Male	58 (69.9)
Female	25 (30.1)
Age	66.75 ± 12 (65)
BMI kg/m^2	26.16 ± 3.74 (26)
ASA score	
2	36 (43.9)
3	45 (54.9)
4	1 (1.2)
Neoadjuvant treatment	
Receive	40 (48.1)
Not-receive	43 (51.8)
Operation type	
Open	35 (42.2)
Laparoscopic	48 (57.8)
Tumor localization	
Lower rectum	31 (37.3)
Middle rectum	17 (20.5)
Upper rectum	35 (42.2)
T stage	
T0	2 (2.4)
Tis	2 (2.4)
T1	8 (9.6)
T2	16 (19.3)
T3	44 (53)
T4	11 (13.3)
Pathologic stage	
0	4 (4.8)
1	22 (26.5)
2A	17 (20.5)
2B	4 (4.8)
3A	12 (14.5)
3B	13 (15.7)
3C	11 (13.3)
Adjuvant treatment	
Receive	49 (62)
Not received	29 (35.4)
Average tumor size (cm)	4.08 ± 2.58 (3.5)
Lymphovascular invasion	25 (30.1)
Average number of lymph nodes	15.82 ± 7.68 (15)
Open	16.17 ± 6.8 (16)
Laparoscopic	15.56 ± 8.33 (14)
Average operation time (min)	245 ± 68.69 (240)
Open	247.71 ± 51.1 (240)
Laparoscopic	243.02 ± 79.58 (240)
Average length of stay (day)	9.71 ± 5.73 (8)
Open	11.57 ± 5.52 (10)
Laparoscopic	8.35 ± 5.55 (7)
Average hemoglobin level HB mg/dL	122.87 ± 21.95 (123)
Average lymphocyte level LYM 10^3/L	1.51 ± 0.69 (1.4)
Average platelet level PLT 10^3/L	266.97 ± 147.97 (237)
Average albumin level ALB gr/dL	42.91 ± 40.33 (39)

(Continues)

Table 1. General characteristics of the patients *(continued)*

Parametres	n (%) or mean ± SD (M)
Average HALP score	29.39 ± 18.48 (26)
Anastomotic leak	8 (9.6)
Readmission	13 (16.5)
30 day morbidity	30 (36.1)
Local recurrence	17 (21.8)
Mortality	5 (6)

(n = 83); HALP: hemoglobin, albumin, lymphocyte, and platelet; BMI: body mass index; M: median; ASA: American Society of Anesthesiologists.

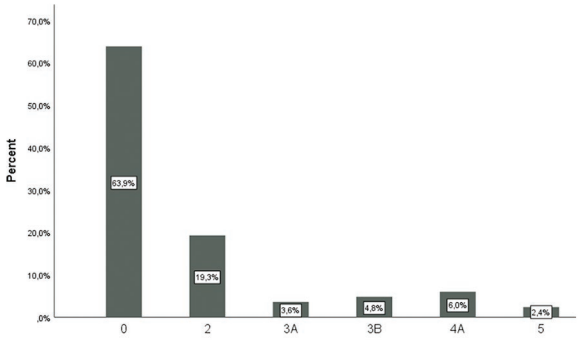

Figure 2. *Bar graph of the distribution of surgical morbidity according to the Clavian-Dindo classification.*

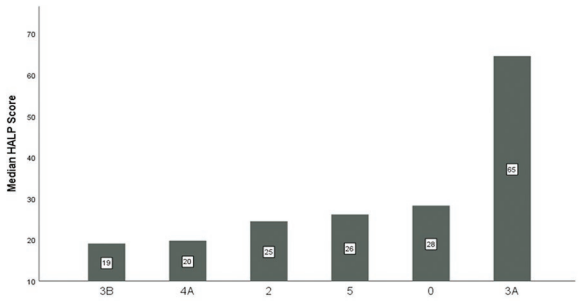

Figure 3. *Median hemoglobin, albumin, lymphocyte, and platelet scores according to the Clavien–Dindo classification.*

in 42.2%, 53% in stage 3, 26.5% in stage 1, and 62% in adjuvant therapy. The average tumor size of the cases was 4.08 ± 2.58 cm, the average number of lymph nodes was 15.82 ± 7.68, the average operation time was 245 ± 68.69 min, the average hospital stay was 9.71 ± 5.73 days, the average HB was 122.87 ± 21.95 mg/dL, the average LYM was 1.51 ± 0.69 10^3/L, the average PLT was 266.97 ± 147.97 10^3/L, the average ALB was 42.91 ± 40.33 gr/dL, and the average HALP score was calculated as 29.39±18.48. In addition, anastomotic leakage was observed in 30.1% of the cases, re-admission in 9.6%, morbidity in 36.1%, and mortality in 6%. The surgical mortalities of the cases are presented with a bar graph, and it was determined that according to the Clavien–Dindo classification, 63.9% of the cases had a morbidity score of 0, 19.3% had 2, 6% had 4A, and 2.4% were classified as 5 according to the Clavien–Dindo classification (Fig. 2).

The effects of the patients' clinical and surgical characteristics on morbidity were investigated using logistic regression models (Table 2). Univariate LR (Logistic Regression) analysis identified sex and age as statistically significant risk factors for morbidity ($p = 0.017$ and $p = 0.016$, respectively). Males carried a 4.266 times higher morbidity risk than females (95% CI: 1.3-13.992, $p = 0.017$), and patients aged over 65 carried a 3.323 times higher morbidity risk (95% CI: 1.256-8.795, $p = 0.016$). The significant factors observed in the univariate LR analysis were further examined together in a multivariate LR (enter method) model to determine their combined effect on morbidity risk. Accordingly, it was determined that age and sex significantly contributed to morbidity risk at a statistical level ($p = 0.029$ and $p = 0.031$, respectively).

The median HALP scores according to the Clavien–Dindo classification are summarized in Fig. 3. Accordingly, it was determined that the cases in the 3A morbidity class had the highest median HALP score, while the lowest median HALP score was seen in 3B cases, according to the Clavian-Dindo classification.

Univariate and subsequent multivariate linear regression analyses identified factors that were significantly associated with HALP scores. In the univariate linear regression models, operation duration and tumor size were determined to be factors that significantly affected the variation in HALP scores ($p < 0.05$) (Table 3). A 1 cm increase in tumor size was associated with an average decrease of 1.62 units in the HALP score ($R^2 = 0.024$; $p = 0.042$), while a 1-min increase in operation time led to an average decrease of 0.07 units in the HALP score ($R^2 = 0.062$; $p < 0.001$). In the multivariate linear regression model, only operation duration and tumor size continued to have a significant relationship with the change in the HALP score, with their respective coefficients being $\beta = -1.57$, $p = 0.044$, and $\beta = -0.06$, $p = 0.025$.

The effects of the patients' clinical and surgical characteristics on local recurrence were investigated using logistic regression models (Table 4). Univariate

Table 2. Investigation of the impact of clinical and surgical characteristics on perioperative morbidity through the utilization of univariate and multivariate logistic regression analyses

Parametres	Univariate LR		Multivariate LR	
	OR (95% CI)	p	OR (95% CI)	p
Gender male (ref: female)	4.266 (1.3-13.992)	0.017	3.864 (1.146-13.031)	0.029
Age > 65 (ref ≤ 65)	3.323 (1.256-8.795)	0.016	3.027 (1.11-8.255)	0.031
BMI > 26 (ref ≤ 26)	2.286 (0.916-5.705)	0.076		
ASA (ref = 2)	1	0.353		
3	0.508 (0.202-1.275)	0.149		
4	2.021 (0.01-235.56)	0.990		
Localization of tumor (ref = lower)	1	0.415		
Middle	0.426 (0.113-1.608)	0.208		
Upper	0.818 (0.304-2.201)	0.691		
Pathological stage > 2 ([ref ≤ 2])	1.233 (0.5-3.038)	0.649		
Operation type (open [ref = lap])	1.65 (0.667-4.082)	0.279		
Operation duration > 240 min ([ref ≤ 240])	1.193 (0.475-2.997)	0.707		
Number of lymph node > 15 ([ref ≤ 15])	1.141 (0.464-2.806)	0.773		
T stage > 2 ([ref ≤ 2])	0.649 (0.254-1.655)	0.365		
HALP score > 26 ([ref ≤ 26])	0.511 (0.206-1.270)	0.116		

HALP: hemoglobin, albumin, lymphocyte, and platelet; LR: logistic regression; OR: odds ratio; ASA: American Society of Anesthesiologists; BMI: body mass index.

Table 3. Univariate and multivariate linear regression analyses for HALP score

Parametres	Univariate linear regression			Multivariate linear regression	
	β (95% CI)	R^2	p	β (95% CI)	p
Gender	–1.66 (–10.50-7.19)	0.1%	0.710		
Age	0.12 (–0.22-0.46)	0.1%	0.486		
ASA score	–1.19 (–9.04-6.65)	0.1%	0.763		
Tumor size	–1.62 (–3.21- –0-60)	0.2%	0.042	–1.57 (–3.11- –0.04)	0.044
Tumor stage	–0.62 (–4.43-3.19)	0.1%	0.001		
Operation time	–0.07 (–0.12- –0.01)	3%	0.023	–0.06 (–0.12- –0.01)	0.025
Anastomotic leak	–9.05 (–22.66-4.57)	2%	0.190		
readmission	–490 (–16.35-6.55)	0.1%	0.397		
Length of stay	0.38 (–0.33-1.09)	0.1%	0.291		
Morbidity	–0.95 (–9.40-7.51)	0.1%	0.825		
Local recurrence	–2.25 (–12.68-8.18)	0.1%	0.669		

HALP: hemoglobin, albumin, lymphocyte, and platelet; ASA: American Society of Anesthesiologists; CI: confidence interval.

LR analysis identified age and readmission variables as significant risk factors for recurrence (p = 0.013 and p = 0.005, respectively). On examination of the results, it was found that patients aged over 65 carried a 5.5 times higher risk of recurrence (95% CI: 1.433-21.106, p = 0.013), and patients who were readmitted had a 6.3 times higher risk of recurrence (95% CI: 1.748-22.711, p = 0.005). The significant factors observed in the

Table 4. Investigation of the impact of clinical and surgical characteristics on local recurrence through the utilization of univariate and multivariate logistic regression analyses

Parametres	Univariate LR		Multivariate LR	
	OR (95% GA)	p	OR (95% GA)	p
Age > 65 (ref ≤ 65)	5.5 (1.433-21.106)	0.013	4.654 (1.160-18.669)	0.030
Gender male (ref: female)	1.206 (0.388-3.743)	0.746		
ASA score (ref = 2)	1	0.866		
3	0.733 (0.236-2.276)	0.592		
4	0.010 (0.001-345.45)	0.990		
Tumor size > 3.5 cm (ref ≤ 3.5)	1.476 (0.497-4.384)	0.483		
T stage > 2 (ref ≤ 2)	1.435 (0.476-4.328)	0.521		
Lymphovascular invasion (1)	1.172 (0.357-3.848)	0.794		
Anastomotic leak (1)	0.573 (0.064-5.114)	0.618		
Readmission	6.3 (1.748-22.711)	0.005	4.903 (1.279-18.792)	0.020
Length of stay > 8 day (ref ≤ 8)	0.806 (0.269-2.417)	0.700		
Perioperative morbidity	0.646 (0.214-1.956)	0.440		
Halp score > 26 (ref ≤ 26)	0.919 (0.313-2.695)	0.877		

LR: logistic regression; OR: odds ratio; ASA: American Society of Anesthesiologists.

univariate LR analysis were further examined together in a multivariate LR (enter method) model to determine their combined effect on recurrence risk. Accordingly, it was determined that age and readmission variables significantly contributed to the risk of recurrence at a statistical level (p = 0.030 and p = 0.020, respectively).

Discussion

This retrospective observational study aimed to explore the predictive value of pre-operative HALP scores for perioperative morbidity in patients undergoing rectal cancer surgery. Contrary to our hypothesis and the existing literature suggesting a potential link between HALP scores and outcomes in various cancers[11], our findings did not demonstrate a statistically significant correlation between pre-operative HALP scores and perioperative morbidity in rectal cancer patients. This discrepancy underscores the potential limitations of the HALP scores in capturing the nuanced interplay of factors that contribute to surgical risks and complications.

On comparing our surgical outcomes with those in the existing literature, it can be asserted that we exhibit similarity in terms of the average duration of operations[19-21] and the average quantity of lymph nodes harvested[22-24]. Nevertheless, the anastomotic leak rate observed in our study is notably elevated compared to the existing literature[18,25], while the local recurrence frequency aligns with the findings reported in the literature[14]. Based on the existing literature, it can be inferred that the quality of oncological surgery is acceptable. However, there is a need for improvement in terms of anastomotic leakage reduction.

When our short-term surgical and clinical parameters, such as average length of stay (11.5 day open, 8.3 day laparoscopic), readmission rate (16.5%), and perioperative morbidity rate (%36), are compared with the existing literature, it becomes evident that our average length of stay is above that of the literature (7 days open, 6 days laparoscopic)[26], and our readmission rate is beyond that of the literature series (6.4%)[27]. The observed rate of perioperative morbidity in our study seems to be higher than that reported in other studies[28]. Based on the data presented, it is evident that certain areas exist within the clinical management of patients that require improvement.

When analyzing the literature on perioperative morbidity in low anterior resections, anastomotic leaks are commonly highlighted as a significant factor. A study conducted by Matthiessen et al.[29] identified several independent risk factors, namely, low anastomosis, preoperative radiation, presence of intraoperative adverse events, and male sex. In a separate investigation, the

use of pre-operative steroids, extended duration of surgical procedures, and contamination of the operative field were identified as distinct risk factors[30]. In addition, Malika et al.[31] conducted a study on perioperative morbidity in the context of rectal cancer surgery. Their findings revealed a statistically significant requirement for perioperative transfusion. In our analysis, we found that age 65 years and male gender were associated with perioperative morbidity. This raises important considerations for pre-operative assessment and risk stratification, indicating that a more comprehensive approach that potentially incorporates a wider range of clinical and biological markers may be necessary to accurately predict and manage perioperative risks.

Notably, our study sought to understand the relationship between pre-operative HALP scores and the risk of local recurrence post-surgery. Despite the expectation that lower HALP scores would correlate with higher recurrence rates given the association between poor nutritional and immunological status and cancer aggressiveness, our data did not reveal a statistically significant link. This lack of correlation may suggest that while HALP scores can provide a snapshot of a patient's general health status, they might not be sufficiently sensitive to specifically predict local recurrence in rectal cancer. Waldenstedt et al.[32] identified several factors associated with local recurrence. These factors include intraoperative adverse events, non-radical resection, high pathological T stage, and the presence of lymph node metastases. Another study revealed a correlation between tumor size, T stage, and local recurrence[33]. The findings of our study indicated a significant association between age, readmission, and local recurrence.

The HALP score has been assessed in the literature with regard to survival in colorectal cancer, and its statistical significance has been established[34]. The study conducted by Yalav et al. revealed that there was no significant association between the HALP score and surgical morbidity in patients with colorectal cancer[35]. Based on our data, there is no correlation between HALP score and surgical morbidity or local recurrence. However, a high HALP score is associated with reduced tumor size and shorter operative time.

Our study has certain limitations. The limitations of this study include its retrospective design, the contribution of multiple surgeons in clinical operations, and the inability to establish a relationship between our data and survival due to the study's specific date range. The findings also prompt a reevaluation of the role of systemic inflammation and nutritional status in rectal cancer surgery outcomes. Although HALP scores were not predictive of morbidity in our cohort, this does not negate the importance of these factors in patient care. Instead, this may indicate the need for more sensitive or specific markers to assess and address these dimensions of patient health.

Conclusions

Our retrospective observational study explored the predictive value of pre-operative HALP scores on perioperative morbidity and local recurrence in rectal cancer surgery. Contrary to our hypothesis and the previous literature, we did not find a statistically significant correlation between pre-operative HALP scores and perioperative morbidity or local recurrence rates. This outcome challenges the presumed universal applicability of HALP scores as a prognostic tool in oncological surgeries and underscores the necessity of considering a multifaceted approach to risk assessment and management in patients with rectal cancer.

Interestingly, our study revealed a significant positive correlation, where a higher HALP score was associated with a reduced tumor size and shorter operative time. This finding suggests that while HALP scores may not directly predict perioperative morbidity or the likelihood of local recurrence, they may still offer valuable insights into certain aspects of the surgical outcome, such as the potential for a less complex surgical procedure and favorable tumor pathology.

The significant associations between perioperative morbidity and factors such as age and sex reinforce the importance of a multifaceted approach to pre-operative risk assessment. Future studies should aim to develop and validate comprehensive models that integrate a broad spectrum of clinical, nutritional, and inflammatory markers to better predict and mitigate the risk of perioperative morbidity in rectal cancer surgery.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that the procedures followed complied with the ethical standards of the responsible human experimentation committee and adhered to the World Medical Association and the Declaration of Helsinki. The procedures were approved by the Institutional Ethics Committee.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. Artificial intelligence (AI) assistance was employed for grammatical review and language editing of this manuscript. Specifically, AI tools were utilized to ensure clarity, coherence, and grammatical accuracy in the text. The scientific content, data analysis, and interpretation of results were exclusively carried out by the authors, without any influence or contribution from AI. The authors take full responsibility for the originality, accuracy, and integrity of the manuscript's content.

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ORIGINAL ARTICLE

Changes in prostate specific antigen value in patients with COVID-19

Cambios en el valor del antígeno prostático específico en pacientes con COVID-19

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Abstract

Objectives: *To evaluate changes in prostate-specific antigen (PSA) values in patients with coronavirus disease 2019 (COVID-19).* **Method:** *Male patients who were admitted to our flu outpatient clinic with cough, fever, weakness, and bone and joint pain were evaluated. The acute phase reactants of erythrocyte sedimentation rate, C-reactive protein, ferritin, and fibrinogen were measured both at the time the patients first presented at the clinic and 1 month after recovery from COVID-19 infection. PSA and free PSA were also measured at the same time. The difference in acute phase reactants and PSA values during active COVID-19 infection and after recovery was assessed using the paired samples t-test.* **Results:** *The mean PSA values of the patients were 2.73 ± 3.7 μg/L in the period of active infection, and 2.04 ± 2.32 μg/L 1 month later (p = 0.12). In the 29 patients with PSA values in the gray zone, the PSA values were determined as 6.6 ± 4.4 μg/L during infection and 4.1 ± 2.9 μg/L after treatment (p = 0.001).* **Conclusion:** *The results of this study showed that PSA values in the gray zone during COVID-19 infection decreased after treatment when the patient recovered.*

Keywords: *COVID-19. Infection. Prostate. Prostate-specific antigen.*

Resumen

Objetivo: *Evaluar cambios en los valores de antígeno prostático específico (PSA) en pacientes con COVID-19.* **Método:** *Se evaluaron pacientes de sexo masculino que ingresaron a nuestra consulta externa de gripe con tos, fiebre, debilidad, dolor óseo y articular. Los reactivos de fase aguda de la velocidad de sedimentación de eritrocitos, la proteína C reactiva, la ferritina y el fibrinógeno se midieron tanto en el momento en que los pacientes se presentaron por primera vez en la clínica como un mes después de la recuperación de la COVID 19. El PSA y el PSA libre también se midieron al mismo tiempo. La diferencia en los reactivos de fase aguda y los valores de PSA durante la infección activa por COVID-19 y después de la recuperación se evaluó mediante la prueba t de muestras pareadas.* **Resultados:** *Los valores medios de PSA de los pacientes fueron 2.73 ± 3.7 μg/L en el periodo de infección activa y 2.04 ± 2.32 μg/L un mes después (p = 0.12). En los 29 pacientes con valor de PSA en la zona gris, los valores de PSA se determinaron como 6.6 ± 4.4 μg/L durante la infección y 4.1 ± 2.9 μg/L después del tratamiento (p = 0.001).* **Conclusión:** *Los resultados de este estudio mostraron que los valores de PSA en la zona gris durante la COVID-19 disminuyeron después del tratamiento cuando el paciente se recuperó.*

Palabras clave: *COVID-19. Infección. Próstata. Antígeno prostático específico.*

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Introduction

The use of prostate-specific antigen (PSA) as a serum marker has revolutionized the diagnosis of prostate adenocarcinoma[1]. Although PSA is organ-specific, it is not cancer-specific, so elevated PSA values may be seen in benign prostatic hypertrophy (BPH), prostatitis, and other non-malignant conditions[2]. PSA is a serine protease from the human kallikrein family, also known as kallikrein-3, which is a glycoprotein produced by the prostate gland[3]. Kallikreins are acute phase reactants, have proteolytic properties, and play an important role in many infections[4-6].

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causing coronavirus disease 2019 (COVID-19) resulted in a global pandemic on a scale unprecedented for the last 100 years. The diagnosis and treatment of many diseases, especially cancers, was delayed due to the COVID-19 pandemic. Articles have been published about the duration of this reasonable delay in urological cancers[7]. This situation has highlighted the importance of cancer screening during a pandemic. Is it logical to see PSA for screening purposes in patients with COVID-19 at the time of active disease? Is it reasonable to take a biopsy from patients with PSA levels in the gray zone after COVID-19 treatment? The aim of this study was to evaluate changes in PSA values in patients with COVID-19.

Method

This study was conducted between April 2020 and September 2021 after obtaining the approval of the Local Ethics Committee (E-21-594). The Clinical Trials number is NCT05009186. Male patients who were admitted to our flu outpatient clinic with cough, fever, weakness, and bone and joint pain were evaluated. Samples were taken from all of these patients for polymerase chain reaction (PCR) tests with both oral and nasopharyngeal swabs. All patients provided written informed consent. Patients with positive PCR test results were included in the study. The age of the patient and urea, leukocyte, hemoglobin, platelet, and creatinine values of the patients were recorded. Urinalysis and urine culture were taken from all patients. The acute phase reactants of erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), ferritin, and fibrinogen were measured both at the time the patients first presented at the clinic and 1 month after recovery from COVID-19 infection. PSA and free PSA were also measured at the same time. Patients whose symptoms improved and with a negative PCR test result were considered recovered.

Patients were excluded from the study if they were aged < 45 or > 70 years, if they had lower urinary tract symptoms, urinary tract infection, a history of prostate biopsy and previous high level of PSA, or a history of prostatitis.

Statistical analysis

Data analyses were performed with PASW 18 software (Statistical Packages for the Social Sciences/ IBM, Chicago, IL, USA). The Kolmogorov-Smirnov and P-P plot tests were used to verify the normality of the distribution of continuous variables. The results were reported as mean ± standard deviation values for data showing normal distribution or median (minimum–maximum) values when data distribution was skewed. All statistical tests were two-tailed. The difference in acute phase reactants and PSA values during active COVID-19 infection and after recovery was assessed using the paired samples t-test. There was determined to be a 91% chance of correctly rejecting the null hypothesis of no difference between active disease and control conditions with 30 participants. A value of $p < 0.05$ was considered statistically significant.

Results

A total of 130 patients who met the study criteria were enrolled, and as 39 did not attend follow-up appointments, they were excluded and an analysis was made of 91 patients. The mean age of the patients was 59 ± 6.7 years. The mean PSA values of the patients were 2.73 ± 3.7 μg/L in the period of active infection, and 2.04 ± 2.32 μg/L 1 month later ($p = 0.12$). The values of the patients before and after treatment are shown in table 1.

In the 29 patients with PSA values in the gray zone, the PSA values were determined as 6.6 ± 4.4 μg/L during infection and 4.1 ± 2.9 μg/L after treatment ($p = 0.001$) (Fig. 1). The PSA values decreased in 25 of the 29 patients in the gray zone and an increase was observed after treatment in four.

A statistically significant improvement was determined in the ferritin and fibrinogen values, as the other acute phase reactants ($p = 0.0001$, $p = 0.04$, respectively). The mean ESR and CRP values were determined as 30.6 ± 20.8 mg/L and 71.5 ± 56.9 mg/L during COVID-19 infection and as 11.9 ± 11.5 mg/L

Table 1. Changes in serum parameters of patients during COVID-19 and after 1 month of COVID-19

Parameters	Values during COVID-19	Values post COVID-19	p
ESR	30.6 ± 20.8	11.9 ± 11.5	0.10
Ferritin (ng/mL)	701.2 ± 600.8	153.7 ± 180.2	0.0001*
Fibrinogen (mg/dL)	580.4 ± 168.7	344 ± 92.4	0.04*
CRP(mg/L)	71.5 ± 56.9	5.5 ± 9.4	0.97
WBC (mcL)	7.48 ± 2.9	9 ± 8	0.57
Platelet (mcL)	207.8 ± 73.4	257 ± 54	0.01*
Hemoglobin (g/dL)	14.3 ± 1.3	14.5 ± 1.5	0.0001*
Urea (mg/dL)	38.7 ± 18.2	34.2 ± 13.7	0.0001*
Creatinine (mg/dL)	1.08 ± 0.51	0.97 ± 0.44	0.0001*
PSA (µg/L)	2.7 ± 3.7	2.04 ± 2.3	0.12
fPSA (µg/L)	0.52 ± 0.93	0.5 ± 0.49	0.01*

*Statistically significant (paired samples t-test). ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; COVID-19: coronavirus disease 2019; PSA: prostate-specific antigen; WBC: white blood cell; fPSA: free prostate-specific antigen.

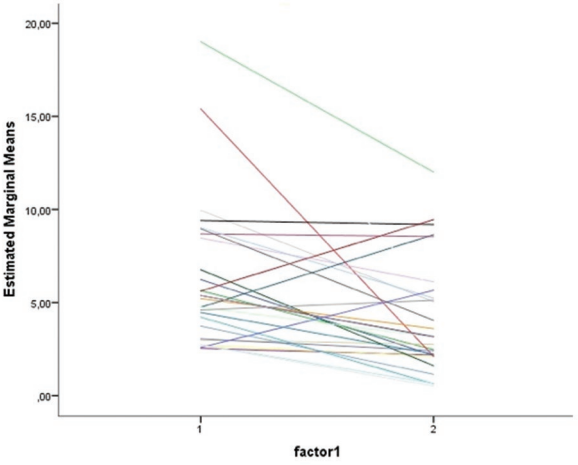

Figure 1. *The change in mean prostate-specific antigen values after treatment is shown in the gray zone with a spaghetti plot.*

and 5.5 ± 9.4 mg/L after recovery (p = 0.10, p = 0.97, respectively) (Table 1). When the relationships between ferritin, ESR, fibrinogen, CRP, and tPSA were evaluated with bivariate correlation analysis, with the exception of ESR, no acute phase reactant was determined to be statistically significantly correlated with PSA. A statistically significant but weak positive correlation was determined between ESR and PSA (p = 0.04, r = 0.21).

Discussion

Acute phase reactants are inflammation markers that vary at a significant rate in serum concentrations during inflammation. They can be separated into two main groups as those showing positive and negative changes according to the serum concentrations during inflammation. The acute phase reactants showing a positive change which are used most in clinical practice are CRP, ferritin, and fibrinogen. The concentrations of these increase during acute and chronic inflammation. The most well-known negative acute phase reactants are albumin, transferrin, and retinol-binding protein. Positive acute phase reactants reach the highest levels during acute trauma and acute inflammation[8,9]. ESR measures the distance that red blood cells in anticoagulated blood fall in a vertical tube after 1 h. Fibrinogen reduces the load on the red blood cell surface and this causes them to collect together rapidly, and as a result ESR increases[10].

Plasma kinins are another acute phase reactant, which is an important part of the inflammatory response as an important mediator of increased vascular permeability[11]. During septicemia, the plasma kallikrein-kinin system is activated, and components of this protease system are seen to function during sepsis[12]. PSA is a serine protease of the human kallikrein group[3], and is expected to be elevated in the plasma as a response to infection. This antigen has an important place in the screening and diagnosis of prostate cancer.

Prostate cancer is the second most commonly seen cancer in males in the USA and Europe[13,14] and is the second most common cancer-related cause of death in males[13]. However, an elevated PSA value is not cancer-specific and may be related to other prostate pathologies such as inflammation and BPH[15]. As the structure of the prostate tissue deteriorates in prostate cancer, prostatitis, and prostate infarction, the amount of PSA released into the blood increases. Therefore, PSA in the blood may be elevated. As PSA synthesis is increased in BPH, this also increases PSA[16]. Despite the disadvantages, PSA measurement remains the gold standard method in current prostate cancer screening as no new biomarker has been determined[17].

Prostate inflammation can cause an increase in PSA level, and this can lead to confusion on the subject of the use of PSA and PSA kinetics in the diagnosis of prostate cancer. The use of empirical antibiotics followed by repeated PSA measurement

is a matter of debate. In a previous study that analyzed patients with Type IV prostatitis and high PSA levels (National Institutes of Health classification), no significant difference was determined in the fall in PSA between the group given antibiotics and the group given placebo (59.2% vs. 53.1%). There was also no significant difference in respect of patients with a decrease in PSA and diagnosis of prostate cancer after treatment with antibiotics or placebo (31% vs. 26.9%)[16]. In the European Association of Urology guidelines, empirical antibiotic treatment is not recommended to lower PSA in the gray zone, but if the patient has an active urinary tract infection, it is recommended that PSA is measured again after antibiotic therapy.

Although there are many studies in literature related to prostatic inflammation, elevated PSA, and empirical antibiotic treatment, to the best of our knowledge there are few studies that have investigated the relationship between systemic infection and serum PSA level. In the patients in the current study, the mean PSA value was 2.73 ± 3.7 μg/L in the period of active COVID-19 infection and 2.04 ± 2.32 μg/L 1 month later. Despite the fall in the mean plasma PSA values, the difference was not statistically significant (p = 0.12). In the 29 patients with PSA values in the gray zone, the mean values were determined as 6.6 ± 4.4 and 4.1 ± 2.9 μg/L during COVID-19 infection and at 1 month later, respectively. The difference was determined to be statistically significant (p = 0.001). Correspondingly, In a newly published study by Cinislioglu et al., which similarly evaluated the relationship between COVID-19 and PSA, the total PSA values obtained during COVID-19 infection were found to be higher than the PSA values obtained before the infection and in the follow-up after the infection[18].

In the early periods of the pandemic, it was thought that the SARS-Cov-2 only involved the lungs, whereas over time it was understood that the virus could target tissues which express angiotensin-converting enzyme 2, which is the SARS-CoV-2 receptor[19]. Moreover, this virus uses transmembrane protease serine 2 receptor to enter the host cells and spread the infection. This receptor is found in the prostate as well as in organs such as the lungs, colon, and liver[20]. This makes the prostate a target organ for the virus[21]. As a result, impairment of the basal membrane structure of the prostate by the virus involving the prostate and causing inflammation could be a reason for elevated PSA. What is more, when it is considered that PSA is an antigen of the kallikrein group and kallikreins have an important role against inflammation during systemic infection, an increase can be expected in plasma PSA level. Therefore, when evaluating the results of this study, it can be said that COVID-19 infection may lead to an increase in PSA values in males aged > 45 years. A significant decrease was observed after recovery from the systemic infection, especially in the gray zone PSA values (2.5-10 μg/L).

In four of the current study patients with gray zone PSA values, the PSA value was determined to have increased after treatment. When these patients were evaluated, it was found that the other acute phase proteins had also increased. The reason for this was thought to be a continuation of the systemic inflammatory effect of COVID-19 infection despite the negative PCR test.

The main limitation of this study was that prostate biopsies were not taken from the patients. If prostate biopsies had been taken, the importance of the fall in the PSA values in respect of cancer would have been able to be determined more objectively. However, it would not have been ethical to take a biopsy from each patient in this type of study.

Conclusion

The results of this study showed that PSA values in the gray zone during COVID-19 infection decreased after treatment when the patient recovered. It can be recommended that for males aged > 45 years with COVID-19 infection, plasma PSA measurements are taken after recovery from the infection. When it is considered that a large proportion of the population has been exposed to COVID-19 and the majority of those have had a mild symptomatic course with the effect of vaccination, it can be recommended that if PSA is measured and a gray zone PSA value is determined, the PSA measurement should be repeated at least 1 month after recovery from the infection.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that the procedures followed complied with the ethical standards of the responsible human experimentation committee and adhered to the World Medical Association and the Declaration of Helsinki. The procedures were approved by the institutional Ethics Committee.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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ORIGINAL ARTICLE

Retrospective evaluation of the effects of different anesthesia methods on emergence agitation in patients undergoing vitreoretinal surgery

Evaluación retrospectiva de los efectos de diferentes métodos de anestesia sobre la agitación de emergencia en pacientes sometidos a cirugía vitreorretiniana

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Abstract

Objective: *The agitation that can occur in patients undergoing vitreoretinal surgery on awakening from general anesthesia is a serious post-operative problem. In our study, we aimed to compare the effects of different anesthesia methods on emergence agitation in patients undergoing vitreoretinal surgery.* **Method:** *Patients undergoing vitreoretinal surgery were divided into two groups: Total intravenous anesthesia (Group T) and inhalation anesthesia (Group D) according to the maintenance of anesthesia applied by consulting the records. Patients' heart rate, mean blood pressure, extubation quality scores, and Richmond Agitation and Sedation Scale values were examined.* **Results:** *For the study, data were available from 100 patients undergoing vitrectomy surgery. It was observed that in the total intravenous anesthesia group the quality of extubation and the patients' additional analgesic requirements were better, and the patients' agitation levels at min 0 were lower.* **Conclusion:** *In our study, it was observed that the choice of total intravenous anesthesia as an anesthetic method in patients undergoing vitreoretinal surgery reduced agitation upon awakening compared to those receiving inhalational anesthesia.*

Keywords: *Vitreoretinal surgery. General anesthesia. Emergence agitation.*

Resumen

Objetivo: *La agitación que puede ocurrir en pacientes sometidos a cirugía vitreorretiniana al despertar de la anestesia general es un problema postoperatorio grave. En nuestro estudio, el objetivo fue comparar los efectos de diferentes métodos de anestesia sobre la agitación de emergencia en pacientes sometidos a cirugía vitreorretiniana.* **Método:** *Los pacientes sometidos a cirugía vitreorretiniana se dividieron en dos grupos: anestesia intravenosa total (grupo T) y anestesia inhalatoria (grupo D), según el mantenimiento de la anestesia aplicado consultando los registros. Se examinaron la frecuencia cardiaca, la presión arterial promedio, las puntuaciones de calidad de la extubación de la Escala de sedación y agitación de Richmond.* **Resultados:** *Para el estudio se dispuso de datos de 100 pacientes sometidos a cirugía de vitrectomía. Se observó que en el grupo TIVA (total intravenous anesthesia) la calidad de la extubación y los requerimientos analgésicos adicionales de los pacientes fueron mejores, y los niveles de agitación de los pacientes en el minuto 0 fueron menores.* **Conclusión:** *En nuestro estudio se observó que la elección de la anestesia intravenosa total como método anestésico en pacientes sometidos a cirugía vitreorretiniana redujo la agitación al despertar en comparación con los que recibieron anestesia inhalatoria.*

Palabras clave: *Cirugía vitreorretiniana. Anestesia general. Agitación de emergencia.*

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Introduction

Vitreoretinal surgery is defined as the removal of deformed vitreous that fills the cavity at the back of the eye and surgically intervening in retinal problems. This surgery is performed in situations that affect the structure of the vitreous and hamper vision such as diabetic retinopathy, retinal detachment, trauma, and uveitis.[1,2]

Emergence agitation is a complication of anesthesia that occurs in the early wake-up period of general anesthesia and is characterized by mental fog, agitation, aggressive behavior disorders, and disruption in perceiving the environment.[3]

The objective in vitreoretinal surgery is not to elevate intraocular pressure with a slight induction. The Valsalva effect that is caused by cough, gagging, and yelling along with pain seen in patients following the surgery can lead to sudden elevation in venous pressure, venous ruptures, and severe post-operative subchoroidal hemorrhage.[4]

There are studies in the literature on preventing or reducing emergence agitation especially in nasal surgeries and maxillofacial surgeries.[5,6] However, the data on vitreoretinal surgeries in this regard are limited. In this study, we aimed to compare the effects of total intravenous anesthesia and inhalation anesthesia with desflurane on post-operative emergence agitation in patients who underwent vitreoretinal surgery.

Method

The study was planned as retrospective research including patients aged between 18 and 70 years who underwent vitreoretinal surgery in the Eye Diseases Clinic between April 30 and 2018 and November 01 2020 and whose American Anesthesiologists Association (ASA) risk scores were I-III. After obtaining ethics committee approval (2021/384), the patient files in the hospital archives were screened.

In the hospital where the study was conducted, following the standard monitorization and premedication of the patients, 1 μg/kg fentanyl, 3 mg/kg propofol and 1 mg/kg rocuronium are applied for anesthesia induction, and anesthesia maintenance is provided with desflurane and 2-3 mcg/kg/dk remifentanil with 50% oxygen mixture, while in some patients, the maintenance is ensured with 6 mg/kg/h propofol and 0.5 mcg/kg/min remifentanil with 50% oxygen mixture. Following induction, in addition to standard monitorization, the Train-of-Four Ratio monitorization is applied. After the completion of the surgery, 2 mg/kg sugammadex is administered to the patients, and when muscle power is recovered, the patient is extubated. In the recovery unit, as a routine application, 5-point extubation quality scale and Richmond Agitation Sedation Scale (RASS) scores are recorded. In the follow-up, it is checked whether the patients have nausea and vomiting and additional analgesics requirements. In addition, Numerical Rating Scale values of the patients' pain levels are recorded in patient files.

In light of this information, the patients were divided into two groups as total intravenous anesthesia group (Group T) and desflurane anesthesia group (Group D) according to the anesthesia maintenance they received. For the study parameters, anesthesia follow-up forms and hospital computer records were examined. The patients who had drug allergy, a neurological or psychiatric disorder, cirrhosis and chronic renal failure, severe cardiovascular and respiratory disorders, coagulation disorder, and whose surgery lasted more than 3 hours were excluded from the study.

As follow-up parameters, the patients' demographic data (age and gender), body mass indices, ASA risk scores, and surgery and anesthesia durations were noted by examining the records. Besides, intraoperative and recovery unit post-operative records were analyzed, and hemodynamic data, history of nausea/vomiting, additional analgesic requirements, emergence agitation levels, extubation quality scale, and RASS scores were recorded.

The study data obtained were analyzed through "Statistical Package for the Social Sciences" for Windows Release 22.0 software. In the comparison of qualitative data, $\chi 2$ was used, while in the comparison of the data obtained through measurement, compliance with normal distribution was checked by Kolmogorov-Smirnov test, and if the normal distribution assumption is met, Student's t test was used, if not, Mann-Whitney U test was employed. In the comparison of the measurements made from the beginning, repetitive measurement variance analysis or Friedman test was used. The data obtained through measurement were expressed as mean and standard deviation, while the data obtained through counting were given as percentage (%). Statistical significance level was accepted as $p < 0.05$.

Results

In the study, of 143 patients who underwent vitreoretinal surgery in the Eye Diseases clinic between April 30, 2018, and November 01, 2020, the data of 100 patients were accessed. It was found that 60 of these patients received total intravenous anesthesia (Group T) and 40 patients were administered desflurane anesthesia (Group D) (Fig. 1).

The patients' ASA risk scores, age, gender, body mass index, and surgery durations are presented in table 1, and no statistically significant difference was determined between the groups ($p > 0.05$).

In terms of the patients' heart rates and mean arterial pressure, no statistically significant difference was found between the groups (Figs. 2 and 3) ($p > 0.05$).

The patients' RASS scores are presented in table 2. Accordingly, emergence agitation levels of Group D at 0^{th} min were significantly higher compared to Group T ($p < 0.001$).

Regarding the patients' extubation quality levels, extubation quality levels of the patients in Group D were found to be significantly higher compared to the patients in Group T ($p < 0.001$) (Table 3). Similarly, additional analgesic requirement levels of the patients in Group D were determined to be significantly higher compared to the patients in Group T ($p = 0.005$) (Table 3).

Table 1. Patient characteristics and duration of anaesthesia and surgery

Parameters	Group T (n = 60)	Group D (n = 40)
Age (year)	61.6 ± 11.9	60.7 ± 12.2
Gender (M/F)	34/26	15/25
Body mass index (kg/m^2)	28.6	29.2
ASA physical status (I/II/III)	9/27/24	4/15/21
Duration of anaesthesia (min)	90.5 ± 29.3	94.4 ± 27.9
Duration of surgery (min)	86.4 ± 22.4	91.7 ± 25.7
Extubation time (min)	4.5 ± 2.3	4.4 ± 2.1
Remifentanyl infusion (mcg/h)	653.5 ± 101.2	651.5 ± 123.3

ASA: american society of anesthesiologists classification. Values are expressed as mean ± standard deviation, number (n).

Table 2. Comparison of emergence agitation levels of the Groups

Emergence agitation (RAAS > +1)	Group T (n = 60)	Group D (n = 40)	p
0 min	0	7 (17.9%)	< 0.001*
15 min	0	0	
30 min	0	0	

*p < 0.001 Group D has higher emergence agitation levels than group T.
RASS: richmond agitation-sedation scale; min: minute.

Table 3. Continuous variables of study between groups

Outcome	Group T (n = 60)	Group D (n = 40)	p
Extubation quality score (1-5)	1.21 ± 0.64	1.77 ± 0.96	< 0.001*
Need for rescue medication (number of patients) Incidence of vomiting and nausea (number of patients)	1 (1.6%) 2 (3.3%)	7 (17.9%) 2 (5%)	0.005*

*p < 0.001, extubation quality score in group D are compared to group T.

Discussion

The study in which we examined the effects of different anesthesia methods on emergence agitation has shown that TIVA method decreases post-operative emergence agitation and ensures a more comfortable recovery from anesthesia. This situation also contributes to better quality of extubation. In addition, this method reduces the patient's pain levels in the recovery period and keeps additional analgesic requirement at a minimum level, which helps the patients to experience the post-operative recovery period more comfortably and calmly.

In vitreoretinal surgery, different anesthesia methods such as TIVA, inhalation anesthesia, and local anesthesia are used, but when the literature was reviewed, no study on emergence agitation in these patients was encountered. As an important post-operative complication, emergence agitation can lead to surgical complications in patients who underwent vitreoretinal surgery such as increase in intraocular pressure following extubation, venous ruptures as a result of increased pressure caused by gagging, and severe subchoroidal hemorrhages. In determining postoperative agitation, RASS is frequently used[7].

Particularly, young age, male sex, and presence of obesity are independent risk factors, and in terms of demographic data, there was no significant difference between the groups in the present study[3].

When the literature is reviewed in terms of the effects of different anesthesia methods to be used in surgical applications on emergence agitation, it is seen that the use of inhalation anesthesia in children is known to be a risk factor in terms of emergence agitation, but that there is limited data on adults[3,6]. In a randomized controlled trial conducted by Chandler et al. on 112 patients who were operated for diplopia,

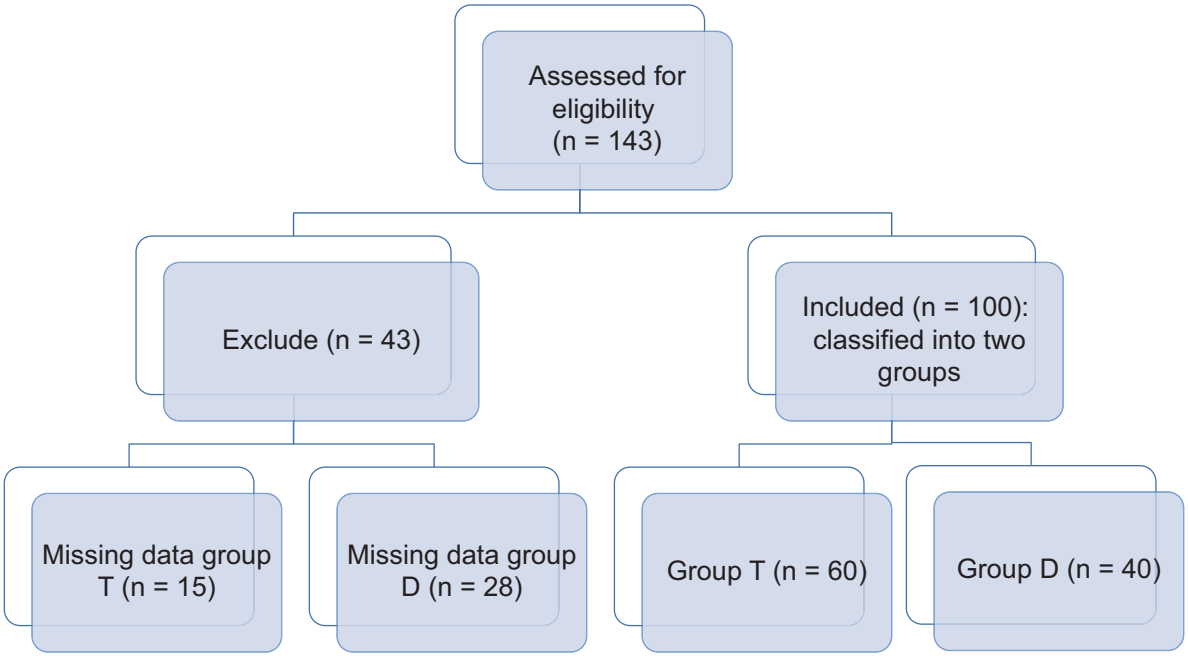

Figure 1. *Consolidated Standards of Reporting Trials flowchart showing the number of patients at each phase of the study.*

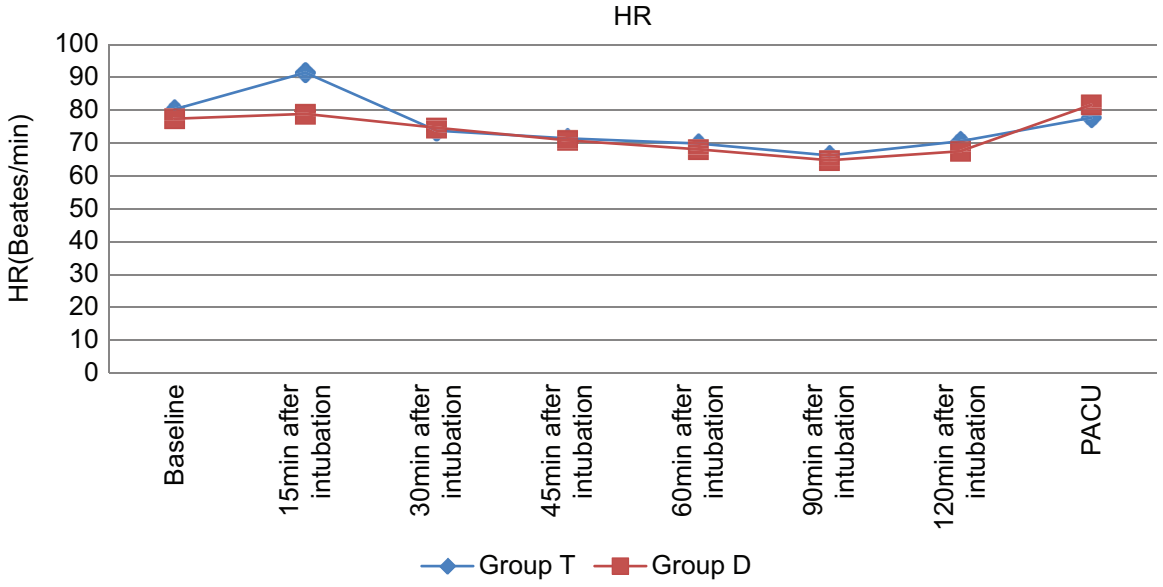

Figure 2. *Changes in heart rate during surgery in groups.*

Pediatric Anesthesia Emergence Delirium was used, and it was demonstrated that TIVA method reduced the incidence of agitation compared to inhalation anesthesia[8].

In a prospective study conducted by Yu et al. on 2000 patients, agitation was followed up by a special nurse with a 3-point scale, and the insidence of agitation was found to be lower in the group which was administered TIVA[9]. In addition, in a retrospective study conducted by Kim et al. on 792 patients, RASS ≥ +1 was accepted to be statistically significant, and the incidence of agitation was found to be lower in TIVA group[5]. In the prospective randomized controlled clinical trial conducted by Jo et al. on

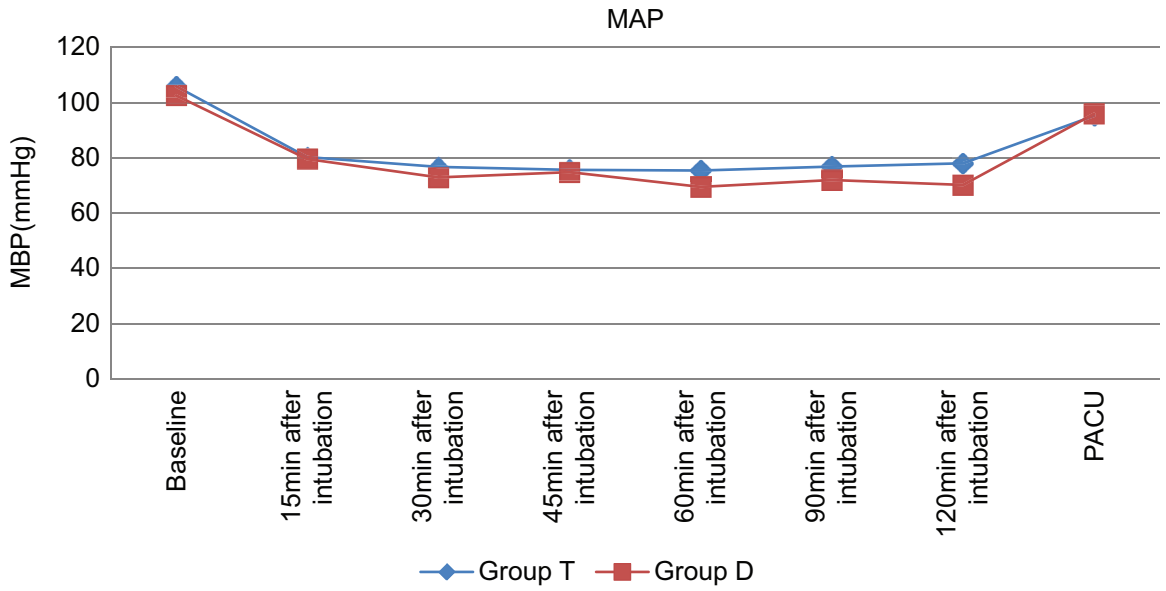

Figure 3. *Changes in mean arterial pressure during surgery in groups.*

80 patients, in addition to RASS, Riker Sedation Agitation Scale (RSAS) was used, RSAS > 1 was accepted to be statistically significant, and TIVA application was found to have decreased agitation incidence compared to the use of sevoflurane inhalation anesthesia[10].

Although there are studies reporting results conflicting with the studies mentioned above[11], in our study, while no agitation was observed in any of the patients who were administered TIVA, determining RASS ≥ 2 at 0th min after extubation in 7 of the 40 patients was found to be statistically significant. This supports the finding that TIVA administration reduced agitation incidence.

As intracranial pressure increase, upper airway obstruction, and situations such as laryngospasm, hypoxia, and hypercarbia that may lead to orientation disorder can increase agitation, necessary measures should be taken and agitation development should be prevented[12]. When extubation quality scores of the patients were compared in our study, extubation quality scores of the patients who were administered TIVA were found to be lower compared to the patients who were administered inhalation anesthesia, and the situation was found to be statistically significant.

The role of pain should not be ignored among the causes of postoperative emergence agitation. An adequate level of postoperative pain palliation has been demonstrated to decrease agitation incidence[9,13-15], However, there are studies which showed less consumption of post-operative analgesics in patients who were administered TIVA[16,17]. When the patient records in the present study were examined, it was seen that all patients were routinely administered 1 g paracetamol and 30 mg meperidine at the 45th min of the operation. In our study, while only one patient out of 60 patients who were administered TIVA needed additional analgesics, seven of the 40 patients who were administered inhalation anesthesia needed additional analgesics, and the difference was found to be statistically significant. This situation supports the finding that in addition to directly reducing agitation incidence, TIVA administration is effective in decreasing agitation induced by pain by reducing post-operative pain level.

Study limitations

Our study has certain limitations. First of all, nor being able to access all patient files due to the long time interval and lack of data in the files caused the number of patients to be limited. Second, as patient protocols and scoring systems contained subjective values as a result of different surgery and anesthesia teams performing the surgeries, a full standardization could not be achieved. Finally, it was observed that Bispectral Index Sensors, which are used to measure anesthesia depth in total intravenous anesthesia, were not used due to proximity to the surgical area.

Conclusion

It can be concluded that total intravenous anesthesia method decreases post-operative emergence agitation, ensures a more comfortable recovery from anesthesia for patients, and thus contributes to a better quality of extubation. In addition, it decreases the need for additional analgesics and helps patients to experience the post-operative recovery process more comfortably and calmly. Thus, complications that can develop depending on emergence agitation in patients who underwent vitreoretinal surgery during which intraocular pressure should not be elevated can be prevented. We believe that identifying more objective markers will be effective in predicting and preventing emergence agitation and that more prospective studies are needed in terms of predicting emergence agitation in adult population, making differential diagnoses, and determining the treatment.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of human and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have obtained approval from the Ethics Committee for the analysis of routinely obtained and anonymized clinical data, so informed consent was not necessary. Relevant guidelines were followed.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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ARTÍCULO ORIGINAL

Procesos para la conversión de una unidad de cirugía mayor ambulatoria en unidad de cuidados intensivos debido a la pandemia por COVID-19. Estudio transversal

Processes for the conversion of a major ambulatory surgery unit into an intensive care unit due to the COVID-19 syndemic. Cross-sectional study

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Resumen

Objetivo: *La pandemia por COVID-19 produjo un déficit de camas en las unidades de cuidados intensivos (UCI). Para optimizar recursos, se utilizaron inicialmente, dada su equipación y personal, las unidades de reanimación posanestésica y los quirófanos, lo que supuso una gran suspensión quirúrgica. Para evitarlo, durante la segunda ola nuestro hospital transformó la unidad de cirugía mayor ambulatoria en una unidad de cuidados críticos. El objetivo principal es desarrollar los procesos llevados a cabo en nuestro hospital para dicha adaptación.* **Método:** *Estudio transversal desarrollado según STROBE que expone los procesos para dicha transformación. Incluimos las adaptaciones logísticas, el número de pacientes atendidos/estancias ganadas y el personal del que fue dotada la unidad. La información fue facilitada por la gerencia y por el servicio de admisión y documentación clínica. Se incluyen encuestas de mejora.* **Resultados:** *Se consiguió, en el momento de máxima ocupación, un total de 44 pacientes sometidos a ventilación mecánica sin el cese de la actividad quirúrgica. Las estancias ganadas desde el 01-03-2020 hasta el 31-12-2020 fueron 755.* **Conclusiones:** *La transformación de la unidad de cirugía mayor ambulatoria en UCI consiguió de manera rápida aumentar la capacidad de camas de críticos sin cesar la actividad quirúrgica. Este proceso de transformación es completamente reversible.*

Palabras clave: *Unidad de cirugía mayor ambulatoria. Conversión. Unidad de cuidados intensivos. Pandemia. COVID-19.*

Abstract

Objective: *COVID-19 pandemic produced a deficit situation of intensive care units (ICU) beds. To optimize resources, the post-anesthetic resuscitation units and operating rooms were initially used in order to care for these patients, due to their equipment and personnel. This meant a significant surgical suspension. To avoid this, during the second wave, our hospital transformed the major ambulatory surgery unit into a critical care unit. The main objective is to develop the processes carried out in our hospital for this adaptation.* **Method:** *Cross-sectional study developed according to STROBE that exposes the processes carried out for this transformation. We include logistical adaptations, number of patients attended/stays won and the staff with which the unit was equipped. The information was provided by management and the admission and clinical docu-*

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mentation service. Improvement surveys are included. **Results:** *A total of 44 patients undergoing mechanical ventilation without cessation of surgical activity were achieved at the time of maximum occupancy. The total number of stays won from 01/03/2020 to 31/12/2020 was 755.* **Conclusions:** *The transformation of the major ambulatory surgery unit into an ICU quickly increased the capacity of critical care beds without relenting surgical activity. This transformation process is completely reversible.*

Keywords: *Major ambulatory surgery unit. Conversion. Intensive care unit. Pandemic. COVID-19.*

Introducción

La pandemia por COVID-19 produjo una modificación sin precedentes de las necesidades hospitalarias. La mayor situación deficitaria se ha generado debido al aumento muy importante de la ocupación de camas, sobre todo de las camas destinadas a pacientes críticos en las unidades de cuidados intensivos (UCI), que se encuentran muy limitadas. En España, a fecha 19-05-2023, se habían confirmado mediante test positivo 13,868,227 casos según el Ministerio de Sanidad[1], con un total de 121,213 fallecidos[1]. Precisaron hospitalización 675,975 personas y 55,959 ingresaron en la UCI, según el Ministerio de Sanidad[2]. A fecha 30-12-2020, al finalizar el primer año de la pandemia, el total de pacientes con COVID-19 hospitalizados en España ascendió a 11,905 lo que supuso un 9.80% de ocupación del total de camas[3]. Los pacientes con COVID-19 ingresados en la UCI ascendieron a 2035, suponiendo esto una ocupación de camas de UCI del 21.34%[3]. Todo ello obligó a realizar importantes adaptaciones, tanto estructurales como del personal sanitario.

La tendencia inicial para optimizar recursos y suplir de manera rápida la falta de camas de UCI fue utilizar aquellas áreas del hospital que, por su fin primario, presentaban una dotación adecuada tanto de equipamiento (respiradores, monitores, etc.) como de personal sanitario (trabajadores que manejan pacientes en situaciones críticas, con necesidad de monitorización, intubación orotraqueal o utilización de fármacos inotrópicos u otras drogas vasoactivas). Las áreas que de base cumplían estos requerimientos y que se utilizaron al inicio fueron fundamentalmente las unidades de reanimación posanestésica (URPA) y los propios quirófanos, así como su personal.

Todo ello permitió aumentar, con los criterios antes definidos, el número de camas de UCI, aunque supuso en la mayoría de las ocasiones una disminución o la desaparición de otros procesos que precisaban estos espacios, como es la cirugía programada o electiva.

En los servicios quirúrgicos, tal redistribución de recursos supuso la desaparición de un importante número de quirófanos y de camas en las URPA para poder atender a los pacientes que se encontraban en un posoperatorio inmediato. Esta situación obligó a realizar una importante suspensión de la actividad quirúrgica en la mayoría de los centros en todo el mundo[4-8], quedando relegada en muchas ocasiones a la cirugía urgente y la cirugía no demorable.

Por ende, la situación obligó a reducir en gran cuantía el número de patologías que, por sus características, eran subsidiarias de ser atendidas en el ámbito de las unidades de cirugía mayor ambulatoria (UCMA), las cuales quedaron prácticamente inutilizadas.

Dado que no se preveía una mejora real de la pandemia de COVID-19 a corto plazo, se hizo necesario plantear alternativas que permitieran seguir atendiendo la carga importante de pacientes que requerían UCI sin que ello supusiera un cese grave de la actividad quirúrgica.

Durante la primera ola de la pandemia, en los meses de marzo y abril de 2020, debido a la falta de previsión inicial por lo inesperado de esta, en el Hospital Universitario de Guadalajara (HUG) se improvisaron nuevas camas de UCI utilizando las URPA, así como sus quirófanos, para dar cobertura a los pacientes críticos. La UCMA se cerró debido al cese de la actividad quirúrgica programada y se utilizó con nuevos respiradores adquiridos para la atención de pacientes críticos, pero sin una adecuada adaptación de las instalaciones por lo inesperada que fue la sobrecarga del sistema.

Debido a ello, desde la Gerencia de Atención Integrada (GAI) del HUG, del Servicio de Salud de Castilla-La Mancha, y en previsión de la llegada de una segunda ola dentro de la pandemia, se decidió realizar una serie de procesos para transformar la UCMA en una UCI de manera reglada, y con ello dar cobertura a la necesidad de camas de críticos, quedando como

último recurso la utilización de quirófanos y de las URPA para tal fin, y evitando así el bloqueo total que se produjo durante los meses de marzo y abril de 2020 en la actividad quirúrgica. Ello permitiría atender a los pacientes críticos, aumentar los quirófanos disponibles y, por tanto, incrementar el número de patologías atendidas y de procedimientos realizables.

El objetivo principal es desarrollar los procesos llevados a cabo en la GAI del HUG para la adaptación de la UCMA en UCI con la finalidad de cubrir la necesidad urgente de camas de cuidados críticos creada por la COVID-19. Como objetivos secundarios tenemos:

- Análisis de resultados: pacientes atendidos y estancias conseguidas.
- Análisis de las deficiencias objetivadas por los responsables de las unidades y los profesionales destinados en ellas.
- Medidas de mejora para la adaptación, en el caso concreto estudiado.
- Proponer unas dotaciones básicas para las UCMA que permitan la reconversión en un breve espacio de tiempo ante una crisis sanitaria similar.

Método

Diseño del estudio

Estudio transversal diseñado siguiendo la lista de verificación de elementos de la declaración STROBE[9,10]. Se estudiaron los procesos llevados a cabo por la GAI de Guadalajara para la transformación de la UCMA en UCI. Se distinguen dos periodos de recogida de datos: el primero, del 20-03-2020, fecha en la que se recibieron los primeros pacientes críticos en la UCMA, hasta el 11-05-2020, cuando esta se cerró por la reducción del número de ingresos; el segundo va del 01-09-2020 al 31-12-2020, periodo de reapertura tras la reestructuración programada para la adaptación de las instalaciones ante la elevada probabilidad de una segunda ola.

Participantes

Se incluyeron todos los pacientes atendidos en la nueva UCI tras la transformación de la UCMA desde el 20/03/2020 hasta el 31/12/2020, sin criterios de exclusión. Para reclutarlos, se solicitó toda la información al servicio de admisión.

Por otro lado, se incluyó al personal de gestión que planificó el proceso de transformación, al personal sanitario desplazado para tal fin y a la dirección hospitalaria para los datos de coordinación.

Como aspectos éticos cabe destacar:

- Para la realización del presente trabajo se obtuvo el consentimiento de la dirección de gestión del HUG.
- Las entrevistas realizadas al personal sanitario y de gestión que participaron tanto en la transformación de la UCMA como en su funcionamiento como UCI fueron anónimas y destinadas única y exclusivamente a la mejora del proyecto.
- Los datos de uso de la UCMA no incluyeron información de pacientes y se obtuvieron con permiso del servicio de admisión y documentación clínica.
- Dado que no aparecen datos de pacientes, no se consideró la solicitud de autorización del Comité Ético de Investigación con Medicamentos.

Variables

Se desarrollaron todas aquellas adaptaciones o modificaciones logísticas que se llevaron a cabo desde el área de gestión de la GAI del HUG para la transformación de la UCMA en UCI. Se solicitó información sobre el material disponible de manera inicial y todo aquel que se asoció posteriormente para la adaptación. Se incluye el tiempo que se necesitó para la transformación.

Se estudió el número de pacientes que fueron atendidos, divididos en ingresos directos en la UCI, traslados recibidos y emitidos, así como el número de estancias ganadas desde el inicio de la actividad de la UCMA como UCI desde el 20-03-2020 hasta el 31-12-2020, y una valoración del aumento de la capacidad total de camas de UCI. Se incorpora el número de fallecimientos.

Se recogió el personal necesario con el que fue dotada la nueva unidad para su funcionamiento.

Fuentes de datos

Se solicitó a la GAI del HUG información sobre el proyecto inicial de adaptación de la UCMA. Una muestra del personal de la UCMA adaptada fue entrevistada para obtener los datos referentes a los defectos y las áreas de mejora de la unidad creada.

Se solicitaron al servicio de admisión y documentación clínica los datos referentes al número de pacientes y estancias de la unidad creada.

Tabla 1. Equipamiento de la unidad de cirugía mayor ambulatoria (UCMA) y modificaciones para la transformación en unidad de cuidados intensivos (UCI)

Equipamiento	UCMA (15-03-2020)	Transformación en UCI
Camas	12 + 1 sillón	10
Camas de diálisis	Ninguna	2
Tomas	1 de oxígeno + 1 de vacío (X12)	1 de oxígeno + 1 de vacío (×2) 2 de oxígeno + 1 de aire + 2 de vacío (×8)
Sistema eléctrico	Sistema general del hospital	Aumento de tomas y potencia + conexión a generador alternativo
Puestos de trabajo	2 ordenadores	4 ordenadores + telemetría
Respiradores	Ninguno	Ventiladores S 1100® (×4) Aeonmed VG70® (×4) Draguer V680® (×10) Puritan Benett®
Monitores	Nellcor (X4)	Philips Intellivue MP5® (×11)
Desfibrilador	Ninguno	Lifepak 20e®
Enfermeras	3*	23†
Auxiliares	2*	16†

*Repartidas en doble turno de mañana y tarde.
†La distribución por turnos es de cuatro enfermeras en el de mañana, tres en el de tarde y tres en el de noche, de lunes a viernes. Los sábados, domingos y festivos son tres por turno. Las auxiliares de enfermería son siempre tres por turno.

Posibles sesgos

Se trata de un trabajo retrospectivo y, por tanto, parte de los datos del proceso y sus costes pueden perderse.

Las entrevistas se realizaron a trabajadores de la unidad creada y como entrevista directa, por lo que parte de los aspectos negativos o deficiencias pueden no haber sido consideradas. Para disminuir los sesgos, los entrevistados fueron informados de que los datos y las opiniones que aportaron se manejarían de manera anónima.

Es probable que los resultados obtenidos no puedan ser extrapolados a otros centros, por la idiosincrasia de cada uno (validación externa).

Tamaño del estudio

Para la realización del presente estudio no se ha precisado cálculo de tamaño muestral, pues se han incluido todos los pacientes atendidos en el periodo considerado. Así mismo, se han incorporado todas las modificaciones realizadas.

Métodos estadísticos

Se recopilaron los datos obtenidos de las encuestas realizadas a las diferentes partes implicadas en la transformación. Una vez incorporados, como parte del análisis descriptivo, se realizó una distribución de variables. Dependiendo del tipo de variable, el análisis se presenta como proporción, tasa, razón o promedio. Debido a ello, no se han objetivado datos faltantes en las variables analizadas.

Resultados

De manera previa al inicio de la pandemia, la UCMA del HUG, a fecha 15-03-2020, contaba con 12 camas y un sillón de tratamiento, una sala para familiares y vestuarios. Cada una de las camas disponía del equipamiento pormenorizado en la tabla 1.

La UCI del HUG, a fecha 15-03-2020, contaba con 14 camas, de las cuales estaban operativas 10. El equipamiento del que se disponía se describe en la tabla 2.

Con el inicio de la primera ola de la pandemia de COVID-19 y el aumento exponencial de pacientes con necesidad de cuidados críticos, la GAI del HUG decidió utilizar de manera rápida la UCMA como UCI. Los primeros pacientes fueron recibidos el 20-03-2020, iniciándose aquí la primera etapa del estudio.

Para llevar a cabo esta adaptación inicial se utilizaron respiradores de la URPA, de los quirófanos y de la atención prehospitalaria, consiguiendo en el momento de máxima ocupación un total de 44 pacientes sometidos a ventilación mecánica.

Tabla 2. Equipamiento de la unidad de cuidados intensivos (UCI) inicial

Equipamiento	UCI inicial (15-03-2020)
Camas	10
Tomas	2 de oxígeno + 1 de aire + 2 de vacío (×10)
Respiradores	Draguer Evita XL® (×2) Draguer Evita 2® (×2) Draguer Evita 4® (×2) Draguer Infinity® Servo I® (×4) Philips V680® (×2)
Monitores	Philips Intellivue® (×14)
Enfermeras	33*
Auxiliares	23*

*La distribución por turnos es de cuatro enfermeras en el de mañana, tres en el de tarde y tres en el de noche, de lunes a viernes. Los sábados, domingos y festivos son tres por turno. Las auxiliares de enfermería son siempre tres por turno.

El número total de pacientes atendidos durante el periodo de estudio se describe con detalle en la tabla 3, desglosados por meses y servicios. Como se puede objetivar, el número de estancias ganadas que se consiguió con la adaptación inicial de la UCMA en UCI fue de 153. Ninguno de los pacientes fue excluido o no participó en el estudio.

El día 11-05-2020, debido a la reducción del número de pacientes con necesidad de cuidados críticos, se procedió a cerrar la unidad y se recuperó su actividad como UCMA hasta el 31-08-2020.

La segunda fase del estudio comienza tras la primera ola de la pandemia. La dirección de la GAI de Guadalajara decidió someter a la UCMA del hospital a las adaptaciones necesarias para que pudiera ser transformada en UCI de manera rápida y eficaz en caso de una segunda ola. La reforma se llevó a cabo durante los meses de julio y agosto de 2020, y debido a la necesidad nuevamente de ampliación de camas por el aumento exponencial de la incidencia de pacientes COVID-19 positivos críticos tras el verano, se procedió a la reapertura de la UCMA como UCI el 01-09-2020.

Las modificaciones llevadas a cabo se pormenorizan en la tabla 1. Cabe destacar la aportación realizada por la Reserva Estratégica de Toledo, que incluyó ocho respiradores adicionales, la modificación de la instalación eléctrica y la creación de dos puestos de diálisis.

Por tanto, tras la reforma realizada, se disponía en su conjunto de 24 camas de críticos, sin tener en cuenta en ningún momento los puestos de la URPA y los quirófanos, los cuales fueron ocupados de manera íntegra en la primera ola de la pandemia.

Los pacientes atendidos en esta segunda fase de utilización de la UCMA como UCI (hasta el 31-12-2020) se detallan en la tabla 4. Las estancias ganadas durante este segundo periodo ascienden a 602. En esta segunda fase tampoco se realizó la exclusión de ningún paciente. Con todo lo anterior, el total de estancias ganadas desde el 01-03-2020 hasta el 31-12-2020 conseguido por la transformación de la UCMA en UCI fue de 755.

Por otro lado, como parte de la reforma realizada en el verano de 2020, la sala de espera de acompañantes de la UCMA se adaptó para ser utilizada como hospital de día, debido a que la ubicación antigua se destinó a pacientes no candidatos a UCI para ser manejados con ventilación mecánica no invasiva. Se habilitaron cuatro de los seis puestos de tratamiento que existían previamente para mantener la distancia adecuada de seguridad. En dichos puestos de tratamiento se administraba medicación de todos los servicios del hospital, a excepción de oncología, hematología y geriatría, por la complejidad de estos y de los pacientes.

Se realizó una encuesta de mejora a cinco miembros de la nueva UCI, cuyos resultados se exponen en la tabla 5.

Discusión

La transformación de la UCMA en UCI en el HUG durante la pandemia de COVID-19 supuso la obtención de 755 estancias en dos periodos: 153 en el primero, con la transformación provisional, y 602 en el segundo, con la transformación definitiva. Dicho aumento de estancias ganadas supuso, fundamentalmente en el segundo periodo, el mantenimiento funcional de la URPA y de los quirófanos, evitando el cese de la actividad quirúrgica y un aumento desmesurado de las listas de espera.

Aunque se han incluido todos los pacientes atendidos en el periodo indicado, dado que se trata de un estudio retrospectivo puede haberse perdido parte de los datos del proceso. Por otro lado, las entrevistas se realizaron a una muestra de los trabajadores de la unidad creada y bajo entrevista directa, por lo que algunos aspectos negativos o deficiencias pueden no haber sido considerados. Para disminuir los sesgos, los entrevistados fueron informados de que los datos y las opiniones que aportaron se manejarían de manera anónima. Así mismo, es probable que los resultados obtenidos no puedan ser extrapolados a otros centros, por la idiosincrasia de cada uno (validación externa).

Tabla 3. Resumen de los pacientes atendidos en la unidad de cirugía mayor ambulatoria (UCMA) transformada en unidad de cuidados intensivos (UCI) de manera temporal en la primera ola de la pandemia de COVID-19 (marzo-mayo de 2020)

Marzo	Ingresos	Traslados recibidos	Traslados emitidos	Estancias	*Exitus*	Abril	Ingresos	Traslados recibidos	Traslados emitidos	Estancias	*Exitus*	Mayo	Ingresos	Traslados recibidos	Traslados emitidos	Estancias	*Exitus*
Cardiología	0	0	0	0	0	Cardiología	0	0	0	0	0	Cardiología	0	0	0	0	0
Cirugía general	0	0	0	0	0	Cirugía general	0	0	0	0	0	Cirugía general	0	0	0	0	0
Cirugía maxilofacial	0	0	0	0	0	Cirugía maxilofacial	0	0	0	0	0	Cirugía maxilofacial	0	0	0	0	0
Cirugía plástica	0	0	0	0	0	Cirugía plástica	0	0	0	0	0	Cirugía plástica	0	0	0	0	0
Cirugía vascular	0	0	0	0	0	Cirugía vascular	0	0	0	0	0	Cirugía vascular	0	0	0	0	0
Dermatología	0	0	0	0	0	Dermatología	0	0	0	0	0	Dermatología	0	0	0	0	0
Digestivo	0	0	0	0	0	Digestivo	0	0	0	0	0	Digestivo	0	0	0	0	0
Endocrinología	0	0	0	0	0	Endocrinología	0	0	0	0	0	Endocrinología	0	0	0	0	0
G. agudos	1	12	3	52	0	G. agudos	0	0	1	21	0	G. agudos	0	0	0	0	0
Ginecología	0	0	0	0	0	Ginecología	0	0	0	0	0	Ginecología	0	0	0	0	0
Hematología	0	0	0	0	0	Hematología	0	0	0	0	0	Hematología	0	0	0	0	0
Medicina interna	1	4	4	9	1	Medicina interna	1	0	0	1	0	Medicina interna	0	0	0	0	0
Nefrología	0	0	0	0	0	Nefrología	0	0	0	0	0	Nefrología	0	0	0	0	0
Neonatología	0	0	0	0	0	Neonatología	0	0	0	0	0	Neonatología	0	0	0	0	0
Neurología	0	0	0	0	0	Neurología	0	0	0	0	0	Neurología	0	0	0	0	0
Oftalmología	0	0	0	0	0	Oftalmología	0	0	0	0	0	Oftalmología	0	0	0	0	0
Oncología	0	0	0	0	0	Oncología	0	0	0	0	0	Oncología	0	0	0	0	0
Otorrinola ringología	0	0	0	0	0	Otorrinola ringología	0	0	0	0	0	Otorrinola ringología	0	0	0	0	0
Pediatría	0	0	0	0	0	Pediatría	0	0	0	0	0	Pediatría	0	0	0	0	0

(Continúa)

Tabla 3. Resumen de los pacientes atendidos en la unidad de cirugía mayor ambulatoria (UCMA) transformada en unidad de cuidados intensivos (UCI) de manera temporal en la primera ola de la pandemia de COVID-19 (marzo-mayo de 2020) ***(continuación)***

Marzo	Ingresos	Traslados recibidos	Traslados emitidos	Estancias	*Exitus*	Abril	Ingresos	Traslados recibidos	Traslados emitidos	Estancias	*Exitus*	Mayo	Ingresos	Traslados recibidos	Traslados emitidos	Estancias	*Exitus*
Psiquiatría	0	0	0	0	0	Psiquiatría	0	0	0	0	0	Psiquiatría	0	0	0	0	0
Neumología	4	6	1	17	0	Neumología	0	0	0	0	0	Neumología	0	0	0	0	0
Reumatología	0	0	0	0	0	Reumatología	0	0	0	0	0	Reumatología	0	0	0	0	0
Tocología	0	0	0	0	0	Tocología	0	0	0	0	0	Tocología	0	0	0	0	0
Traumatología	0	0	0	0	0	Traumatología	0	0	0	0	0	Traumatología	0	0	0	0	0
Urología	0	0	0	0	0	Urología	0	0	0	0	0	Urología	0	0	0	0	0
UCI	0	6	7	12	0	UCI	0	2	4	38	0	UCI	0	3	3	3	0
Totales	6	28	15	90	1	Totales	1	2	5	60	0	Totales	0	3	3	3	0

Tabla 4. Resumen de los pacientes atendidos en la unidad de cirugía mayor ambulatoria (UCMA) transformada en unidad de cuidados intensivos (UCI) tras la reforma (septiembre-diciembre de 2020)

Septiembre	Ingresos	Traslados recibidos	Traslados emitidos	Estancias	*Exitus*	Octubre	Ingresos	Traslados recibidos	Traslados emitidos	Estancias	*Exitus*
Cardiología	0	0	1	0	0	Cardiología	0	0	0	0	0
Cirugía general	0	0	0	0	0	Cirugía general	0	1	0	0	0
Cirugía maxilofacial	0	0	0	0	0	Cirugía maxilofacial	0	0	0	0	0
Cirugía plástica	0	0	0	0	0	Cirugía plástica	0	0	0	0	0
Cirugía vascular	0	1	0	0	0	Cirugía vascular	0	1	1	0	0
Dermatología	0	0	0	0	0	Dermatología	0	0	0	0	0
Digestivo	0	0	0	0	0	Digestivo	0	0	0	0	0
Endocrinología	0	0	0	0	0	Endocrinología	0	0	0	0	0
G. agudos	0	0	0	0	0	G. agudos	0	0	0	0	0
Ginecología	0	0	0	0	0	Ginecología	0	0	0	0	0

(Continúa)

Tabla 4. Resumen de los pacientes atendidos en la unidad de cirugía mayor ambulatoria (UCMA) transformada en unidad de cuidados intensivos (UCI) tras la reforma (septiembre-diciembre de 2020) *(continuación)*

Septiembre	Ingresos	Traslados recibidos	Traslados emitidos	Estancias	*Exitus*	Octubre	Ingresos	Traslados recibidos	Traslados emitidos	Estancias	*Exitus*
Hematología	0	0	0	0	0	Hematología	0	0	0	0	0
Medicina interna	0	0	0	0	1	Medicina interna	0	0	0	0	0
Nefrología	0	0	0	0	0	Nefrología	0	0	0	0	0
Neonatología	0	0	0	0	0	Neonatología	0	0	0	0	0
Neurología	0	0	0	0	0	Neurología	0	0	0	0	0
Oftalmología	0	0	0	0	0	Oftalmología	0	0	0	0	0
Oncología	0	0	0	0	0	Oncología	0	0	0	0	0
Otorrinola ringología	0	0	0	0	0	Otorrinola ringología	0	0	0	0	0
Pediatría	0	0	0	0	0	Pediatría	0	0	0	0	0
Psiquiatría	0	0	0	0	0	Psiquiatría	0	0	0	0	0
Neumología	0	0	0	0	0	Neumología	0	0	0	0	0
Reumatología	0	0	0	0	0	Reumatología	0	0	0	0	0
Tocología	0	0	0	0	0	Tocología	0	0	0	0	0
Traumatología	0	0	0	0	0	Traumatología	0	0	0	0	0
Urología	0	0	0	0	0	Urología	0	0	0	0	0
UCI	17	9	18	104	0	UCI	19	6	30	128	0
Totales	17	10	19	104	1	Totales	19	8	31	128	0
Noviembre	**Ingresos**	**Traslados recibidos**	**Traslados emitidos**	**Estancias**	***Exitus***	**Diciembre**	**Ingresos**	**Traslados recibidos**	**Traslados emitidos**	**Estancias**	***Exitus***
Cardiología	0	0	0	0	0	Cardiología	0	0	0	0	0
Cirugía general	0	0	0	0	0	Cirugía general	0	0	0	0	0
Cirugía maxilofacial	0	0	0	0	0	Cirugía maxilofacial	0	0	0	0	0
Cirugía plástica	0	0	0	0	0	Cirugía plástica	0	0	0	0	0

(Continúa)

Tabla 4. Resumen de los pacientes atendidos en la unidad de cirugía mayor ambulatoria (UCMA) transformada en unidad de cuidados intensivos (UCI) tras la reforma (septiembre-diciembre de 2020) *(continuación)*

Noviembre	Ingresos	Traslados recibidos	Traslados emitidos	Estancias	*Exitus*	Octubre	Ingresos	Traslados recibidos	Traslados emitidos	Estancias	*Exitus*
Cirugía vascular	0	1	0	0	0	Cirugía Vascular	0	0	0	0	0
Dermatología	0	0	0	0	0	Dermatología	0	0	0	0	0
Digestivo	0	1	0	0	0	Digestivo	0	0	0	0	0
Endocrinología	0	0	0	0	0	Endocrinología	0	0	0	0	0
G. agudos	0	0	0	0	0	G. Agudos	0	0	0	0	0
Ginecología	0	0	0	0	0	Ginecología	0	0	0	0	0
Hematología	0	0	0	0	0	Hematología	0	0	0	0	0
Medicina interna	0	0	0	0	6	Medicina Interna	0	0	1	0	5
Nefrología	0	0	0	0	0	Nefrología	0	0	0	0	0
Neonatología	0	0	0	0	0	Neonatología	0	0	0	0	0
Neurología	0	0	0	0	0	Neurología	0	0	0	0	0
Oftalmología	0	0	0	0	0	Oftalmología	0	0	0	0	0
Oncología	0	0	0	0	0	Oncología	0	0	0	0	0
Otorrinola ringología	0	0	0	0	0	O.R.L.	0	0	0	0	0
Pediatría	0	0	0	0	0	Pediatría	0	0	0	0	0
Psiquiatría	0	0	0	0	0	Psiquiatría	0	0	0	0	0
Neumología	0	0	0	0	0	Neumología	0	1	0	0	1
Reumatología	0	0	0	0	0	Reumatología	0	0	0	0	0
Tocología	0	0	0	0	0	Tocología	0	0	0	0	0
Traumatología	0	0	0	0	0	Traumatología	0	0	0	0	0
Urología	0	0	0	0	0	Urología	0	0	0	0	0
UCI	25	16	30	171	0	U.C.I.	33	11	37	199	0
Totales	25	18	30	171	6	Totales	33	12	38	199	6

Tabla 5. Resultados de la encuesta para mejora

Los nuevos monitores adquiridos para las 10 nuevas camas de la antigua unidad de cirugía mayor ambulatoria son pequeños y fijos. Para una correcta visualización, lo recomendable es que al menos sean de 19 pulgadas.
Se requeriría, para un funcionamiento óptimo, la disposición de al menos un 10-20% extra de monitores y respiradores.
Con la nueva ubicación, debería diseñarse una zona de lavado quirúrgico adecuada para la realización de procedimientos estériles, como canalización de vías.
Debería valorarse un aumento de las camas de diálisis disponibles (solo hay dos adaptadas).
La zona de almacenaje habilitada no es lo suficientemente amplia para todo el material necesario.
Para mantener unas correctas medidas de seguridad entre pacientes ingresados en una unidad de cuidados intensivos se debe mantener una separación adecuada entre ellos o bien tenerlos en boxes debidamente aislados. Por la necesidad de espacio y de aumentar el número de camas, esta separación no se cumple en la adaptación de la unidad de cirugía mayor ambulatoria, pero debería valorarse una vez pasada la situación crítica.
Mejorar las zonas de aislamiento entre pacientes.

Conclusiones

A raíz de los datos expuestos, interpretamos que la transformación de una UCMA en una UCI en situación de crisis sanitaria permite, por un lado, ofrecer cobertura a la población en mayor medida, y por otro lado, con dicho aumento de cobertura se consigue demorar la ocupación de las URPA y los quirófanos con pacientes críticos. Con ello es posible el mantenimiento de la actividad quirúrgica y, en consecuencia, la disminución de la lista de espera.

Además, una vez realizada la adaptación, en caso de producirse un aumento de las necesidades sanitarias por otro evento se podría volver a hacer el cambio de una manera rápida, eficaz y eficiente, implicando un aumento de las camas de UCI y el mantenimiento de la actividad quirúrgica.

Financiamiento

Los autores declaran no haber recibido financiamiento para este estudio.

Conflicto de intereses

Los autores declaran no tener conflicto de intereses.

Consideraciones éticas

Protección de personas y animales. Los autores declaran que para esta investigación no se han realizado experimentos en seres humanos ni en animales.

Confidencialidad, consentimiento informado y aprobación ética. El estudio no involucra datos personales de pacientes ni requiere aprobación ética. No se aplican las guías SAGER.

Declaración sobre el uso de inteligencia artificial. Los autores declaran que no utilizaron ningún tipo de inteligencia artificial generativa para la redacción de este manuscrito.

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ORIGINAL ARTICLE

Long-term clinical and radiological outcomes after valgus extension osteotomy and tectoplasty for advanced Legg-Calve-Perthes disease

Resultados clínicos y radiológicos a largo plazo después de osteotomía y tectoplastia de extensión en valgo para la enfermedad de Legg-Calve-Perthes avanzada

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Abstract

Objective: *We evaluated the long-term clinical and radiographic outcomes of femoral valgus extension osteotomy combined tectoplasty in Herring group C Perthes disease patients with hinge abduction.* **Method:** *A total of 13 patients underwent this procedure between 2002 and 2009. In this retrospective study, all patients were classified as Herring group C. The mean age at diagnosis was 8.6 ± 2.2 years. The mean age at surgery was 9.3 ± 1.7 years. The mean age at the most recent follow-up was 23.3 years (range 19-29 years). All patients were followed at least 11.5 years after surgery.* **Results***: All patients had hinge abduction deformity preoperatively. The mean Harris hip score improved from 70.23 ± 10.43 points preoperatively to 91.76 ± 7.25 points at the final follow-up. No patient had a limping gait at the final follow-up. The pre-operative visual analog scale score was 7.84 ± 0.22, and the last follow-up was 1.03 ± 0.25 ($p < 0.001$). According to the Stulberg classification, good radiological outcomes were obtained in 7 hips, whereas fair or poor outcomes were noted in 6 hips.* **Conclusions:** *In severely affected hips of Perthes, patients who underwent femoral valgus extension osteotomy combined tectoplasty revealed satisfactory long-term clinical and radiological outcomes.*

Keywords: *Tectoplasty. Femoral valgus extension osteotomy. Hinge abduction. Herring group C.*

Resumen

Objetivo: *Evaluar los resultados clínicos y radiográficos a largo plazo de la tectoplastia combinada con osteotomía de extensión en valgo femoral en pacientes con enfermedad de Perthes del grupo C de Herring con abducción en bisagra.* **Método:** *Entre 2002 y 2009 se sometieron a este procedimiento 13 pacientes. En este estudio retrospectivo, todos los pacientes fueron clasificados como Herring C. La edad media en el momento del diagnóstico fue de 8.6 años. La edad media en el momento de la cirugía fue de 9.3 años. La edad media en el seguimiento más reciente fue de 23.3 años.* **Resultados:** *Todos los pacientes tenían deformidad en abducción en bisagra preoperatoriamente. La puntuación media de cadera de Harris mejoró de 70.23 puntos antes de la operación a 91.76 puntos en el seguimiento final. La puntuación en la EVA preoperatoria fue de 7.84 y en el último seguimiento fue de 1.03. Según la clasificación de Stulberg, se obtuvieron buenos resultados radiológicos en 7 caderas, mientras que se observaron resultados regulares o malos en 6 caderas.* **Conclusiones:** *En caderas gravemente afectadas de Perthes, los pacientes sometidos a osteotomía de extensión femoral en valgo y tectoplastia combinada revelaron resultados satisfactorios.*

Palabras clave: *Tectoplastia. Osteotomía de extensión en valgo femoral. Abducción en bisagra. Herring grupo C.*

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Introduction

Perthes disease impaired vascularization in the femoral head and may cause incongruence of the hip joint during the hip remodeling period[1]. Hip joint osteonecrosis leads to various deformities of the hip joint, and in later life, secondary end-stage degenerative osteoarthritis may occur[2]. Despite numerous studies, an algorithm could not be established for this clinical entity.

Maintaining hip containment during the disease reduces the deforming forces on the femoral head. During the disease process, the shape of the femoral head and its congruency with the acetabulum affect the prognosis. The "Biological plasticity" concept allows the acetabulum to serve as a mold to the femoral head during the healing process. The treatment goal is to obtain a congruent hip joint with a good range of movement by achieving a spherical femoral head and a well-shaped acetabulum at skeletal maturity. The risk of developing coxarthrosis in the joint may be reduced or delayed[3,4].

In the late stage of LCP (Legg-Calve-Perthes) disease, the anterolateral deformed femoral head protrudes outside the acetabulum, and during hip abduction, impingement occurs. Hinge abduction causes incongruity of the hip joint and restricts hip movement. Various surgical procedures ranging from cheilectomy to shelf acetabuloplasty for surgical containment have been described to overcome "hinge abduction." In the presence of severe femoral head deformity, valgus extension osteotomy may be required as a salvage procedure because it overcomes the hinging and creates a more congruent surface of the femoral head within the acetabulum[5,6]. Tectoplasty provides an extra-articular weight-bearing surface and a more congruent acetabular roof[6].

The basis of treatment in Perthes disease is to provide and maintain containment in the hip joint. According to the lateral colon classification, Hering group C patients have a poor prognosis. Femoral head deformation and decreased acetabular depth cause containment problems and create discongruence in the hip joint. In case of discongruence in the hip joint, remodeling is impaired. In the combined treatment we performed femoral valgus extension osteotomy to overcome the hinged abduction while the anterolateral part of the femoral head impinges during abduction. The aim of tectoplasty is to create an extra-articular load-bearing surface area on the acetabular side.

The purpose of this study was to evaluate the long-term clinical and radiographic outcomes of femoral valgus extension osteotomy combined with tectoplasty in severe LCP patients. In a previous study, we evaluated the short-term clinical and radiographic outcomes of this technique in 11 Herring group C LCP patients[7].

Method

The study had institutional review board approval (reference number 2020/170). We evaluated retrospectively the long-term clinical and radiographic outcomes of 13 LCP patients who underwent femoral valgus extension osteotomy combined with tectoplasty between 2002 and 2009. In our study, all patients were diagnosed with LCP and classified according to lateral pillar classification as Herring group C. All patients had intraoperative radiographic and clinically diagnosed hinge abduction.

The study group of 13 patients analyzed consisted of one female and 12 males; in eight cases, the right hip was affected, and in five, the left (Table 1). The mean age at diagnosis was 8.6 ± 2.2 years. The mean age at surgery was 9.3 ± 1.7 years. The mean age at the most recent follow-up was 23.3 years. All patients were followed at least 11.5 years after surgery (mean 15.5 ± 3.3 years). Clinical assessments of all patients were made in terms of pain, range of hip motion, fixed hip contractures, leg length discrepancy, and presence of limp. All patients were examined preoperatively under general anesthesia to confirm the presence of hinge abduction. With the presence of hinge abduction femoral valgus extension, osteotomy was performed in all the patients in our study. A lateral approach was performed to the proximal femur. The femoral neck was prepared for an angled blade plate or K wires. A transversal cut between the femoral shaft and lesser trochanter was performed, and an extension and valgus were built into the osteotomy. The correction angles required for adequate femoral coverage, were determined by comparison of the contralateral side. After femoral valgus extension osteotomy, fluoroscopic evaluation was performed intraoperatively. Tectoplasty procedure was added to patients who were detected to have inadequate femoral head coverage. The tectoplasty procedure aims to enlarge the weight-bearing area at the hip joint and obtain a more congruent joint. It was performed in a supine position by an anterior Smith-Peterson incision with the technique described by Saito et al.[8]. In this

Table 1. Patients demographics

Number of patients	13
Number of hips	13
Age at diagnosis (years)*	8.6 ± 2.2
Age at surgery (years)*	9.3 ± 1.7
Gender (M/F)	12/1
Involved site (R/L)	(8/5)
Length of follow-up (years)*	15.5 ± 3.3
Length of post-op (months)*	188.4 ± 34.6
Age at last follow-up (years)*	15.5 ± 3.3
Lateral pillar classification (A/B/B/C/C)	-/-/-/13
Patients with Hinge abduction	13

*The values are given as the mean, with the standard deviation in parentheses. M: male; F: female; R: right; L: left.

technique, care was taken not to damage the lateral acetabular growth cartilage. All surgical procedures were led by a single experienced pediatric orthopedic surgeon (C, B). Patients were mobilized non-weight bearing with crutches to the operated side until graft healing was observed. After graft healing and osteotomy union were observed radiologically, partial weight-bearing was permitted, and commencing full weight-bearing began at 3-4 months.

All the patients had pre-operative, early post-operative, and final follow-up clinical and radiographic evaluations (Fig. 1). The radiographic examination included an anteroposterior view of the pelvis in neutral and frog-leg position. Pre-operative staging and severity of disease were determined using modified lateral pillar Herring classification[9]. These subjective assessments were carried out independently by two of the authors (MK and ME-B). The radiographic parameters included Center-Edge angle (CE angle), Sharp angle, femoral head size ratio, neck shaft angle, acetabular depth width index, caput index, subluxation ratio, femoral head coverage ratio, and femoral head extrusion index. Osteoarthritic changes were evaluated using the Tönnis classification[10]. At the final follow-up, the radiographic outcome was assessed using the Stulberg classification to evaluate femoral head sphericity and hip remodeling[11]. The spherical femoral head (Stulberg 1 or 2) was rated as good, the ovoid femoral head (Stulberg 3) as moderate, and the flat femoral head (Stulberg 4 or 5) was rated as poor outcomes. The clinical assessment includes; the hip range of motion, limb-length discrepancy, the presence of a Trendelenburg sign, and a visual analog scale (VAS) (ranging from 0 to 10). All participants completed the Harris hip scoring system (maximum score, 100 points). A total Harris hip score below 80 points was considered a poor or fair result, and 80-100 was a good or excellent result[12].

Statistical analysis

The statistical analysis was performed using Statistical Package for Social Sciences (SPSS) Version 22.0 (SPSS, Chicago, IL) statistical analysis software. Normal distribution was defined by the Shapiro-Wilk test. All values were calculated as the mean and the standard deviation. The pre-operative and post-operative comparisons were performed using repeated measures analysis of variance. Data were analyzed for statistical significance using the paired t-test, and $p < 0.05$ was considered statistically significant. Spearman correlation analysis was conducted to analyze the pre-operative factors that were strongly associated with patient outcomes. Patients who were ≤ 8 years old at the time of diagnosis were compared with those who were > 8 years old. Harris hip score and the Stulberg classification were used to determine patient outcomes.

Results

All children presented with a painful limping gait preoperatively. At the time of surgery, all hips were classified according to lateral pillar classification as Herring group C. The mean Harris hip score improved from 70.23 ± 10.43 preoperatively to 91.76 ± 7.25 points at the final follow-up. The mean leg length discrepancy preoperatively was 1.46 ± 0.51 cm and after skeletal maturity at the last follow-up, was 0.53 ± 0.59 cm ($p < 0.001$). No patient had a limping gait or Trendelenburg sign at the final follow-up. The mean last follow-up hip flexion was 122.30° ± 11.65°. There were no significant complications or need for additional surgery. The pre-operative VAS score was 7.84 ± 0.22, and the last follow-up VAS score was 1.03 ± 0.25 ($p < 0.001$).

Follow-up radiographs were analyzed for 13 patients (13 hips) (Table 2). According to the Stulberg classification, good radiological outcomes were obtained in seven hips (seven hips were class 2), whereas fair or poor outcomes were noted in six hips (four hips were

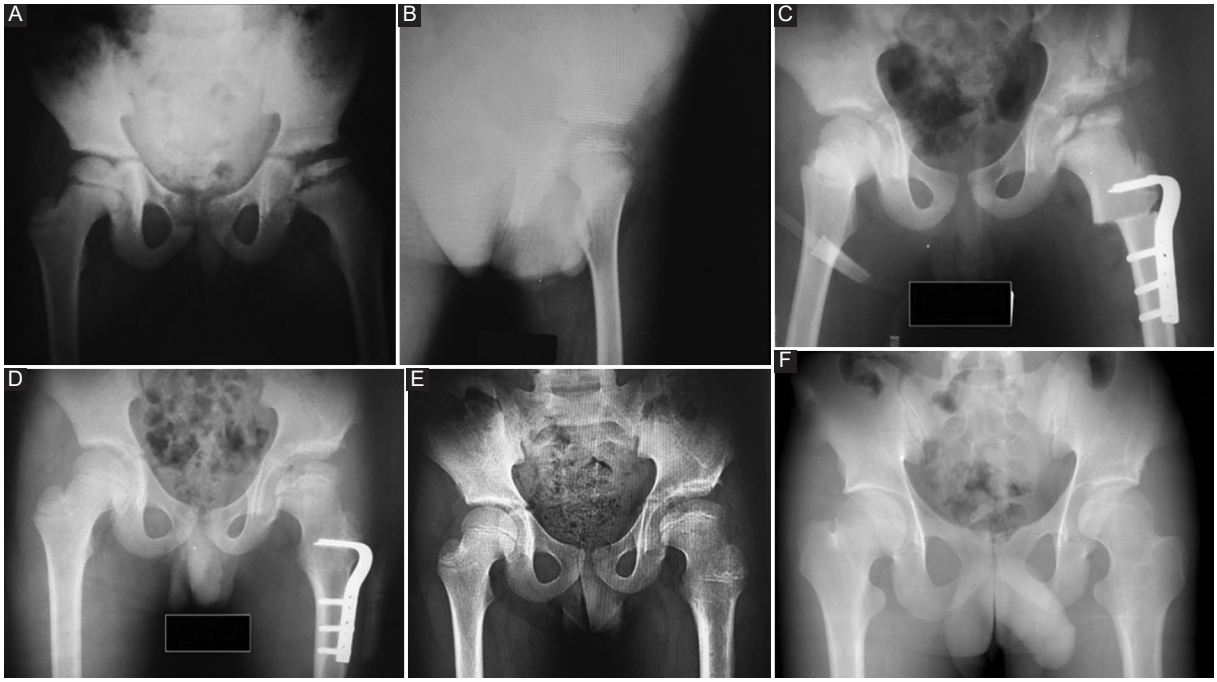

Figure 1. *Plain radiographs of an 11-year-old boy following femoral valgus extension osteotomy combined tectoplasty.* **A:** *pre-operative antero-posterior radiograph. Herring group C Perthes. Femoral head subluxation and flattening* **B:** *pre-operative lateral radiograph* **C:** *early post-operative anterior-posterior radiograph* **D:** *post-operative 1-year anterior-posterior radiograph* **E:** *post-operative 4-years anterior-posterior radiograph* **F:** *last follow-up post-operative anterior-posterior radiograph. There is good and lasting coverage with satisfaction of the femoral head.*

Table 2. Clinical outcomes according to age at diagnosis

Measure	Age at diagnosis		p
	≤ 8 years (n = 5)	> 8 years (n = 8)	
Stulberg classification			
1 or 2	4	2	0.159*
3, 4 or 5	1	5	
Last follow-up Harris hip score			
≥ 80 points	4	7	0.742*
< 80 points	1	1	
Tönnis grade			
0 or 1	3	3	0.471*
2 or 3	2	5	

*No significant difference between ≤ 8 and > 8 (p > 0.05).

class 3 and two hips class 4). Six hips had mild degenerative changes (Tönis grade 1), five had moderate (Tönis grade 2), and two had severe changes (Tönis grade 3). The mean subluxation ratio was 1.66 preoperatively and 1.23 at the last follow-up (< 0.001). The mean femoral head coverage ratio was 67.53% preoperatively and 84.61% at the last follow-up (= 0.009). The mean femoral head size ratio was 1.1 preoperatively and 1.20 at the last follow-up (p = 0.077). Sharp angle decreased from 46.76 to 35.77 (p < 0.001). Centre edge angle increased from 14.30 to 40.07 (p < 0.001). It was no significant change in neck-shaft angle (p = 0.477). The acetabular depth-to-width index improved from 272 to 308 (p = 0.008).

Patients who were ≤ 8 years old at the time of diagnosis were more likely to have a lower Stulberg class; however, the differences were not significant (Table 3). There was no significant relation between age at diagnosis and last follow-up Harris hip score and last follow-up Tönis classification. There were no cases of failure of fixation, and all osteotomies went on to radiologically proven union. There were no significant deep infections.

Discussion

We evaluated the long-term clinical and radiographic outcomes of femoral extension valgus osteotomy combined tectoplasty as a means of surgical containment for Herring group C LCP patients with hinge abduction. In our study, we aimed to provide a spherical femoral head within a well-shaped acetabulum in the final process. Even in the case of collapse and deformation, the femoral head tends to be

Table 3. Comparison of pre-operative and post-operative radiological outcomes

Measure	Pre-operative		1 year post-operative		Last follow-up		p
	Mean	SD	Mean	SD	Mean	SD	
Subluxation ratio	1.66	0.33	1.47	0.26	1.23	0.12	< 0.001*
Femoral head coverage ratio (%)	67.53	11.68	100.30	6.27	84.61	11.75	= 0.009*
Femoral head size ratio	1.13	0.11	1.23	0.18	1.20	0.13	= 0.077
Sharp angle	46.76	6.85	33.38	4.92	35.77	2.95	< 0.001*
Sharp ratio**	1.13	0.11	1.22	0.18	1.19	0.12	= 0.077
Center-Edge angle	14.30	5.21	43.23	6.33	40.07	9.38	< 0.001*
Neck shaft angle	142.61	8.55	152.46	7.63	145.38	10.16	= 0.477
Caput index	0.69	0.12	0.67	0.15	0.74	0.12	= 0.166
Acetabular depth-to-width index	0.27	0.03	0.31	0.05	0.30	0.04	= 0.008*
Femoral head extrusion index	32.13	5.66	0.57	0.22	13.38	6.23	< 0.001*
Acetabular depth-to-width ratio	272.3	31.6	315.3	50.4	308.4	39.1	= 0.008*

*Statistically significant ($p < 0.05$).
**The ratio of the Sharp angle of the affected hip versus the contralateral normal hip.
SD: standard deviation.

remodeled if it is well-contained in the cartilage[13]. All patients in our study were severely affected and had a massive femoral head involvement with lateral subluxation.

The treatment algorithm in severely affected Perthes patients is still controversial. In a multicentric prospective study, it was shown that the lateral pillar classification and age at the time of onset of the disease are strongly correlated with outcomes[13]. Some reports stated that group C hips frequently had poor outcomes unrelated to treatment[14,15]. However, in those studies, the surgically treated group received either a femoral or acetabular osteotomy, not a combination of these procedures. It was shown in a study of severely affected patients, that a femoral varus osteotomy improved the sphericity of the femoral head compared to conservative treatment[16]. Combined procedures in severely affected patients provide better congruency of the hip joint[17]. In another study, the combined procedure group obtained significantly better outcomes both clinically and radiologically in severely affected hips compared with the single procedure group[18].

Hinge abduction is the process of severe Perthes disease, causing the deformed and extruded anterolateral femoral head impingement to the lateral lip of the acetabulum during the abduction. Operative and non-operative treatments were reported to deal with this entity. Traction and bed rest, Shelf acetabuloplasty, and triple pelvic osteotomy treatment methods were performed. Another treatment method is femoral valgus extension osteotomy, which was first described by Catterall. It rotates the deformed extruded femoral head away from the lateral lip of the acetabulum, and the abnormal hinge movement aimed to get resolved. This relieves pain, reestablishes the abductor mechanism, and improves leg length. Unloading the lateral part of the femoral head and the lateral acetabular physis may produce favorable hip remodeling. We added the tectoplasty procedure to enlarge the weight-bearing surface without decreasing the volume of the acetabulum. Thus, the development of femoroacetabular impingement was prevented. A deformed femoral head and acetabulum cause an obliquity of the weight-bearing joint surface that changes the rotation center of the femoral head. As a consequence, the loading pressure in the reduced articular area increases. Osteotomies are designed to reduce the loading of the joint surface by increasing the area of the weight-bearing surface. Femoral valgus extension osteotomy stretches the superior zone of the joint capsule and its synovial membrane. It stimulates the remodeling capacity of the hip[19]. There was no other study that reported the long-term outcomes in the literature of the femoral valgus extension osteotomy combined tectoplasty procedure for hinge abduction in Herring group C perthes patients[20].

Stulberg classification has been used to evaluate the surgical clinical outcomes in the literature[21,22]. In the treatment procedure, we aimed to prevent femoral head subluxation, obtain a congruent hip joint, eliminate hip irritation, restore adequate hip movement, and relieve pain. Treatment modalities performed on patients with severely affected hips vary widely in the literature[20,23,24]. These are femoral valgus osteotomy, shelf acetabuloplasty, tectoplasty, triple pelvic osteotomy, Chiaris' pelvic osteotomy, Salter pelvic osteotomy, and a combination of them. Chang et al. evaluated the outcomes of patients with 21 severely affected hips undergoing the Staheli procedure. According to Stulberg's classification, 33.3% were good (class 1 or 2), 38.1% were fair (class 3), and 28.6% were poor and bad (class 4 or 5)[25]. In another study, the results of patients who underwent Shelf acetabuloplasty were reported as 51.8% good, 29.6% fair, and 18.6% poor[5]. Huang and Huang reported 14 patients' results who underwent triple pelvic osteotomy as good at 35.7%, moderate at 42.8%, and poor at 21.4%[26]. We performed a femoral valgus extension osteotomy combined with tectoplasty, which had not been reported in the literature before. In our study, we evaluated the clinical outcomes as 53.8% good, 30.7% moderate, and 15.3% bad. This rate is comparable to reports using other surgical procedures in severely affected hips.

In our study, the femoral head coverage ratio improved from 67.53% preoperatively to 84.61% at the last follow-up. Chang et al. performed a Shelf acetabuloplasty procedure in severely affected hips, and in this study, the femoral head coverage ratio improved from 74% preoperatively to 98% postoperatively[25]. Huang and Huang performed triple pelvic osteotomy, and improvement was observed from 66% to 101%[26]. Our long-term outcomes concluded that the procedure improves the femoral head coverage ratio and may contribute to remodeling the hip joint. Daly et al. performed Shelf acetabuloplasty and observed that the femoral head coverage ratio decreased from 83% to 75%[5]. In our study, the femoral head size ratio increased from 1.13 preoperatively to 1.19 at the last follow-up. This result can be associated with the development of coxa magna in the follow-ups. In our study, the subluxation ratio decreased from 1.66 to 1.23. Chang et al. performed Shelf acetabuloplasty, and in this study, the subluxation ratio decreased from 1.6 to 1.17[25]. It was shown that the Sharp angle in Perthes' hips is steeper than the unaffected side during the course of the disease[27]. In our study, the Sharp angle decreased from 46.76° preoperatively to 35.77°and the CE angle increased from 14.30° to 40.07°. Ghanem et al. performed Shelf acetabuloplasty in severely affected patients, and the Sharp angle decreased from 45° preoperatively to 35° postoperatively, and the CE angle increased from 12.5° to 44°[3]. In a study, it was shown that the acetabulum is wider and shallower at all stages of Perthes[27]. In our study, our results (272 increased preoperatively-308 postoperatively) show that the combined procedure had a stimulatory effect on the acetabular depth growth with the capsular tension effect.

Age at onset is considered one of the most important predictors of prognosis in perthes patients. Obtaining a spherical femoral head and establishing its congruence within the acetabulum is one of the main goals in Perthes disease treatment[28]. In our study, patients who were ≤ 8 years old at the time of diagnosis were more likely to have a lower Stulberg class, better outcomes, and lower Tönis class, but the differences were not statistically significant (Table 3).

If hinge abduction develops in LCP disease, hip containment is impaired. In this situation, valgus extension osteotomy is an effective method used as a salvage procedure. It is a procedure that reduces the uncovered femoral head into the hip joint and obstructs impingement during the abduction. One of our goals was to induce hip remodeling with this procedure, which we performed in cases where the acetabular growth capacity continued, and the triradiate cartilage was open.

The study has some limitations. The lack of a control group, the relatively small number of patients, and the retrospective study design are some limitations of our study. However, the follow-up was 15 years, which was long enough to evaluate the clinical and radiographical combined surgical procedure. In addition, this study has limited value for femoroacetabular impingement evaluation.

Many reports emphasized that severely affected hips in LCP had poor outcomes. In our study, we aimed to increase joint congruency and achieve satisfactory clinical results. It improved hip functional scores at skeletal maturity and relieved pain scores dramatically. We concluded that valgus extension osteotomy combined tectoplasty procedure in severely affected hips with hinge abduction is an effective treatment method and had satisfactory 15-year follow-up outcomes. Our method could be an alternative treatment option for late-stage Perthes patients.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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ORIGINAL ARTICLE

Utility of opportunistic CT Hounsfield Units determined bone quality in chilean women

Utilidad de las Unidades Hounsfield de tomografía computarizada oportunista para determinar la calidad ósea en mujeres chilenas

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Abstract

Objective: *To describe the correlation between Hounsfield Units in opportunistic computed tomography (CT scan) and T-score measured by dual energy X-ray absorptiometry (DXA) in the Chilean population.* **Method:** *Female patients over 50 years old with CT scan and DXA performed within 6 months. Hounsfield units (HU) were measured by circular regions-of-interest placed on axial slice image of the L1 vertebral body in the CT scan. T-score was obtained through DXA scan in L1-L4 vertebrae.* **Results:** *144 female patients were included with a mean age in years of 68.39 ± 8.75. A moderate correlation was found between T-score and HU (Pearson coefficient of 0.6, p < 0.001). The mean values of HU differ significantly between the groups of Osteoporosis (OP) (89.46 ± 20.20), Osteopenia (110.87 ± 30.74) and normal bone mineral density (154.53 ± 38.90) (p < 0.01). The area under curve for diagnostic capacity was 0.81 (95% CI 0.72-0.9). The HU thresholds for the diagnosis of OP were 101 (sensitivity 75%, specificity 75%).* **Conclusion:** *Opportunistic CT scan is a useful tool in Chilean population to perform a screening for OP.*

Keywords: *Osteoporosis. Spine. Hounsfield Units. Computed tomograo scan. DXA.*

Resumen

Objetivo: *Describir la correlación entre las Unidades Hounsfield (UH) en tomografía computarizada (TC) oportunista y el T-score medido por absorciometría de rayos X de energía dual (DXA) en población chilena.* **Método:** *Pacientes de sexo femenino mayores de 50 años con TC y DXA realizadas dentro de 6 meses. Las UH se midieron mediante regiones circulares de interés colocadas en una imagen de corte axial de L1 en loa TC. Los puntajes T-score se obtuvieron de la exploración DXA para las vértebras L1-L4.* **Resultados***: Se incluyeron 144 pacientes con una edad media de 68.39 ± 8.75 años. Se encontró una correlación moderada entre el T-score y las UH (coeficiente de Pearson: 0.6; p < 0.001). Los valores medios de UH difieren significativamente entre los grupos de osteoporosis (89.46 ± 20.20), osteopenia (110.87 ± 30.74) y densidad*

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mineral ósea normal (154.53 ± 38.90) (p < 0.01). El área bajo la curva para la capacidad diagnóstica fue de 0.81 (intervalo de confianza del 95%: 0.72-0.90). El umbrales de UH para el diagnóstico de osteoporosis fue 101 (sensibilidad del 75% y especificidad del 75%). **Conclusión:** *La TC oportunista es una herramienta útil en la población chilena para realizar tamizaje de osteoporosis.*

Palabras clave: *Osteoporosis. Columna. Unidades Hounsfield. Tomografía computarizada. Absorciometría de rayos X de energía dual.*

Introduction

Osteoporosis (OP) is a common chronic systemic disease, defined by a decrease in bone mineral density (BMD) with a progressive deterioration of bone tissue microarchitecture[1,2]. Worldwide, OP prevalence has been estimated to be 18.6% of the population, mostly in menopausal women[3]. In Chile the population pyramid is inverting as the elderly population is progressively increasing[4]. It is estimated that this demographic group will constitute an escalating proportion of patients treated for osteoporotic pathologies.

Spinal fractures are one of the most frequent OP associated pathologies, leading to an extensive source of morbimortality and resource expense. Therefore, it is essential to diagnose a decrease in BMD since it has been associated with postoperative complications[2,5,6] such as additional fractures (pedicle and vertebral compression fractures), pseudoarthrosis, instrumentation failure due to poor fixation in osteoporotic bone or spinal disease progression due to altered biomechanics[7].

Nowadays, dual-energy X-ray absorptiometry (DXA) through T-score calculator is the gold standard in the determination of BMD when diagnosing OP[8-10].

Its accuracy ranges from 85 and 99%[11]. The World Health Organization (WHO) defines normal BMD within 1 standard deviation (SD) of the young adult mean (T-score > −1); osteopenia between −1 and −2.5 SD (T-score −1-2.5); and OP as BMD −2.5 SD (T-score < 2.5)[10,12]. DXA is a relatively affordable, low radiation and easy technique[13]. Nevertheless, most of osteoporotic fractures occur in patients with values above this threshold[14], and its results may variate in patients with vertebral compression fractures, abdominal vessel calcifications, osteophytes, facet hypertrophy and spinal deformities[15].

These limitations in DXA have prompted the search for other diagnostic methods for OP. Thereby, Hounsfield units (HU) have recently emerged as an alternative to BMD estimation in computed tomography (CT). Studies have shown a 86% sensitivity and 94% specificity for OP diagnosis[16-20].

Over the last years, multiple studies have explored the validity of HU[16-20] and demonstrated an adequate moderate to high correlation (r= 0.4-0.8) between BMD and HU[10,16-20]. Most patients that will undergo spinal surgery already have a CT scan as routine preoperative planning, providing an opportunity for OP examination. Furthermore, within the healthcare context, patients commonly undergo CT scans for various clinical indications, allowing opportunistic detection of OP.

Nowadays, this correlation has not been studied within the Chilean population. Thus, this study aims to determine the correlation between HU measured by opportunistic CT and DXA measured T-score to establish threshold values in healthy patients and female patients with OP in Clinica Alemana de Santiago.

Method

Study design

Analytical observational study with retrospective recruitment. The study was approved by the scientific ethics committee of Clínica Alemana de Santiago (CAS) and Universidad Del Desarrollo faculty of medicine. Code 2021-86.

Participants

Female Patients who had undergone abdomen-pelvic or lumbar CT scan and DXA for any diagnosis in our institution, within 6 months maximum. Recruitment was continuously done in CAS from April 2017 to November 2021. Inclusion criteria were > 50-year-old female. Patients with previous spinal surgery, undergoing tumoral pathology treatment and/or previous radiotherapy, rheumatic

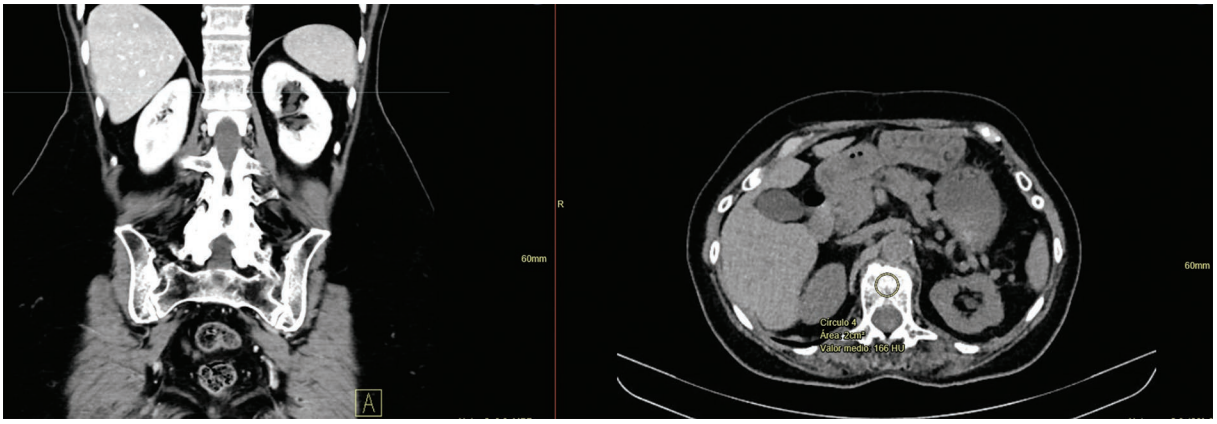

Figure 1. *Hounsfield Units (HU) measurement example. A circular region of interest (ROI) is drawn in an axial image of the L1 midbody and the software automatically calculates the average HU value for the ROI.*

disease, hematological or metabolic bone disorders other than OP, and with a diagnosis of OP receiving medical treatment were excluded.

Measurements

DXA scans were performed using the G.E model ID XA densitometer. Standard CAS method. T-score was obtained through DXA scan in L1-L4 vertebrae. Patients were classified into three groups according to their DXA-obtained T-score (WHO recommendation). T-score < −2.5 was classified as OP, t-score −2.5-1.0 was classified as osteopenia, and t-score > 1.0 classified as Normal.

Imaging studies, abdomen-pelvic and/or lumbar CT, were performed by the following equipment: Siemens brand, 128-channel Somatom Definition AS model, General Electric, 64-channel Revolution GSI model, and Toshiba brand [Canon], 320 channel Aquilion One model. CT parameters included: A 2.0 mm slice thickness and a 1 mm slice interval or a 0.75 mm slice thickness and a 0.5 mm slice interval. All subjects were in a supine position with their arms up for spiral exploration of the lumbar spine, abdomen and pelvis.

To determine HU, axial slice images with soft tissue windows at the L1 level were evaluated retrospectively using Enterprise imaging Xero viewer 8. 1. 4. 150. Soft tissue and bone windows were used to view the images. Coronal slices were used as a reference to locate L1. For measurement standardization, a 2 cm^2 region of interest was determined within the trabecular bone in the L1 vertebral body, excluding the cortical margin. Then, the attenuation was measured through HU (Fig. 1).

Data analysis

Fisher's exact test was used for categorical data. One-way analysis of variance followed by *post-hoc* analysis with Bonferroni correction was used for continuous variables in independent samples. The correlation between HU and T-score was obtained through Pearson's correlation. A 144 subjects minimum sample size was calculated for a 0.4 correlation (r) with 95% confidence level and statistical power of 80%. Sensibility, specificity, and area under curve (AUC) of the receiver operating characteristic (ROC) curve were calculated for all three bone status groups. Maximum sensitivity and specificity criterion was utilized to determine the optimal cut-off point of HU in ROC curves. $p < 0.05$ values were considered statistically significant. Statav. 16 program was used.

Results

144 female patients were included in the data analysis (Table 1). The overall mean age was 68.39 years old. All patients were divided according to T-score. 52.1% were classified as osteopenia (−2.5-−1.0), followed by 36.8% with normal BMD (> −1.0) and 11.1% patients with OP (< −2.5). The mean age in each group was 69.49, 66.7, and 68.8, respectively. No significant differences were identified among them ($p = 0.861$).

The mean HU value was 89.46 HU (SD = 20.2) for the group with OP, 110.87 HU (SD = 30.74) for the osteoporotic group, and 154.53 HU for the normal BMD group. These differences in HU values among

Table 1. Group description according to BMD

BMD			DXA	CT
Classification	n	Mean age (SD)	T-score (SD)	HU (SD)
Normal	53	66.75 (8.7)	0.3 (0.8)	154.52 (38.9)
Osteopenia	75	69.49 (8.5)	–1.72 (0.4)	110.89 (30.7)
Osteoporosis	16	68.68 (9.4)	–3.12 (0.4)	89.4 (20.2)
Total	144	68.39 (8.7)	–1.13 (1.3)	124.56 (40.6)

HU: Hounsfield Units; BMD: bone mineral density; DXA: dual-energy X-ray absorptiometry; CT: computed tomography; SD: standard deviation.

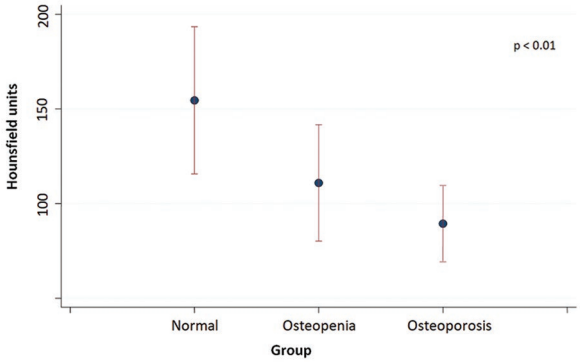

Figure 2. *Mean Hounsfield Units (HU) values (± standard deviation), stratified by normal bone mineral density, osteopenia, and osteoporosis. (According to DXA reference standard). The differences in HU among the three sub-groups are statistically significant (p < 0.01).*

groups were statistically significant (p < 0.01) (Fig. 2).

For all patients, a moderate correlation of 0.6 was found between T-score and HU. This correlation was statistically significant (p < 0.001) (Fig. 3).

HU values as diagnostic cut-off point and ROC curves

The diagnostic capacity of HU through CT to differentiate OP from no OP (osteopenia, normal BMD) with an equilibrated cut-off point was 101 HU (75% sensibility, 75% specificity), (AUC 0.81 [IC 95% 0.72-0.9]). (Fig. 4A) 118 HU was determined as the cut-off value for high-sensitivity results (89% sensibility, 59% specificity). While 80 HU was determined as the cut-off value for high-specificity results (40% sensibility, 90% specificity). 126 HU was found to be the equilibrated cut-off point to discriminate normal BMD patients from osteopenia patients (79% sensitivity, 73% specificity), (AUC 0.8102 [IC 95% 0.766-0.9001]) (Fig. 4B). 155 HU was determined as a high sensibility value (89.3% sensitivity, 48% specificity) while 102 was determined as a high specificity value (52% sensitivity, 88.7% specificity).

Discussion

Although BMD has been historically measured through DXA[10-12-21], HU as a CT attenuation measure is considered an alternative method[21,22-26]. Our findings validate its use as an option for OP opportunistic diagnosis in the Chilean population.

Within our institution, we obtained a balanced cut-off point with adequate sensibility and specificity values compared to Gold Standard, AUC 0.81 (IC 95% 0.72-0.9). Recently, a systematic review by Pinto et al.[24] determined that current data support the possibility of establishing a threshold value to diagnose OP with HU, measured through CT, with HU values ranging from 90.9 and 138.7 (IC 95% p < 0.001). Buckens et al.[27] determined a 99 HU cut-off point in L1 vertebrae to diagnose OP, with balanced sensitivity (Sensibility = 62% and Specificity = 79%). Similarly, Kim et al.[28], reported a 95 HU cut-off point for OP diagnosis (Sensitivity = 82% and Specificity = 66.4%).

Considering the validity, reproducibility, and numerous studies that report excellent interviewer variability[16,21,29], the orthopedic surgeon may use these values in preoperative planning for OP screening. Also, it does not implicate additional costs or side effects[22,26,30]. Thus, low BMD diagnosis in preoperative planning can be timely and valid[26,31,32].

Therefore, preoperative OP identification could optimize its diagnosis, perioperative management through appropriate treatment, and surgical strategies adapted to the patient's needs that would decrease postoperative complications[24,25,33].

Study strengths and limitations

To our knowledge, this is the first study reported on the Chilean population. Literature findings correspond to our results, but we suggest a new study with a larger sample to guarantee the result's credibility. Finally, the population studied was female, which could tend to differences in the cut-off points of the population general. We recommend national studies that include men and women.

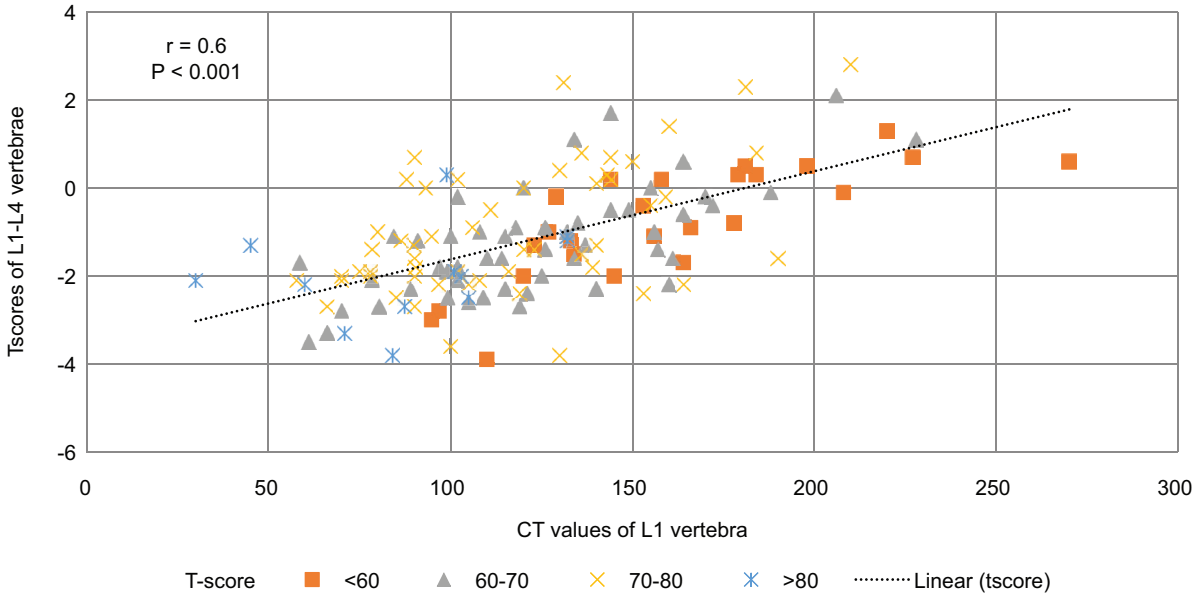

Figure 3. *Scatterplots showing correlation between mean Hounsfield Units (HU) and T-score (r = 0.6, p < 0.001) in L1-4 vertebrae, stratified into age groups: less than< 60, 60-70, 70-80 and more than 80 years.*

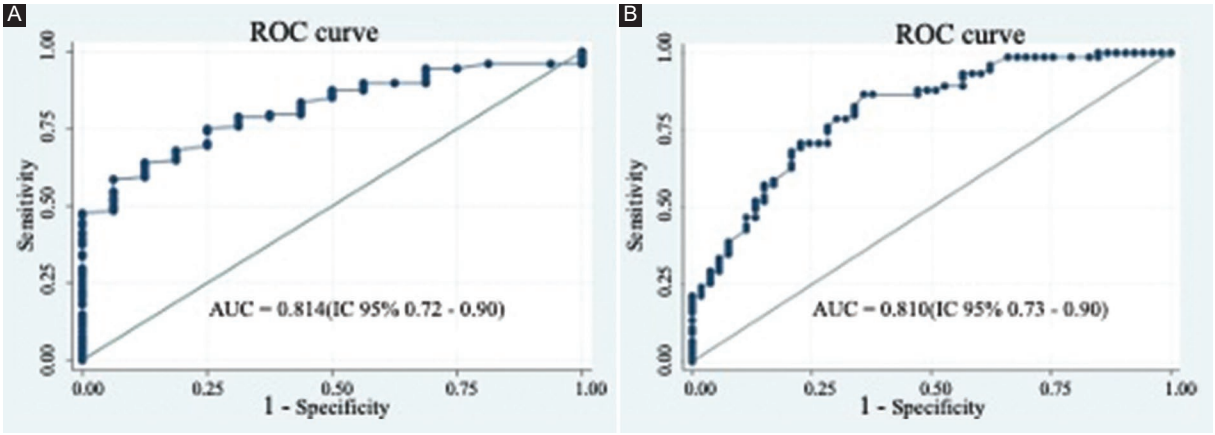

Figure 4. *Receiver operating characteristics curves for computed tomography attenuation prediction performance with hounsfield units in L1 vertebrae, compared to DXA diagnostics.* **A:** *to discriminate non osteoporotic patients (osteopenia-normal bone mineral density [BMD]) from osteoporotic patients.* **B:** *to discriminate patients with normal BMD from osteopenia patients.*

Conclusion

Even though the implementation of CT measured HU for OP diagnosis needs to be corrected for optimal results, our findings suggest that it can be applied to national clinical practice, according to evaluation purposes. Thus, recognizing patients with < 101 HU in L1 vertebrae would allow an optimal identification of OP risk, justifying referral to specialists, additional treatment, and measures in surgical planning. Meanwhile patients with > 126 HU OP diagnosis could be excluded, avoiding further studies.

Funding

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that the procedures followed complied with the ethical standards of the responsible human experimentation committee and adhered to the World Medical Association and the Declaration of Helsinki. The procedures were approved by the institutional Ethics Committee.

Confidentiality, informed consent, and ethical approval. The authors have obtained approval from the Ethics Committee for the analysis of routinely obtained and anonymized clinical data, so informed consent was not necessary. Relevant guidelines were followed.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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CASO CLÍNICO

Asociación VACTERL en una recién nacida producto de embarazo gemelar por donación de óvulos

VACTERL association in a newborn as a product of a twin pregnancy by egg donation

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Resumen

La asociación VACTERL es infrecuente en los recién nacidos, con una alta mortalidad dentro del primer año de vida. Presentamos el caso de una recién nacida producto de un embarazo gemelar asistido por donación de óvulos. Durante la reanimación se evidenció falta de orificio anal e imposibilidad al paso de la sonda orogástrica, por lo que fue ingresada en la unidad de cuidados intensivos neonatales para su estudio y tratamiento, donde se encontró atresia anal, atresia esofágica tipo III, tetralogía de Fallot y atresia duodenal. No existen reportes de esta asociación en embarazos gemelares por donación de óvulos con un gemelo afectado.

Palabras clave: *Asociación VACTERL. Malformaciones congénitas. Embarazo gemelar.*

Abstract

VACTERL association is a rare entity in newborns, with high mortality in the first year of life. We present a case of a female newborn, product of a twin pregnancy assisted by egg donation. During reanimation, absence of anal orifice and impossibility to pass the orogastric tube were evidenced, so she was admitted to the neonatal intensive care unit for study and treatment, where we found anal atresia, esophageal atresia type III, tetralogy of Fallot and duodenal atresia. There are no reports of this association in twin pregnancies by egg donation with an affected twin.

Keywords: *VACTERL association. Congenital malformations. Twin pregnancy.*

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Introducción

En 1972, Quan y Smith realizaron el primer reporte de la asociación VATER, y actualmente se acepta el término VACTERL. Esta asociación es un conjunto de alteraciones congénitas que incluyen anomalías vertebrales (V), atresia anal (A), malformaciones cardiacas (C), atresia esofágica con o sin fístula traqueoesofágica (TE), alteraciones renales (R) y alteraciones de extremidades (L). Se requieren al menos tres de estos criterios para su diagnóstico[1].

La asociación VACTERL es de etiología incierta, presumiblemente multifactorial, con una relativa infrecuencia en los recién nacidos (1:10,000 a 1:40,000) y predilección por el sexo masculino (2.6:1) de acuerdo con lo reportado en diferentes publicaciones[2,3].

La frecuencia de presentación de las anomalías no tiene un patrón establecido, pudiendo encontrarse distintas combinaciones[4]. La prevalencia general de malformaciones congénitas es del 2% en embarazos espontáneos, siendo la ecografía la prueba de elección para el diagnóstico prenatal[5,6]. En la detección de esta asociación, el ultrasonido presenta una sensibilidad del 84% y una especificidad del 99.9%. El pronóstico de estos pacientes es malo, ya que el 50-85% fallecen en el primer año de vida[7].

Caso clínico

Recién nacida de 6 días de vida extrauterina, producto de embarazo gemelar biamniótico bicorial (de acuerdo con el último reporte ultrasonográfico) por donación de óvulos. Madre de 40 años, sangre O + G 1 P 0 C 1 A 0, con infecciones de vías urinarias en trimestre no especificado, tratada con medicamentos no especificados, sin comorbilidad ni enfermedades durante el embarazo, control prenatal desde el inicio de la gestación, ingesta de ácido fólico, hierro y vitaminas, así como ultrasonidos de control trimestrales normales.

Padre de 40 años, sangre O +, con hijos aparentemente sanos con su anterior pareja.

Se programa para cesárea a las 36 semanas de gestación y se aplica un ciclo de esquema de maduradores pulmonares. Se obtienen dos productos, siendo nuestra paciente la gemela 1.

En la reanimación se otorga APGAR 8/9, SA 1 y Capurro de 36 semanas de gestación. Peso 1975 g, perímetro cefálico 31 cm, perímetro abdominal 25 cm, perímetro torácico 27 cm, talla 42 cm, frecuencia cardiaca 150 latidos por minuto y frecuencia respiratoria

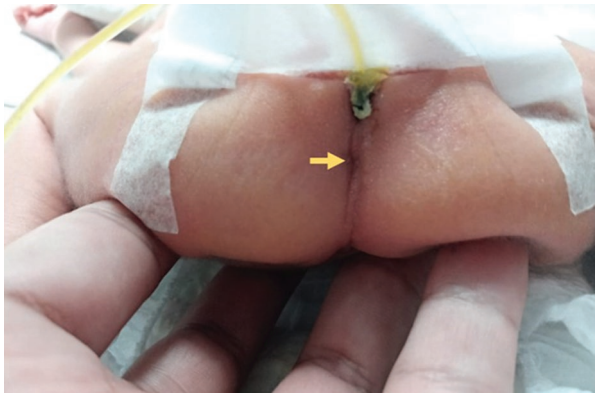

Figura 1. *Fotografía que muestra la ausencia de orificio anal (flecha).*

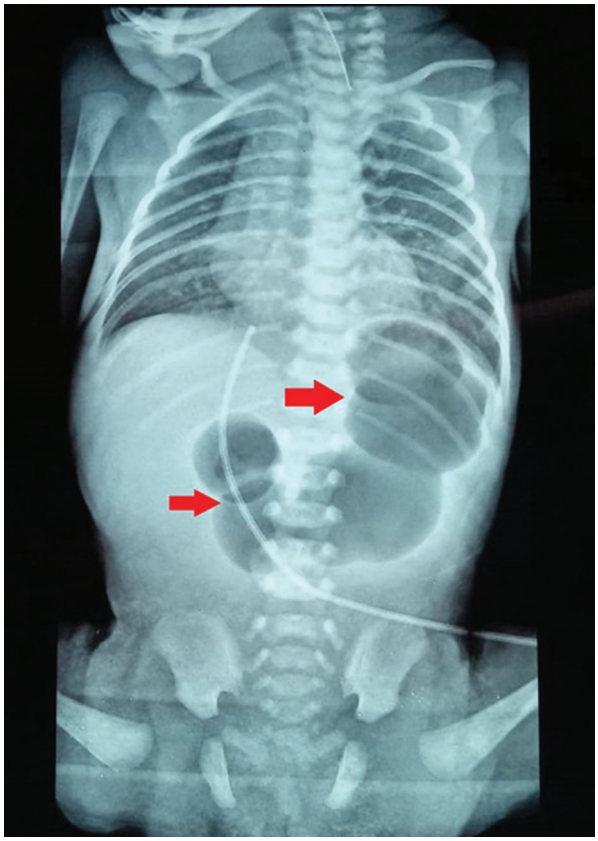

Figura 2. *Radiografía toracoabdominal que muestra una imagen de cuádruple burbuja (flechas).*

29 respiraciones por minuto. Con buen tono muscular, respira y llora enérgicamente. El gemelo 2, aparentemente sano.

Se coloca en cuna radiante a 37 °C con oxígeno libre a 2 l/min. En la exploración se encuentra permeabilidad de coanas, reflejos primitivos presentes, tórax y abdomen sin compromisos, cadera estable, llenado capilar de 3 segundos, fontanela anterior de 1 cm

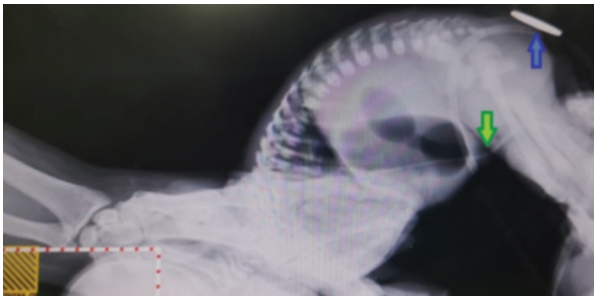

Figura 3. *Invertograma que muestra la altura proximal de la columna de aire (flecha verde) y el sitio anatómico del orificio anal (flecha azul).*

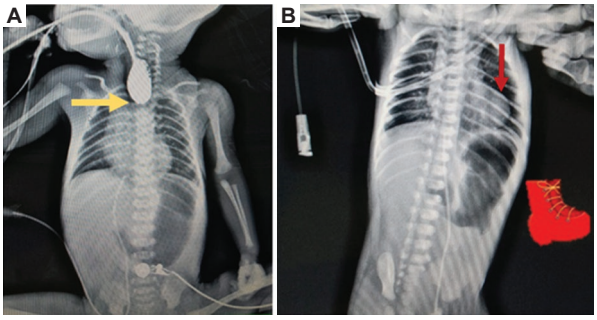

Figura 4. A: *esofagograma baritado que muestra un fondo de saco a nivel de la vértebra T2 (flecha).* **B:** *radiografía toracoabdominal con imagen característica de «zapato sueco» (flecha).*

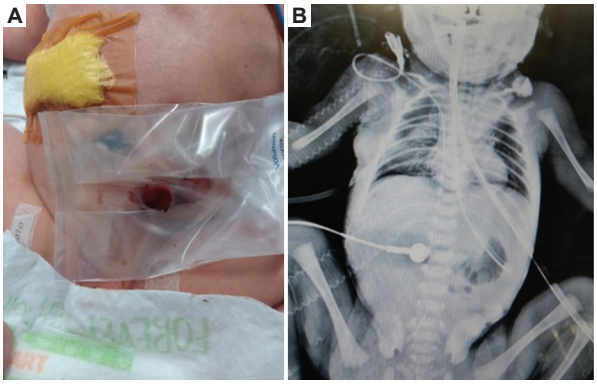

Figura 5. A: *colostomía derivativa.* **B:** *radiografía toracoabdominal de control.*

aproximadamente y posterior parcialmente cerrada; no se encuentra fosa anal (Fig. 1) y existe impedimento para el paso de la sonda orogástrica. Se realiza una radiografía toracoabdominal anteroposterior que evidencia una imagen característica en cuádruple burbuja y ausencia de aire distal, que hace sospechar atresia intestinal (Fig. 2). Ante estas alteraciones, se decide trasladar a la paciente a nuestra institución pública.

Ingresa a la unidad de cuidados intensivos neonatales a las 20 horas de vida extrauterina, donde se auscultan un soplo de intensidad III/IV y un segundo ruido desdoblado, por lo que se decide un manejo multidisciplinario integral.

Se solicita invertograma para determinar la altura del cabo colónico; sin embargo, la probable presencia de atresia duodenal o yeyunal no permite una correcta valoración (Fig. 3). La búsqueda de células meconiales en orina fue negativa.

Al realizar un esofagograma baritado por la sospecha de atresia esofágica se observa el fondo de saco ciego a nivel de T2 (Fig. 4), siendo probable una atresia tipo III, la cual se confirma durante la cirugía.

Por las características radiológicas del corazón, compatibles con la imagen en forma de «zapato sueco» (Fig. 4), el soplo auscultado y la tonalidad de la piel, se solicita valoración por el servicio de cardiología pediátrica, que realiza un ecocardiograma y confirma una tetralogía de Fallot con las siguientes características:

- Ventrículo derecho crecido e hipertrófico.
- Comunicación interventricular de 5.6 × 5.5 mm, con cortocircuito bidireccional con predominio de derecha a izquierda.
- Cabalgamiento aórtico del 50%, con presencia de continuidad mitroaórtica.
- Estenosis pulmonar moderada mixta, infundibular, valvular y supravalvular, con hipoplasia valvular y tronco de la arteria pulmonar con una velocidad máxima de 3.9 m/s, gradiente máximo de 60 mmHg y medio de 34 mmHg.

Se evidencia foramen oval permeable de 3.4 mm con cortocircuito bidireccional, y funciones sistólica y diastólica biventriculares conservadas. La anatomía es desfavorable.

Se planea y realiza cirugía por un cirujano pediatra, corrigiendo la atresia esofágica mediante anastomosis de cabo proximal y distal por abordaje torácico posterior derecho, así como cierre de la fístula traqueoesofágica, dejando sello pleural. Se corrige la atresia intestinal, siendo esta duodenal de tipo 1, y se encuentra atresia rectal, por lo que se realiza una colostomía derivativa en el mismo acto quirúrgico, a los 4 días de vida extrauterina (Fig. 5).

Es intubada antes de iniciar la cirugía y se mantiene así en la unidad de cuidados intensivos neonatales para evitar la dehiscencia de la anastomosis. Se da por terminada la cirugía sin complicaciones ni incidentes, y se realiza una radiografía de control a las 12 horas (Fig. 5).

Se plantea la realización de una derivación subclaviopulmonar por parte de cirugía cardiovascular en cuanto los vasos tengan el diámetro necesario para el procedimiento.

Los días posteriores, la paciente permaneció bajo sedación y comenzó a presentar episodios de hipoxia que remitían con sulfato de magnesio, esteroides y agonistas beta, llegando a saturaciones de hasta el 20%. Tuvo un paro cardiorrespiratorio al octavo día de vida, logrando una buena respuesta con reanimación cardiopulmonar. Falleció a los 6 días de vida, de un segundo paro cardiorrespiratorio. La causa de la muerte es incierta, pero probablemente fue por las alteraciones cardiacas inherentes a la tetralogía de Fallot, ya que los estudios de laboratorio no mostraron datos de infección ni desequilibrio hidroelectrolítico, y la radiografía de control no mostró ningún patrón de alarma.

Discusión

Un estudio de 25 pacientes con asociación VACTERL en nuestro país reportó que los factores de riesgo encontrados fueron diabetes gestacional y consumo de estatinas, cocaína o marihuana, entre otros[8].

De acuerdo con lo reportado por otros autores, las alteraciones cardiacas son las más comunes en la asociación VACTERL, seguidas por las anales y las vertebrales[4].

En un estudio de casos del Hospital para el Niño Poblano se reportó que las combinaciones más frecuentes fueron la tríada (35.7%), la tétrada (37.5%), la péntada (21.43%) y la héxada (7.14%), reportando un solo caso de tetralogía de Fallot[9].

Así mismo, otro grupo de investigadores de la University of California, Irvine Medical Center, Miller Children's Hospital Long Beach and Children's Hospital of Orange County, reportaron una serie de 36 pacientes de los que el 61.1% tuvieron atresia anal, se encontraron 6 pacientes con atresia duodenal y 6 pacientes con tetralogía de Fallot, y el 69.44% de los pacientes tenían algún tipo de fistula traqueoesofágica y atresia esofágica[10]. La presencia de atresia duodenal junto con la asociación VACTERL se ha reportado únicamente en el 5% de los casos[11].

En un estudio de casos del Joint Research Centre-European Surveillance of Congenital Anomalies publicado en 2019, el 6% de los casos fueron en pacientes con antecedentes de embarazo gemelar[4]. Un estudio retrospectivo con 142 pacientes con esta asociación reportó que los embarazos con terapia de reproducción asistida (TRA) que incluye la donación de óvulos, tienen mayor riesgo de presentar el complejo VACTERL, con una *odds ratio* (OR) de 4.8[12]; este mismo estudio sugiere que la primiparidad, el sobrepeso, la obesidad y la ausencia de ingesta de ácido fólico también son factores de riesgo.

El compendio de 28 registros de 15 países de la Red Europea para la Vigilancia de Anomalías Congénitas (EUROCAT) demostró que las TRA en general presentan un aumento de esta entidad (OR: 2.3)[13]. Actualmente, cerca del 2% de los embarazos son logrados con TRA[14]. En ambos estudios, el embarazo gemelar no fue un factor de riesgo[13,14].

La presencia de atresia duodenal junto con la asociación VACTERL se ha reportado únicamente en el 5% de los casos; por sí sola, la atresia duodenal tiene una mortalidad general del 13%[11,15].

Por sí sola, la atresia duodenal tiene una mortalidad general del 13%[15]. Cabe destacar que la coexistencia de atresia esofágica (con o sin fístula traqueoesofágica) y cualquier tipo de cardiopatía tiene una sobrevivencia de alrededor del 25%, lo que complicó aún más la esperanza de vida de nuestra paciente[16].

La escasa sobrevida en este tipo de pacientes puede deberse a las complicaciones propias de la asociación, como la falla renal que es característica, las complicaciones de las malformaciones o las secuelas de las complicaciones de las múltiples intervenciones quirúrgicas, como traqueomalacia, fístula traqueoesofágica recurrente, dehiscencia o fugas de anastomosis esofágicas o duodenales (en los casos que se acompañen de atresia duodenal), y sepsis. La muerte súbita de causa cardiaca secundaria al desarrollo de arritmias en las cardiopatías es un factor que debe tomarse en cuenta. El desarrollo neurocognitivo se encuentra íntegro, y por ello es indispensable un manejo integral y oportuno[15,17-19].

En este caso, a pesar de seguir un control prenatal adecuado, no se identificaron signos ultrasonográficos que hicieran sospechar esta afección, quizá por tratarse de un embarazo gemelar.

En México existen pocas series y casos reportados de asociación VACTERL, y en todo el mundo prácticamente son inexistentes los casos gemelares con un recién nacido afectado y el otro sano, asociados a TRA. Por ello, este reporte puede considerarse el primero de este tipo. Además, la presencia de tetralogía de Fallot es inusual, así como la coexistencia de atresia duodenal.

Conclusión

La asociación VACTERL es infrecuente y no se le conoce una etiología específica; sin embargo, las edades materna y paterna elevadas, la deficiencia de complementación con ácido fólico, el consumo de sustancias psicoactivas, algunos fármacos y las TRA, entre otros, son factores que pueden contribuir a su aparición. El control prenatal puede prevenir y detectar de manera temprana esta asociación. No obstante, la poca esperanza de vida puede estar ligada a las múltiples afecciones, ya que cada una cuenta con un riesgo de mortalidad individual, así como por las posibles complicaciones derivadas de los procedimientos quirúrgicos para la corrección de las malformaciones.

A pesar de no ser frecuente, es indispensable difundir los hallazgos, ya que con solo la exploración física se puede sospechar este y otros tipos de enfermedades catalogadas como raras.

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Conflicto de intereses

Los autores declaran no tener conflicto de intereses.

Consideraciones éticas

Protección de personas y animales. Los autores declaran que los procedimientos seguidos se conformaron a las normas éticas del comité de experimentación humana responsable y de acuerdo con la Asociación Médica Mundial y la Declaración de Helsinki. Los procedimientos fueron autorizados por el Comité de Ética de la institución.

Confidencialidad, consentimiento informado y aprobación ética. Los autores han seguido los protocolos de confidencialidad de su institución, han obtenido el consentimiento informado, y cuentan con la aprobación del Comité de Ética. Se han seguido las recomendaciones de las guías SAGER, según la naturaleza del estudio.

Declaración sobre el uso de inteligencia artificial. Los autores declaran que no utilizaron ningún tipo de inteligencia artificial generativa para la redacción de este manuscrito.

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CLINICAL CASE

Modified stent for the treatment of tracheomegaly combined with a tracheoesophageal fistula: a case report

Stent modificado para el tratamiento de traqueomegalia combinada con fístula traqueoesofágica: reporte de un caso

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Abstract

Tracheoesophageal fistulas (TEFs) are common in clinical practice and we address them in different ways according to their etiologies. Herein, we present a case of tracheomegaly combined with a TEF after long-term tracheotomy. We placed a modified silicone stent into the trachea to simultaneously cover the fistula and maintain an artificial airway for ventilation. After migration of the modified stent, we replaced it with a prolonged tracheotomy tube. This modified stent is a novel clinical attempt at addressing TEFs that should be more thoroughly explored.

Keywords: *Modified stent. Silicone stent. Tracheomegaly. Tracheoesophageal fistula.*

Resumen

Las fístulas traqueoesofágicas son frecuentes en la práctica clínica y las abordamos de diferentes formas según sus etiologías. Aquí, presentamos un caso de traqueomegalia combinada con una fístula traqueoesofágica después de una traqueotomía a largo plazo. Colocamos un stent de silicona modificado en la tráquea para cubrir simultáneamente la fístula y mantener una vía aérea artificial para la ventilación. Después de la migración del stent modificado, lo reemplazamos con un tubo de traqueotomía prolongado. Este stent modificado es un intento clínico novedoso para abordar las fístulas traqueoesofágicas que debe explorarse más a fondo.

Palabras clave**:** *Stent modificado. Stent de silicona. Traqueomegalia. Fístula traqueoesofágica*

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Introduction

Acquired tracheoesophageal fistulas (TEFs) are abnormal channels between the trachea and esophagus caused by acquired factors and can be divided into malignant TEFs and benign TEFs according to their etiology. Long-term tracheal intubation or tracheotomy is one of the most common causes of benign TEFs. Tracheomegaly is dilatation of the trachea to a transverse diameter > 25 mm in men and 21 mm in women[1]. Common causes include Mounier-Kuhn syndrome, long-term smoking, chronic bronchitis, emphysema, pulmonary cystic fibrosis, connective tissue disease, and pulmonary fibrosis[2]. Long-term tracheal intubation or tracheotomy can also cause secondary tracheomegaly[3]. Few reports have described tracheomegaly complicated with TEF[4]. We report a case of tracheomegaly combined with TEF due to long-term tracheotomy that was treated with a modified stent.

Case report

Chief complaints

A 57-year-old man was admitted to our hospital with the chief complaints of craniocerebral trauma for more than 1 year and a TEF for 1 week.

History of present illness

More than 1 year prior, the patient experienced severe craniocerebral injury after trauma and then underwent tracheotomy after intracranial operation. Chest computed tomography (CT) was performed for the month-long recurrent fever and suggested a TEF. Then, the patient was transferred to our hospital.

History of past illness

The patient had craniocerebral injury 1 year ago.

Personal and family history

The patient denied smoking and drug use. His father died of the unknown cause and his mother died of a heart attack.

Physical examination

The patient's vital signs were stable and the Glasgow Coma Scale score was 4 + T + 1. Pupillary reflexes were delayed. The patient was uncooperative with the physical examination. His right skull was depressed, which was considered a post-operative change. He was tracheotomized and breath sounds were low.

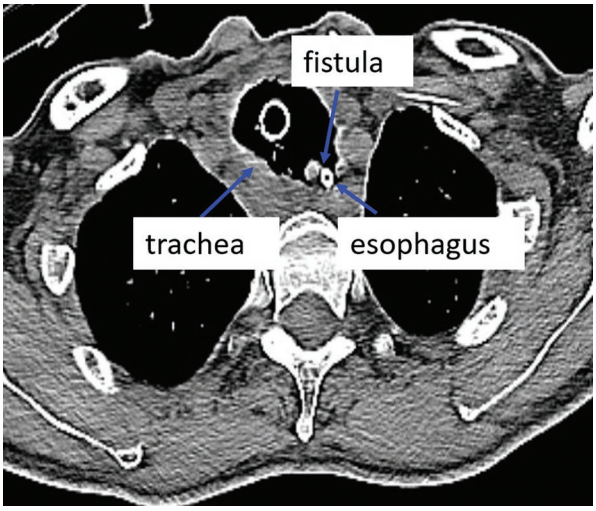

Figure 1. *Trachea and fistula in the chest computed tomography.*

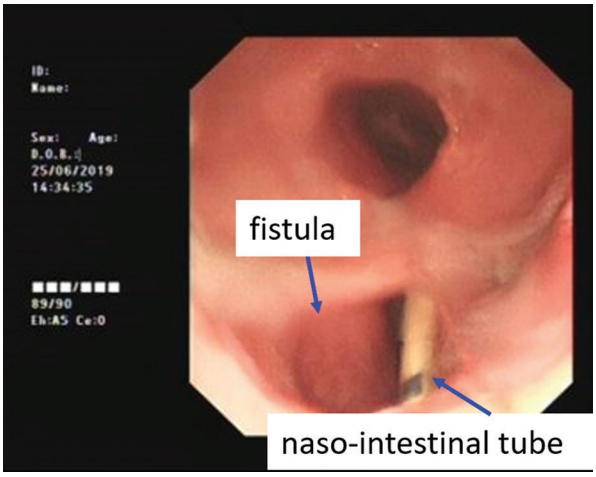

Figure 2. *The tracheoesophageal fistulas by the bronchoscopy.*

Laboratory examinations

No obvious abnormalities in routine laboratory examinations were found.

Imaging examinations

Chest CT revealed severe dilation of the trachea, with a maximum diameter of approximately 38 mm, and the local formation of a TEF (Fig. 1). Bronchoscopy

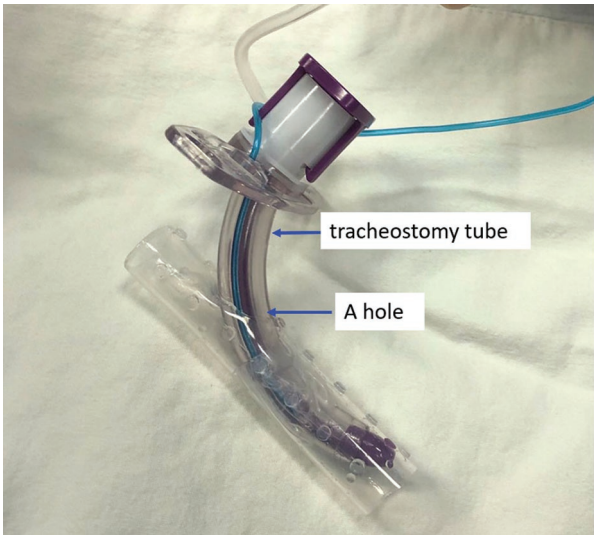

Figure 3. *The demonstration of modified silicone stent.*

showed that the upper segment of the trachea was obviously dilated, and a TEF with a diameter of approximately 1.2 cm could be observed; the nasointestinal tube in the esophagus could also be seen (Fig. 2).

Final diagnosis

The final diagnosis was TEF.

Treatment

We chose a Y-shaped silicone stent, truncated it to a length of 60 mm, and cut a hole in the surface for the insertion of a tracheostomy tube (Fig. 3). After the induction of anesthesia, we inserted a rigid bronchoscope into the trachea up to the air incision and removed the previous tracheostomy tube under bronchoscopic guidance. Then, we placed the modified silicone stent (15 mm × 60 mm) into the trachea to completely cover the fistula, ensuring that the hole in the stent was directly facing the air incision. After the stent was well supported, we inserted a No. 7 tracheostomy tube through the air incision and the hole into the stent (Fig. 4).

Outcome and follow-up

After the operation, the patient was well ventilated and discharged. Two months later, he came to our hospital again because of difficulty sputum suctioning and chest CT suggested migration of the stent. Then, we removed the stent and replaced it with a lengthened tracheotomy tube (70 mm).

Discussion

The principles for treating malignant and benign TEFs are different. Malignant TEFs mainly involve lung cancer and esophageal cancer, and their treatment should involve systematic support first due to the limited life expectancy. A covered self-expandable metal stent is often recommended for this kind of TEF[5] but not for benign TEFs as it can adhere strongly to the esophagus, which makes it difficult to remove after prolonged placement. For benign TEFs, closing the fistula by surgery is the first choice, but recently, stents have been explored more frequently for treating benign TEFs that are not suitable for surgery[5].

Post-tracheotomy or post-intubation TEFs are mostly caused by overinflation of the cuff of endotracheal or tracheotomy tubes, which results in ischemic necrosis of tracheal membrane tissue. In the presence of severe underlying diseases and atypical symptoms and due to late diagnoses, the fistula is always large and accompanies a locally dilated trachea. Therefore, surgery is the first choice[6]. Our patient became comatose after a severe craniocerebral contusion, which means that he was unsuitable for surgery. Maintaining a tracheotomy tube was necessary, indicating that closing the fistula was paramount. The extremely dilated trachea also increased the difficulty of treatment. We reviewed the literature on tracheomegaly complicated with TEF and found a report on only one similar case. The patient had an extremely dilated trachea with a transverse diameter of 4.6 cm on chest CT and a giant fistula with a diameter of 3 cm after long-term tracheotomy. Conservative treatments such as total parenteral nutrition and pressure control of the tracheotomy cuffs were chosen because of the poor general condition of the patient. The final outcome was not mentioned in the report[4].

Silicone stents are currently widely used because of their biocompatibility, good tolerance, ease of removal, and wide choice of diameters and lengths. Conventional Y-type or straight silicon stents cannot meet the needs of complex cases in the clinic, however. Therefore, the use of modified silicone stents has been increasingly reported, such as for massive hemoptysis[7]. The use of lengthened tracheotomy tubes is common for patients with a TEF after long-term tracheotomy or intubation[8]. However, the balloon of the tube increases the risk of recurrent tracheal dilatation and TEF formation;

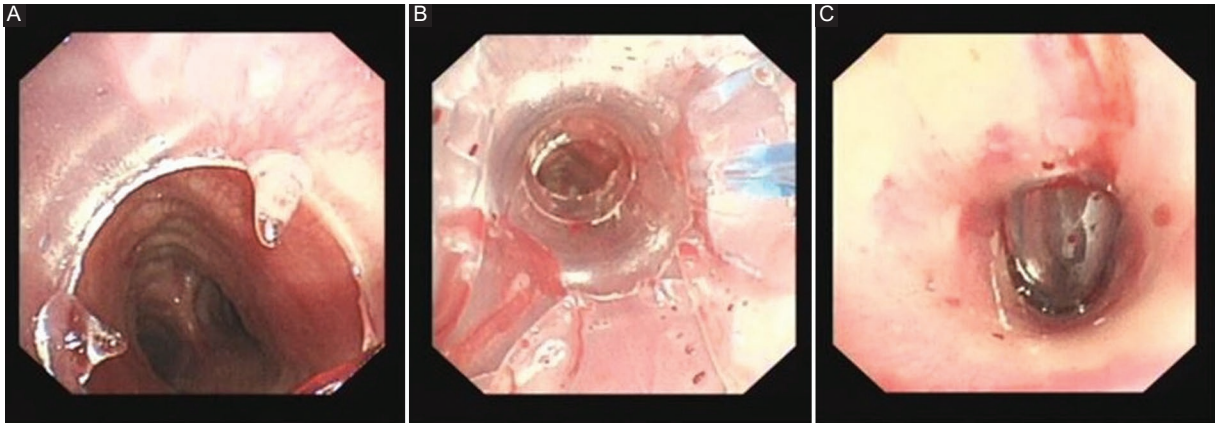

Figure 4. *Post-implantation of modified stent and tracheotomy tube.* **A:** *the bottom of modified stent.* **B:** *trachea by bronchoscopy through tracheotomy tube.* **C:** *the upper side of modified stent.*

therefore, in this case, a modified stent was inserted. First, the stent can cover the fistula; second, it preserves the air incision and, consequently, the artificial airway, thus allowing continued use of the balloon of the tracheotomy tube. The most common drawback of silicone stents is migration, which inevitably occurred 2 months later in our patient. We chose to replace it with a lengthened tracheotomy tube, which is the common method for treating TEFs caused by long-term tracheotomy.

Conclusion

This is the first report describing the novel, clinical application of a modified stent in the treatment of tracheomegaly complicated with a TEF. We expect to continue to explore this procedure in the treatment of benign TEFs.

Funding

No funding was received for this study.

Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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CLINICAL CASE

Thoracic lipoblastoma in a 6-year-old African male: a case report

Lipoblastoma torácico en varón africano de 6 años: reporte de un caso

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Abstract

Lipoblastoma is a very infrequent tumor, characteristic of early childhood. The thoracic location is infrequent, with isolated reports to date. We present the case of a 6-year-old male patient with a right thoracic tumor of months of evolution that was surgically removed by right anterolateral thoracotomy and in which the diagnosis of classic well-differentiated lipoblastoma was histologically confirmed. The patient evolved favorably and was discharged. He is currently under follow-up and without recurrence 1 year after surgery. This is, to our knowledge, the first thoracic lipoblastoma reported in an African pediatric patient. The importance of knowing the clinical, semiological, and intraoperative characteristics of this tumor becomes even more important, as in our case, in the context of international cooperation, where in many cases, there is no possibility of performing pre-operative imaging studies or subsequent genetic studies.

Keywords: *Lipoblastoma. Thoracic. Pediatric. African. Male.*

Resumen

El lipoblastoma es un tumor muy infrecuente, característico de la primera infancia. La localización torácica es infrecuente, con reportes aislados hasta la fecha. Presentamos el caso de un paciente varón de 6 años con una tumoración torácica derecha de meses de evolución que fue extirpada quirúrgicamente mediante toracotomía anterolateral derecha y en la que se confirmó histológicamente el diagnóstico de lipoblastoma clásico bien diferenciado. El paciente evolucionó favorablemente y fue dado de alta. Actualmente se encuentra en seguimiento y sin recidiva un año después de la cirugía. Este es, hasta donde sabemos, el primer lipoblastoma torácico reportado en un paciente pediátrico africano. La importancia de conocer las características clínicas, semiológicas e intraoperatorias de este tumor cobra aún más importancia, como en nuestro caso, en el contexto de la cooperación internacional, donde en muchos casos no existe la posibilidad de realizar estudios de imagen preoperatorios ni estudios genéticos posteriores.

Palabras clave:*Lipoblastoma. Torácico. Pediátrico. Africano. Varón.*

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Introduction

Lipoblastoma is a very infrequent tumor, characteristic of early childhood. Its origin is related to the proliferation of embryonic fat in the post-natal period[1]. There are multiple localizations described, with a predominance of extremity localization (where embryonic fat persists longer). Thoracic localization is infrequent[2-6], as is mediastinal[7]. Clinically, these lesions usually have an insidious course and are usually asymptomatic, although the thoracic location may be associated with extrinsic pulmonary compression. Imaging tests can help characterize the extent of the lesion and the degree of involvement of adjacent structures, but the radiologic features of lipoblastomas are generally non-specific, requiring a high degree of diagnostic suspicion on the part of the surgeon. In most cases, complete surgical resection is curative, although local recurrences have been described[4].

Case report

A 6-year-old male patient with no previous medical history presented with a right thoracic tumor of months of evolution. There was no relevant family history of neoplastic disease. He had no associated symptoms. Physical examination revealed the presence of a fixed, fluctuant, relatively soft mass in the anterolateral segment of the right thorax, measuring approximately 15 cm in its major axis (Fig. 1). No cutaneous involvement was observed. Due to the patient's care setting (a surgical cooperation campaign in Velingara, Senegal), pre-operative imaging studies could not be performed. The lesion was approached by right anterolateral thoracotomy. An encapsulated lipomatous tumor was identified, with an extrathoracic and an intrathoracic component, clearly different macroscopically (Fig. 2). The lesion seemed to be dependent on the costal wall. The lung and the rest of the thoracic cavity were free. A complete resection was performed, including the two costal arches that were in direct relation to the tumor. A thoracic drain was placed. The surgical specimen is shown in figure 3. The post-operative course was favorable and without complications. After 1 year, the patient is asymptomatic and without clinical recurrence. Although a cytogenetic study of the specimen could not be performed due to the limitations of the care context, the diagnosis of classic well-differentiated lipoblastoma was histologically confirmed.

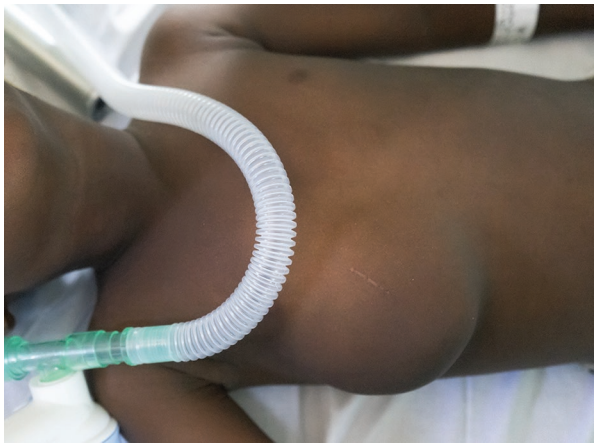

Figure 1. *Clinical photograph of the patient before surgery. Note the presence of a large rounded tumor involving the anterior and lateral wall of the right hemithorax.*

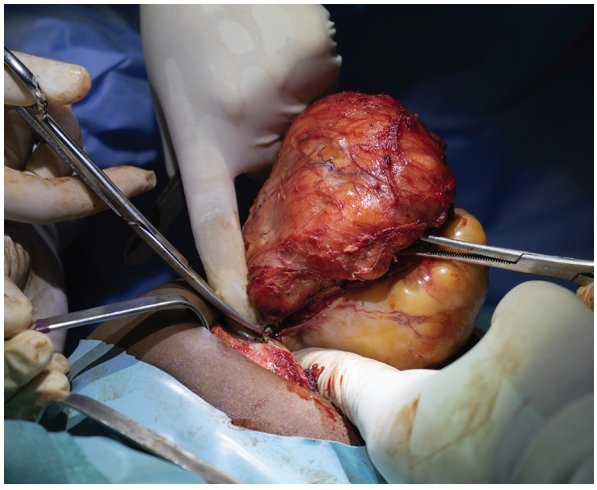

Figure 2. *Intraoperative photograph. Large encapsulated lipomatous tumor, with two clearly differentiated components (above, extrathoracic component. Below, intrathoracic component).*

Discussion

Regarding chest wall lipoblastomas, there are 15 cases reported to date in the medical literature[2-4,6,8,9]. The non-specificity of the radiological findings (absence of bone destruction or pathological fractures, absence of calcifications, and absence of adenopathies) sometimes determines the need for diagnostic biopsies[2,3,6], the result of these being inconclusive in some cases (non-specific fibrocollagenous tissue)[2]. In other cases, however, radiological studies establish a formal diagnostic suspicion of lipoblastoma[3] and directed biopsies confirm the diagnosis[3,6].

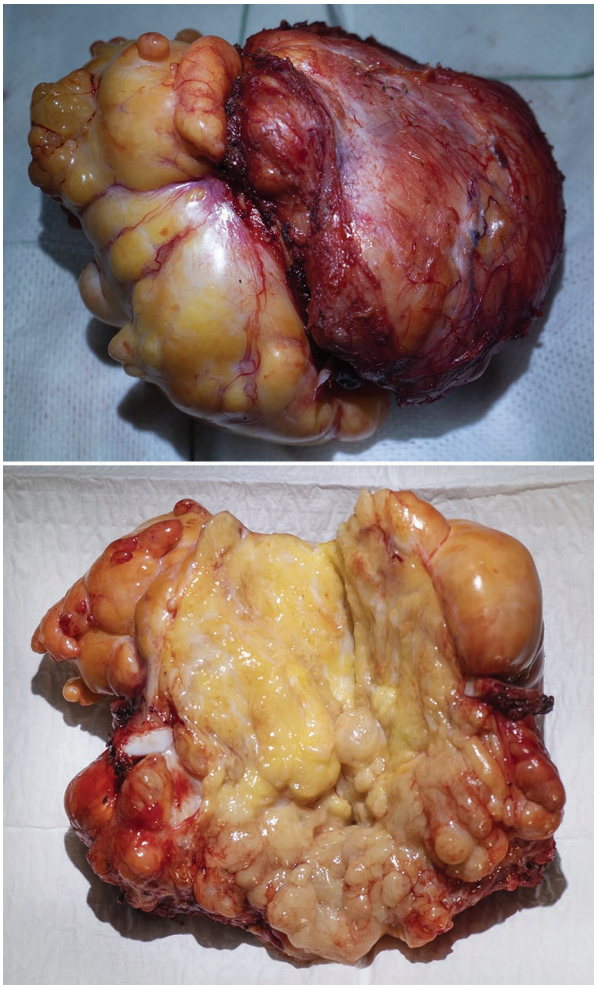

Figure 3. *Macroscopic photograph of the tumor after excision. Above: whole specimen. Encapsulated lipomatous tumor, with two clearly differentiated zones and with a narrow transition in the central zone. Below: open tumor following the major axis. Note the difference between the internal aspect of the intrathoracic zone (above) and the extrathoracic zone (below), with the extrathoracic zone presenting a more cystic aspect and a more grayish tone. Note the presence of the resected costal arches, marking the transitional boundary between the intra- and extrathoracic sections of the tumor.*

Regarding the surgical approach, it should be noted that no standardisation exists to date. It is known that lipoblastoma is a locally aggressive tumor and that resection should be, as far as possible, radical and complete. However, it is also known that in incomplete resections, a close evolutionary surveillance attitude can be taken with the remaining lesion, and maturation of residual lesions to typical lipomas or fibrolipomas has been demonstrated[4].

In most cases published to date, the surgical approach has been by thoracotomy[3,4,5]. However, in isolated cases, the thoracoscopic approach has been successfully described[6]. In smaller and localized tumors, there are authors who have reported performing wide excisional biopsies with subsequent close follow-up[2]. Intraoperative findings can be highly variable, with exclusively extrathoracic tumors[2] and tumors with both intra- and extrathoracic components with pleural involvement[3]. In the case presented here, we documented a tumor with both an intra-and extrathoracic component, although the pleura was intact and separated from the tumor.

It should be noted that in thoracic wall tumors, depending on the histology and the degree of bone involvement, resection of the ribs adjacent to the lesion may be indicated. This is the case of the two patients reported in the series of Maistry et al.[9]: both had the two ribs involved in the lesion resected, followed by reconstruction with Biodesign® with good oncologic and functional results. In our case, we opted for a limited resection, considering that such resection would not limit the closure or condition the integrity of the costal wall.

From the point of view of international cooperation, the diagnostic challenge posed by the presence of a thoracic tumor in this context is multiple: on the one hand, the absence of imaging tests prevents us from having useful information for the surgical approach, such as the degree of extension of the tumor, the potential involvement of vascular or neural structures, and the presence of other associated lesions. On the other hand, the absence of a conventional hospital structure with resources such as an intensive care unit makes it necessary to act with caution, limiting the surgical procedure to those acts that do not result in the need for non-existent post-operative support. Therefore, we believe that this type of patients should be approached by experienced surgeons who can calibrate well the benefit-risk balance of the procedure. In relation to the differential diagnosis and as previously mentioned, it is complex to establish a pre-operative suspicion of thoracic lipoblastoma given the scarcity of the existing literature and given the low specificity of the radiological findings. In our case, this complexity was increased by the absence of studies. We believe that anatomical and functional criteria should prevail in cooperation, so we chose to approach the patient with the widest possible resection within the previously described safety limits. The presence of an adequate cleavage plane with the pulmonary parenchyma and adequate tolerance to the anesthetic procedure were the keys to complete resection of the lesion. When approaching a

lipoblastoma surgically, the potential costal involvement and the eventual need for costal resection should be foreseen as far as possible, knowing that in the context of cooperation, it is difficult to count on prosthetic resources for the reconstruction of the thoracic wall.

Conclusion

This is, to our knowledge, the first thoracic lipoblastoma reported in an African pediatric patient. The age of the patient is also noteworthy, given that this type of tumor is notably more frequent in children under 3 years of age. The importance of knowing the clinical, semiological, and intraoperative characteristics of this tumor becomes even more important, as in our case, in the context of international cooperation, where in many cases, there is no possibility of performing pre-operative imaging studies or subsequent genetic studies. A surgical approach based on the principles of safety and performed by an experienced surgeon is an indispensable pre-requisite.

Funding

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Conflicts of interest

There are no conflicts of interest to declare.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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CASO CLÍNICO

Malformaciones cavernomatosas del tallo cerebral en pediatría: reporte de un caso y revisión de la literatura

Brainstem cavernous malformations in pediatrics: case report and literature review

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Resumen

Las malformaciones cavernomatosas tienen una prevalencia del 0.4% al 0.8% en la población. Su sintomatología incluye convulsiones, cefalea y déficit motor y de nervios craneales. Presentamos el caso de una niña de 10 años con cefalea, hemiparesia derecha, ataxia y afección de nervios craneales izquierdos VI, VII, IX y X. La resonancia magnética de encéfalo evidenció una lesión pontobulbar izquierda. Se realizó resección de una malformación cavernomatosa. La paciente presentó resolución de los síntomas al año de la cirugía. Las malformaciones cavernomatosas del tallo cerebral en pediatría son infrecuentes; cuando sangran, se recomienda la cirugía, y en las asintomáticas solo vigilancia neurológica.

Palabras clave: *Malformación cavernomatosa cerebral. Pediatría. Tallo cerebral. Neurocirugía.*

Abstract

Cavernous malformations have a prevalence of 0.4% to 0.8% in the population. Its symptoms are seizures, headache, and motor and cranial nerve deficits. We present the case of a 10-year-old girl with headache, right hemiparesis, ataxia, and involvement of left cranial nerves VI, VII, IX and X. Magnetic resonance imaging of the brain showed a left pontobulbar lesion. A cavernous malformation was resected. The patient showed resolution of the symptoms one year after surgery. Cavernous malformations of the brainstem in pediatrics are infrequent; when they bleed, surgery is recommended, and in asymptomatic lesions only neurological surveillance.

Keywords: *Brain cavernous malformation. Pediatrics. Brainstem. Neurosurgery*

Introducción

Las malformaciones cavernomatosas (MC), también conocidas como angiomas venosos o cavernomas, son malformaciones vasculares formadas por grupos de sinusoides dilatados, organizados en canales con una sola capa de endotelio. Representan del 10% al 15% de todas las malformaciones neurovasculares y tienen una prevalencia del 0.4% al 0.8% en la población[1,2]. Las MC pueden ser familiares (genéticas) o espontáneas; las genéticas se asocian a MC múltiples con un patrón autosómico dominante, relacionadas

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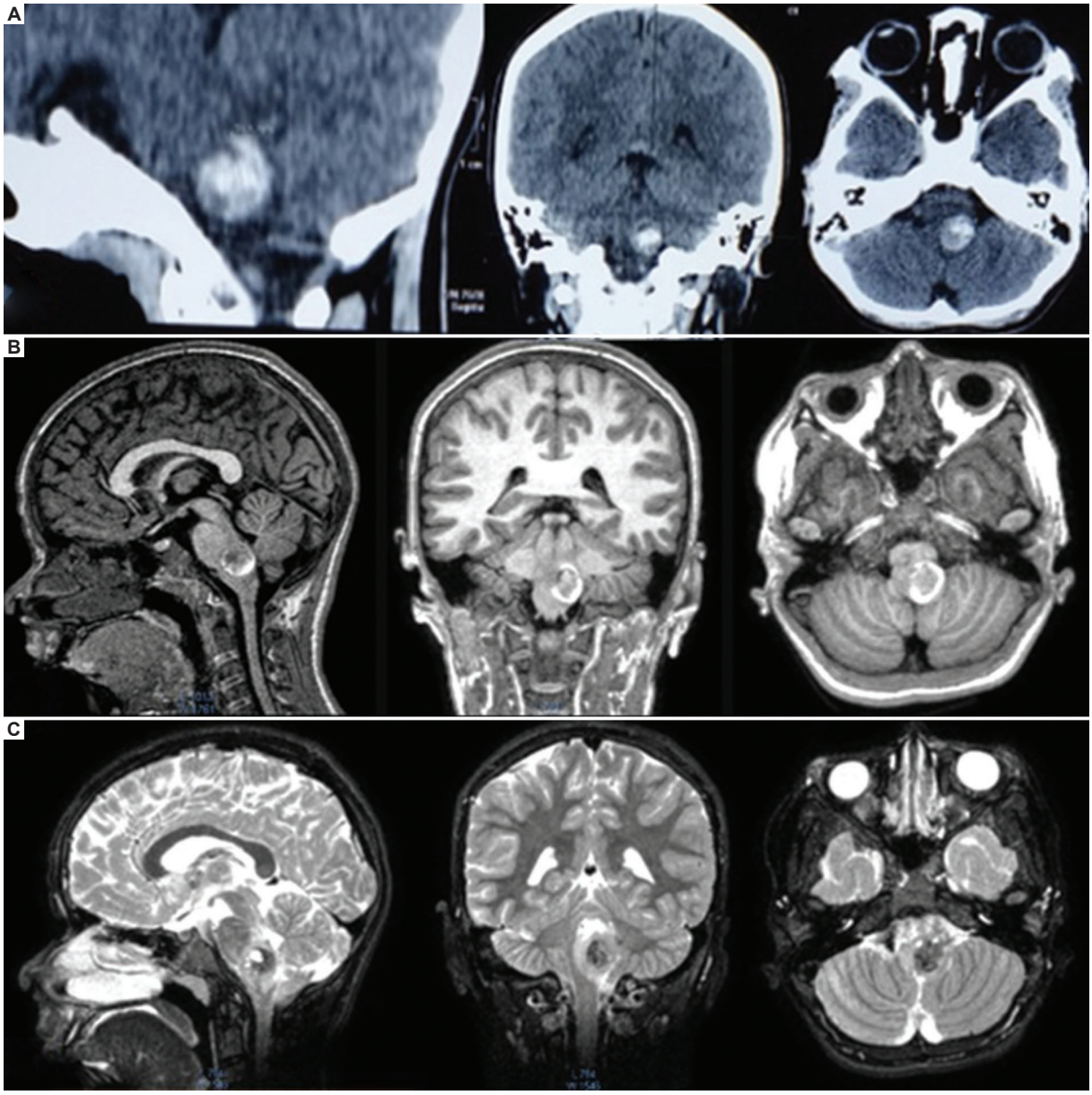

Figura 1. *La tomografía computarizada simple de cráneo en cortes sagital, coronal y axial (***A***) evidenció una lesión hemorrágica heterogénea en la unión pontobulbar izquierda. La resonancia magnética (RM) en secuencias T1 (***B***) y T2 (***C***) en cortes sagital, coronal y axial mostró una lesión subpial a nivel pontobulbar izquierdo, con diferencia en las intensidades, sugestiva de probable malformación cavernomatosa.*

con la mutación en uno de tres genes: KRIT1(CCM1), MGC4607 (CCM2) y PDCD10 (CCM3). Existe predisposición por grupos étnicos (50% en hispanos y 10-20% en caucásicos). Su etiología se ha relacionado con la exposición a la radiación[3,4]. La sintomatología incluye crisis convulsivas, cefalea, déficits motores y disfunción de nervios craneales, dependiendo de su localización, y se atribuye al sangrado intra- o extralesional y efecto de masa. La localización más frecuente es supratentorial (70-80%), seguida de la infratentorial (10-20%) y medular (5-10%)[5]. La hemorragia por MC en el tallo cerebral (que comprende el mesencéfalo, la protuberancia anular y el bulbo raquídeo), al tener mayor densidad los núcleos de los nervios craneales y los tractos motores, incrementa la sintomatología y la discapacidad, en comparación con su contraparte supratentorial[6]. Por su tamaño, las MC se clasifican en pequeñas (< 2 cm), grandes (2-4 cm) y gigantes (> 4 cm). La resonancia magnética (RM) se considera como primera opción

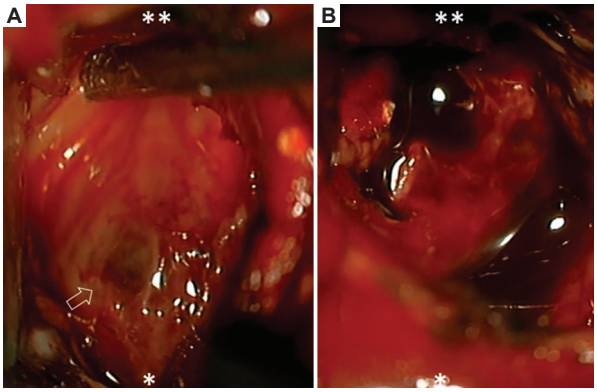

Figura 2. *Fotografía intraoperatoria del piso del ventrículo IV, con la paciente en decúbito prono.* **A***: colículo facial izquierdo incrementado de volumen (flecha).* **B***: salida de material hemático antiguo posterior a la incisión infracolicular. Con dos asteriscos se indica la posición superior y con un asterisco la posición inferior.*

para su diagnóstico[7-9]. El manejo de las MC incluye observación, cirugía o radiocirugía, dependiendo de su presentación clínica y localización anatómica[10,11].

Caso clínico

Presentamos el caso de una niña de 10 años que 7 días previos a su ingreso tuvo cefalea y pérdida transitoria del estado de consciencia con posterior recuperación, y desarrolló hemiparesia en el hemicuerpo derecho con fuerza 2/5, ataxia y afección de los nervios craneales izquierdos VI, VII, IX y X. Se le realizó una tomografía de cráneo simple y fue enviada a nuestro hospital para valoración por neurocirugía pediátrica, complementando su abordaje con RM de encéfalo y columna, que evidenció una lesión intraaxial, subpial del tallo cerebral en la unión pontobulbar izquierda, sugestiva de una MC (Fig. 1). Se realizó cirugía a los 10 días de iniciada la sintomatología. Con la paciente en decúbito prono, bajo monitorización neurofisiológica intraoperatoria y con técnicas de microcirugía, se realizó un abordaje telovelar, localizando el piso del ventrículo IV y el colículo facial izquierdo, presentando el colículo un incremento de volumen y un halo de hemosiderina. Se hizo una incisión infracolicular, obteniendo material hemático antiguo, y se identificó una MC de 7 mm que fue resecada totalmente, se corroboró la hemostasia y se cerró por planos de manera convencional (Fig. 2). La paciente fue extubada a las 72 horas. Al persistir con dificultades para la deglución, requirió una gastrostomía endoscópica. Fue egresada a su domicilio a los 7 días del posoperatorio. Se le dio seguimiento en la consulta externa, confirmando el diagnóstico de MC por histopatología. A los 4 meses logra deambular de forma independiente, con una fuerza 4/5 en el hemicuerpo derecho, resolución de la parálisis facial y capacidad de deglución, y se le retira la gastrostomía por lograr un adecuado peso para su talla y edad; aún persistía afección del VI nervio craneal izquierdo. Al año de la cirugía recupera totalmente la fuerza del hemicuerpo derecho y la función de los nervios craneales. Se realiza una RM de encéfalo de control que evidencia la ausencia de la MC (Fig. 3). La paciente no tiene antecedentes de exposición a radiación ni historia familiar de MC, y se descartó una alteración genética.

Discusión

El sangrado de las MC es más común en los niños (36-78%) que en los adultos (8-37%)[5]. El tratamiento de las MC del tallo cerebral es controversial; sin embargo, cuando el paciente presenta sangrado y afección clínica se recomienda cirugía para evitar un nuevo resangrado y un mayor déficit neurológico permanente, ya que se han reportado resangrados anuales del 18.1% al 32.3%[2,6]. En los casos asintomáticos no se recomienda cirugía[4,10-13]. Comparando nuestro caso con los de otros autores, encontramos que Di Rocco C et al.[14] reportan su experiencia con tres MC del tallo cerebral en pacientes pediátricos; si bien reconocen que presentan un déficit posquirúrgico transitorio, los pacientes tienden a recuperarse y a la resolución de los síntomas, recomendando la cirugía. También Lena et al.[15], en 13 años, reportan 9 MC del tallo cerebral en niños y operaron al 66.6%, recomendando resecar toda la lesión para evitar resangrados, y logran mejoría de los síntomas con la cirugía. Abla et al.[16], en 40 pacientes pediátricos con MC del tallo cerebral operadas, concluyen que la cirugía es la mejor opción en las lesiones sintomáticas. Constatando nuestros hallazgos, Bhardwaj et al.[17] reportan 20 MC del tallo cerebral en niños, de las que operaron 7 y manejaron de forma conservadora 13, reportando morbilidad transitoria en el grupo quirúrgico; en el grupo no quirúrgico se agregaron déficits neurológicos, recomendando la cirugía como mejor opción terapéutica. Sawarkar et al.[5] reportan 10 MC del tallo cerebral pediátricas sintomáticas, y de estas resangraron el 50% antes de la cirugía, operaron a 9, el 88.9% mejoraron y el 11.1% empeoraron, concluyendo que la cirugía es el mejor tratamiento. Rennert et al.[18] reportan 8 MC del tallo cerebral en niños, logrando una resección total en el 87.5% de los pacientes y

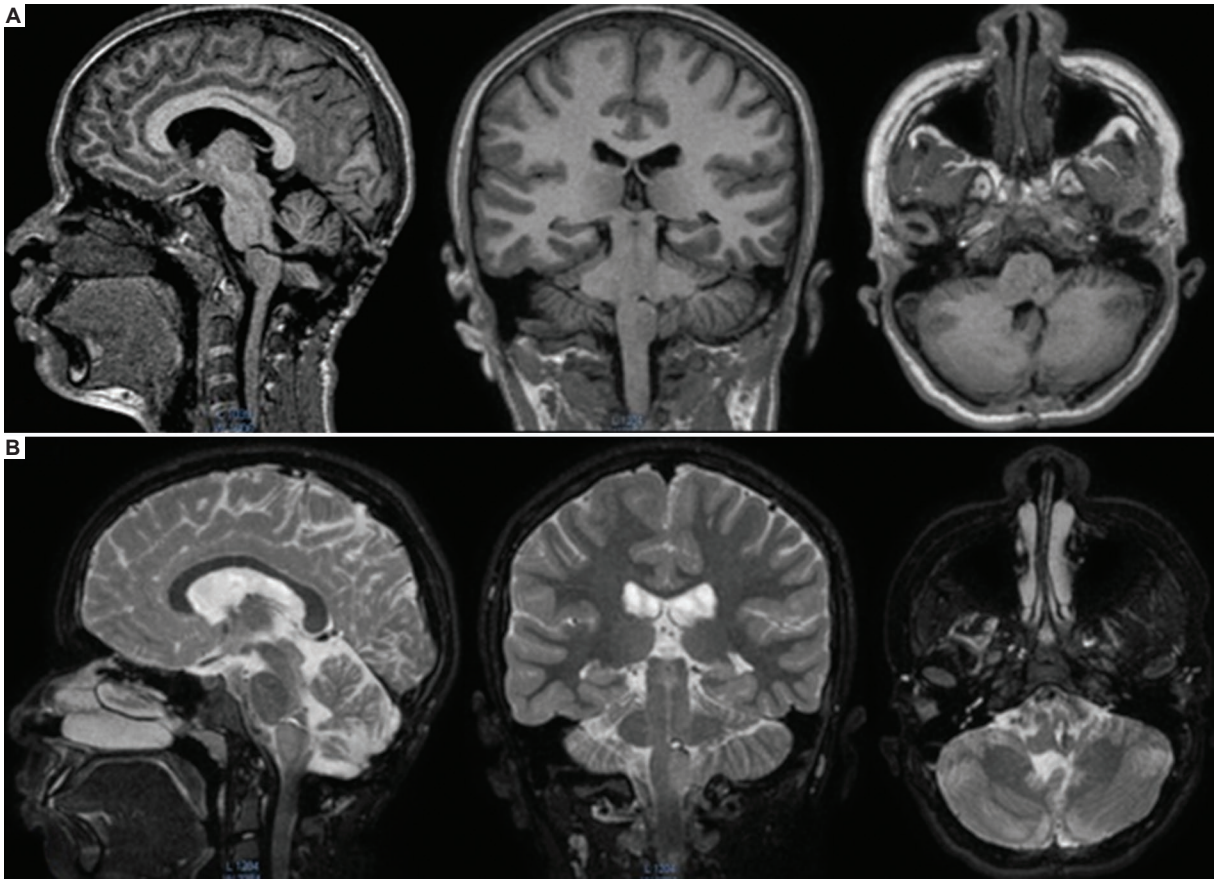

Figura 3. *Resonancia magnética posoperatoria en secuencias T1 (***A***) y T2 (***B***), en cortes sagital, coronal y axial, que evidencian la ausencia de la lesión en la unión pontobulbar izquierda (compárese con la figura 1).*

subtotal en el 12.5%, con mínima morbilidad y resolución total de los síntomas. Li et al.[19] operaron 52 MC del tallo cerebral en pediatría, recomendando la resección total de la lesión; los pacientes presentaron mejoría clínica posterior a la cirugía. Velz et al.[20] reportan 40 pacientes pediátricos con MC del tallo cerebral, de los que operaron a 13 sintomáticos y en los 27 asintomáticos realizaron vigilancia neurológica; los pacientes sintomáticos mostraron mejoría clínica con la cirugía. Florian et al.[21] reportan 2 pacientes, de 6 y 5 meses, con MC del tallo cerebral sintomáticas, evidenciando su naturaleza congénita y la resolución de los síntomas con cirugía. En Latinoamérica, Braga et al.[22] y Suárez et al.[23] reportan MC del tallo cerebral operadas en niños, con 2 y 6 casos respectivamente, recomendando cirugía en los pacientes sintomáticos y logrando mejoría clínica con la cirugía, como se evidenció en nuestro caso.

En las MC del tallo cerebral de adultos, en un metaanálisis realizado por Gao et al.[24] se comparan la microcirugía y la radiocirugía, concluyendo una ventaja de la microcirugía sobre la radiocirugía en cuanto a incidencia de resangrados y resolución de los síntomas. De igual forma, Kearns et al.[25] y Harris et al.[26] recomiendan la cirugía para MC del tallo cerebral sintomáticas, con un riesgo de mortalidad menor del 4% y mejoría de la sintomatología. En México, Nathal et al.[27] reportan 50 MC del tallo cerebral sintomáticas operadas en adultos, encontrando resolución de los síntomas posterior a la cirugía.

Comparando los resultados en el manejo del presente caso, se evidencia que la cirugía en las MC del tallo cerebral sintomáticas es la mejor opción terapéutica, tanto en adultos como en niños.

Conclusiones

Las MC del tallo cerebral en pediatría son infrecuentes. Su sangrado tiene una presentación clínica catastrófica y tiende a presentar nuevos resangrados, en comparación con los adultos; por ello, se recomienda su manejo neuroquirúrgico mediante microcirugía una

vez diagnosticadas, considerando la mayor expectativa de vida en los niños. En lesiones incidentales no se recomienda cirugía, sino solo vigilancia neurológica.

Financiamiento

Los autores declaran no haber recibido financiamiento para este estudio.

Conflicto de intereses

Los autores declaran no tener conflicto de intereses.

Consideraciones éticas

Protección de personas y animales. Los autores declaran que para esta investigación no se han realizado experimentos en seres humanos ni en animales.

Confidencialidad, consentimiento informado y aprobación ética. Los autores han seguido los protocolos de confidencialidad de su institución, han obtenido el consentimiento informado de los pacientes, y cuentan con la aprobación del Comité de Ética. Se han seguido las recomendaciones de las guías SAGER, según la naturaleza del estudio.

Declaración sobre el uso de inteligencia artificial. Los autores declaran que no utilizaron ningún tipo de inteligencia artificial generativa para la redacción de este manuscrito.

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LETTER TO THE EDITOR

Correspondence on incidence and factors associated with adverse reactions after the first dose of COVID-19 vaccine

Correspondencia sobre incidencia y factores asociados con las reacciones adversas tras la primera dosis de vacuna contra la COVID-19

Amnuay Kleebayoon[1], and Viroj Wiwanitkit[2,3]

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To the Editor,

Dear Editor, we would like to comment on the article "Incidencia y factores asociados con las reacciones adversas tras la primera dosis de la vacuna Pfizer-BioNTech en trabajadores de la salud[1]." In order to estimate the frequency of adverse reactions (AR) following the initial dosage of the Pfizer-BioNTech vaccine and to pinpoint some risk variables for AR, López-Contreras et al. According to López-Contreras et al. There is a 20% chance that a health care worker will get an AR as a result of the Pfizer-BioNTech vaccination[1].

The relationship that exists in reality might or might not be different from what is stated in the report. It is an interesting clinical problem when COVID-19 immunization has negative side effects. Articles may provide case-specific data, but it is impossible to establish with certainty how confounding factors affect results. It could be challenging to choose the right action to take. The objective of the current study, which aims to examine the effects of COVID-19 vaccine aversion, appears to be highly subjective. Determining the precise reason of a vaccination reaction may be challenging due to a paucity of clinical data defining the physiological and immunological status of COVID-19 vaccine recipients prior to vaccine injection. It is challenging to prove that there is no confounding factor given the registry's retrospective analysis.

Comorbidities are rarely mentioned in clinical records, even when they exist. Due to a lack of expertise, determining the precise patho-immuno-pharmacological link can be difficult at times. It can be difficult to understand how concurrent medical problems affect clinical outcomes. Genetics is the least important[2]. More information is difficult to obtain when no new data can be used to support any of the existing study's conclusions. At the end, it is possible to say that the proposed "no association" can be verified. However, another possible investigation that takes into account factors would be needed.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

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Confidentiality, informed consent, and ethical approval. The study does not involve patient personal data nor requires ethical approval. The SAGER guidelines do not apply.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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CARTA AL EDITOR

Carta al editor sobre el artículo "Procalcitonina y proteína C reactiva séricas como biomarcadores predictivos de dehiscencia de anastomosis intestinal en cirugía colorrectal"

Letter to the editor about the article "Procalcitonin and C-reactive protein as predictive biomarkers of anastomotic leak in colorectal surgery"

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Con atención he revisado el artículo publicado por Jiménez-Lizaola et al.[1] referente a biomarcadores predictores de dehiscencia. Los autores presentan un estudio de prueba diagnóstica con 11 pacientes. Describen el manejo estadístico de las variables clínicas y cuantitativas laboratoriales, pero no presentan el cálculo del tamaño de muestra, condición básica para un estudio de esta naturaleza, y este más parece una serie de casos a la que se adapta el diseño de prueba diagnóstica. El trabajo tiene serias deficiencias, ya que desde su título y objetivo busca predictores para dehiscencia de anastomosis en cirugía colorrectal, pero solo seis de sus casos lo fueron, pues cinco fueron ileocólicas. En ningún caso se describe el nivel preciso de las anastomosis, la técnica empleada (manual o mecánica) ni el abordaje (abierto o laparoscópico). Hay una gran variación de los resultados de las variables cuantitativas que se presentan con medias y desviaciones estándar, sin aclarar si se llevó a cabo un análisis para establecer la distribución de los resultados, como la prueba de Kolmogórov-Smirnov. Las variables cuantitativas fueron analizas con prueba t de Student de una muestra o prueba de Wilcoxon. En ambos casos fue incorrecto, pues debió aplicarse prueba t de Student para muestras independientes o prueba U de Mann-Whitney si la distribución de resultados era anormal.

La prevalencia del fenómeno dehiscencia fue del 36.4%, resultado marcadamente alto en pacientes con condiciones de preparación preoperatoria óptima al ser cirugía electiva, y además una paciente murió al undécimo día por un supuesto infarto agudo del miocardio, pero egresó del hospital con proteína C reactiva elevada, y no describen si se mantuvieron vigilancia estrecha y si el diagnóstico de infarto agudo del miocardio se sustentó bajo criterios estrictos o murió por sepsis abdominal. En todo caso, debió contabilizar como mortalidad operatoria. Tampoco los autores describen cuál fue el manejo de los pacientes complicados con dehiscencia (¿nueva ostomía?, ¿drenaje percutáneo?, ¿abdomen abierto?) ni si ayudó en algo la detección temprana. En conclusión este estudio tiene pobre utilidad por la escasa muestra, no presenta valores predictores ni las áreas bajo la curva, y el análisis estadístico es inadecuado. Concuerdo con los autores en que se requieren más estudios con muestras mayores para confirmar o descartar la proteína C reactiva y la procalcitonina como predictores de dehiscencia de anastomosis.

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Conflicto de intereses

El autor declara no tener ningún conflicto de intereses.

Consideraciones éticas

Protección de personas y animales. El autor declara que para esta investigación no se han realizado experimentos en seres humanos ni en animales.

Confidencialidad, consentimiento informado y aprobación ética. El estudio no involucra datos personales de pacientes ni requiere aprobación ética. No se aplican las guías SAGER.

Declaración sobre el uso de inteligencia artificial. El autor declara que no utilizó ningún tipo de inteligencia artificial generativa para la redacción de este manuscrito.

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CARTA AL EDITOR

Miopatía, fatiga y COVID-19 larga: consideraciones de la nueva histopatología neuromuscular

Myopathy, fatigue and long COVID-19: considerations of the new neuromuscular histopathology

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Estimado editor:

Actualmente, la comprensión de las secuelas neurológicas y musculares posteriores a la infección por SARS-CoV-2 representa un tema de interés creciente para los profesionales de la salud y el deporte, debido a que se ha dado especial énfasis a las secuelas ocasionadas por la COVID-19 larga en el componente neuromuscular, dada su asociación con la calidad de vida y la morbimortalidad.

Por ejemplo, en un trabajo realizado por Agergaard et al.[1] se evaluó con electromiografía cuantitativa y electromiografía de fibra única a pacientes con síntomas musculoesqueléticos prolongados de COVID-19, encontrando anomalía de la electromiografía de fibra única asociada con daño de los nervios terminales y de la placa terminal motora determinado por biopsias musculares.

Por otra parte, Hejbøl et al.[2] analizaron pacientes con molestias de fatiga, mialgia o debilidad posteriores a COVID-19 y evidenciaron que se presentó debilidad muscular en un 50% y electromiografía miopática en un 75%, y del mismo modo se notificaron cambios histológicos (mitocondriales, inflamación y lesión capilar).

Estos cambios histológicos en el tejido muscular indudablemente ocasionan complicaciones en el bienestar y la salud de las personas, más aún cuando se ha sugerido que los factores no modificables y la morbilidad psicológica pueden ayudar a mantener la fatiga continua y retrasar la recuperación[3], por lo que un abordaje individualizado del paciente sería lo más adecuado para la disminución y el tratamiento de estas secuelas.

Aún queda mucho por investigar sobre la histopatología neuromuscular de la COVID-19 larga, pues otro trabajo notificó que no existen cambios miopáticos, sino autonómicos, en los pacientes con síndrome de COVID-19 prolongada[4]; en consecuencia, hasta el momento no se puede asociar la fatiga en la COVID-19 larga solo a cambios miopáticos.

Por lo anterior, se concluye que la COVID-19 larga y su histopatología neuromuscular son un problema de salud pública y se requiere la participación de neurólogos, fisiólogos, médicos, fisioterapeutas y profesionales afines para continuar abordando los cambios histológicos en estos pacientes, así como proponer estrategias de rehabilitación interdisciplinarias para disminuir los síntomas persistentes, como la fatiga continua.

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Los autores declaran no tener conflicto de intereses.

Consideraciones éticas

Protección de personas y animales. Los autores declaran que para esta investigación no se han realizado experimentos en seres humanos ni en animales.

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Declaración sobre el uso de inteligencia artificial. Los autores declaran que no utilizaron ningún tipo de inteligencia artificial generativa para la redacción de este manuscrito.

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CARTA AL EDITOR

Medición del deseo de comer tras la pandemia

Measuring the desire to eat after pandemic

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Sr. Editor:

La obesidad en el mundo es un problema sanitario relevante. Esta patología es causa de diversas enfermedades asociadas. Los datos de la Organización Panamericana de la Salud indican que, en 2021, la obesidad fue causa de 2.8 millones de muertes por enfermedades no transmisibles en las Américas[1]. Además, el reporte menciona que se ha triplicado la cifra en los últimos 50 años y que el 62.5% de nuestra población sufre esta afección[1]. Por tanto, es relevante conocer los factores que influyen en la obesidad.

Un factor que ha sido objeto de diversos estudios en todo el mundo es el deseo intenso de comer, que se entiende como el detonante de la consecuente obesidad. En este contexto, el artículo «Deseo intenso de comer: estandarización del *Food Cravings Questionnaire-State* en México»[2] buscó estandarizar el FCQ-S (medición el estado de intensidad del deseo de ingerir un alimento específico) con una población de 1059 adultos, en los años 2018-2019, en la Ciudad de México. Se obtuvieron resultados satisfactorios en validez, confiabilidad y adaptabilidad a la población adulta mexicana.

Una acotación a esta valiosa investigación[2] es que, si bien el FCQ-S se ha aplicado en diversas partes del mundo, siempre fue por debajo de 1000 personas, por lo que es de suma valía esta considerable ampliación del margen de población.

A partir de este artículo[2], una línea indagatoria interesante podría ser medir el FCQ-S nuevamente después de la pandemia. En Perú, por ejemplo, entre 2020 y 2021, la ansiedad tuvo una prevalencia del 36.4%, la depresión del 26.6%, el estrés del 44.2% y el trastorno por estrés postraumático del 5.9%[3]. Tales indicadores, sin duda alguna, tienen una significancia transversal con algunos componentes evaluados en esta investigación[2], como la pérdida de control y el deseo intenso.

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