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ORIGINAL ARTICLES

Osseointegration of Dental Implants in Atrophic Regions. The use of Densah Burs, Osseodensification Technique, in Sinus Lift Procedures. A Clinical Case and Review Literature

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Abstract

Introduction: Atrophic posterior maxillary regions pose a significant challenge in dental medicine, where dental implant stability is hard to achieve. The innovative osseodensification, a new biomechanical technique that aims to solve this problem without removing any bone tissue, is a topic of great interest and potential in our field.

Case report: The patient, A.K., a 44-year-old smoking female, was presented to the clinic concerned with the lack of ability to eat from her left side as a result of the extraction of her upper molars. After a 3D radiographic scan was conducted, it was confirmed that there was considerable bone loss in the upper left posterior region and a proximity with the maxillary sinus. As part of the treatment plan, an Osseo-densification technique in crystal maxillary sinus elevation would be used for two implant placements in the first and second molar regions.

Conclusions: The Osseo-densification technique in crestal sinus lifting was shown to be a dependable and less invasive option for treating considerable posterior maxillary bone loss. However, conclusive findings are still needed for this technique, emphasizing the need for continuous research and learning in our field.

Keywords: Osseodensification, maxillary sinus lift, implant stability, Densah burs.

Introduction:

Osseodensification is a new biomechanical bone preparation technique for dental implant placement using Densah burs, the Versah system, which rotates counterclockwise at 800 to 1500 rpm. Osseodensification differs from other methods in that it does not remove any bone tissue. Instead, the bone tissue is simultaneously compacted and autografted in directions that extend outward from the osteotomy [1].

The osteotomes formed by the Densah burs don't damage or shatter the bone trabeculae, improving secondary implant stability and helping the healing process [4].

With the Osseodensification process, the Densah® Burs can widen the cylindrical osteotomy without removing bone tissue, causing controlled plastic deformation. In total, 12 burs achieve the desired osteotomy diameter by being used in ascending order, one after the other. The burs can be used in two ways: either in the 'Densification Method' to densify and preserve bone by rotating in a counterclockwise direction or the 'Cutting Method' to precisely cut bone by spinning in a clockwise direction. The 'Densification Method' is beneficial in cases where bone preservation is a priority, while the 'Cutting Method' is preferred when precise bone cutting is necessary [2].

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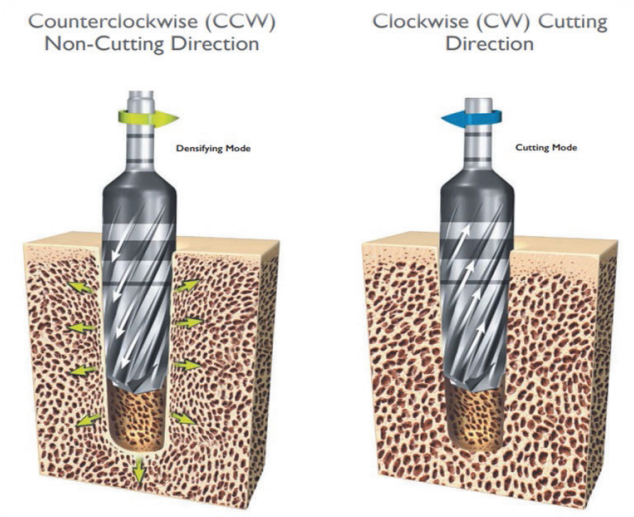

Figure 1- Densah Burs methods of use [2]

The Densah® burs are used with an ‹Advance-Retract› motion. This technique involves applying slight vertical pressure to advance the bur into the osteotomy, then retracting to relieve pressure and repeating this process periodically. This motion helps in the efficient preparation of the implant site. Additionally, the burs should always be used with continuous irrigation to prevent overheating and ensure the patient's safety [2].

There are a lot of different clinical situations where the osseo-densification technique can be used: sub-antral bone grafts, immediate implant placement in post-extraction sockets, narrow alveolar bone crests, and low-density bone areas [3].

Histological studies done in animals show that osseodensification allows a better healing process and even provides a broader implant bed preparation without any adverse effects on primary stability (Figure 2) [9].

However, there are also contraindications, such as performing osseodensification on cortical bone or xenografts [4].

Case Introduction:

The patient, A.K., a 44-year-old smoker, presented to the clinic concerned about her inability to eat from her left side due to missing her upper molars. When the patient smiled, the absence of the upper molars was slightly visible, causing her a sense of discomfort. No systemic complications or medical conditions affecting oral health were reported during the subjective examination.

The patient's clinical examination found minimal tartar accumulation and a good condition of existing fillings. Proximal caries lesions on teeth 44 and 45 were also noted. The patient said that teeth 26 and 27 were extracted more than 4 years ago after suffering from periapical lesions at both teeth' apex (Figure 3).

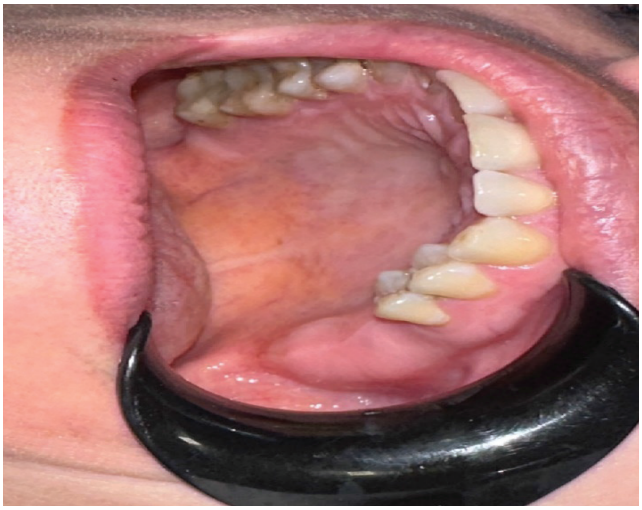

Figure 3- Clinical presentation

After a 3D (CBCT) radiograph was conducted, it was confirmed that there was considerable bone loss at the upper left posterior region and in proximity to the maxillary sinus (Figure 4).

As part of the treatment plan, it was decided that after oral prophylaxis and caries treatment, the osseodensification

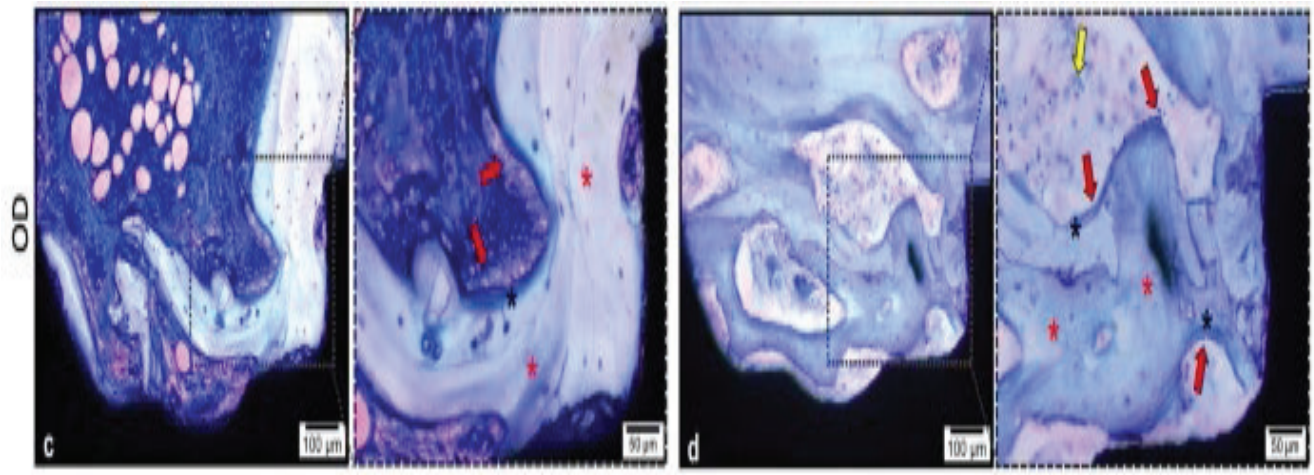

*Figure 2- Osseodensification healing, (**c**, **d**) 14 and 28 days after implantation, respectively*

technique in crystal maxillary sinus elevation would be used for two-implant placements in the first and second molar regions. A sinus lift was necessary due to the maxillary sinus's natural proximity to the planned implant site and the bone resorption resulting from the absence of the molar maxillary teeth for more than four years.

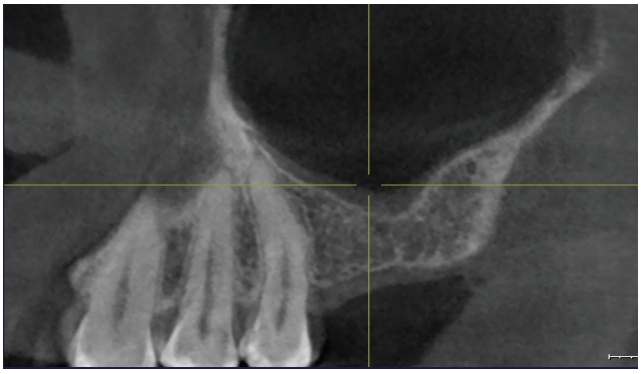

Figure 4- Preoperative 3D radiographic scanner

Two hours before the surgery, the patient took 2 mg of amoxicillin as a prophylactic antibiotic and 1 mg of etason to prevent postoperative inflammation. She was also instructed to rinse with chlorhexidine digluconate solution (0.2%) for 1 min. The local anesthetic chosen was articaine hydrochloride 4% with epinephrine (1:100.000). A limited full mucoperiosteal flap was lifted using a #15 scalpel. The first cut was made on the top of the edentulous ridge, and two releasing incisions were made at the back ends of the ridge to allow for better flap movement and to avoid tension.

To prepare the site for implant placement, Densah® Burs (Versah, LLC, Jackson, MI, USA) were used in a counterclockwise (CCW) direction. The manufacturer's recommendations were followed by using sufficient irrigation to avoid overheating. The Densah® bur was chosen according to the intended implant size, aiding sinus lift and bone drilling (Figure 5).

After gently elevating the sinus floor, the final Densah® bur was utilized without irrigation to compact Raptos® Allograft Bone Particulates into the sinus space.

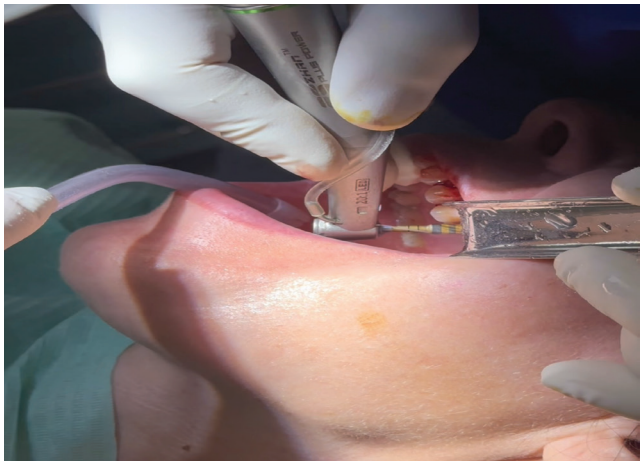

Figure 5- Implant placement preparation

Two 4.5 x 8.5 mm implants were inserted into the designated teeth at 26 and 27 sites. The implants were placed strategically to guarantee maximum initial stability and submerged without immediate temporary restorations, creating ideal circumstances for osseointegration while healing (Figure 6).

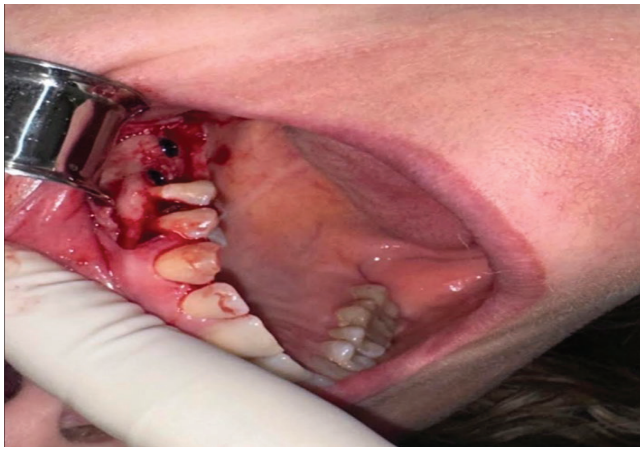

Figure 6- Implant placement

The patient reported that after the anesthesia, the postoperative pain was little to none. She only needed to take two tablets of analgesics the day of the surgery. During future appointments, a thorough examination was performed. X-rays showed a successful integration of the implants and no sign of over-elevation or perforation of the Schneiderian membrane (Figure 7). Probing at six locations around the implants was also performed to confirm the health of the soft tissues around the implants. The patient's successful recovery and anticipated successful implant integration provide reassurance and confidence in the efficacy of the osseo-densification technique. The long-term outlook remains optimistic.

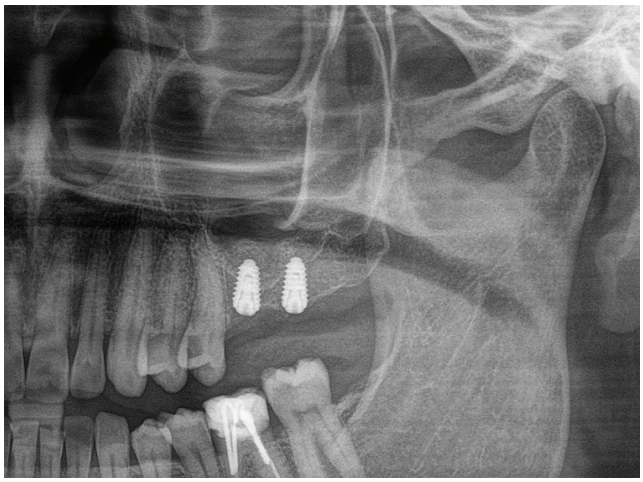

Figure 7- Panoramic x-ray after surgery

Discussion:

The osseodensification technique in crystal maxillary sinus elevation is being studied for advantages over conventional methods. Meanwhile, less invasive surgery enhances the implant's stability by preserving and increasing bone density through compact autografting [5].

Studies have shown that when compared with other methods, OD does not negatively affect osseointegration, as supported by the successful implant integration and absence of complications during the healing phase [6].

Understanding OD in sinus lift procedures is essential to understanding potential risks. While there have been good case reports, conclusive findings in osseodensification still need to be made [7].

Methods for transrectal sinus floor elevation utilizing osseodensification drilling are outlined for regions with a remaining bone height of ≥2 and ≤6 mm, and residual bone height of 2–3 mm is cited as a potential danger for sinus membrane perforations when utilizing osseodensification burs [8].

In our case, osseodensification proved to have positive results. There were no signs of pain, inflammation, or other negative factors, and promising radiographic and clinical findings were obtained. However, the patient's smoking habits remain a risk factor for long-term stability.

Conclusions:

The osseodensification method used in crestal sinus lifting was shown to be a dependable and less invasive option for treating considerable posterior maxillary bone loss, such as in this case. However, it is essential to acknowledge that this technique has no conclusive findings.

COI Statement: This paper has yet to be submitted in parallel, published, or considered beforehand.

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Materials and Methods

Our study design is a retrospective cohort study. The population included in this study is 600 adult patients who underwent cardiac surgery between January and December 2023 at a single tertiary care center, University Hospital Center "Mother Teresa," in Tirana, Albania. We used the inclusion criteria for patients undergoing elective or emergency coronary artery bypass grafting (CABG), valve surgeries, or combined procedures.

Patients with preoperative myocardial infarction (MI) within 48 hours of surgery or incomplete postoperative data in the last year, 2023, were excluded from the study. The data collected were patient demographics (age, sex, comorbidities) and surgery type (CABG, valve surgery, combined). We studied diagnostic methods for PMI (ECG, biomarkers, echocardiography), management strategies (medical therapy, IABP usage), and outcomes (ICU stay, mortality).

Acute PMI after cardiac surgery is usually asymptomatic because patients are often incapable of reporting classic ischemic indicators in the early period due to the effects of postoperative pain management (anesthesia and analgesia) and the masking effect of symptoms related to surgery (pain, nausea, fatigue). Furthermore, acute PMI is difficult to distinguish from myocardial infarction. In the Fourth Universal Definition of Myocardial Infarction, there is no consensus on the troponin cutoff points that differentiate cardiac procedural myocardial ischemia from myocardial infarction.

PMI was diagnosed based on the Fourth Universal Definition of Myocardial Infarction, requiring a significant elevation in cardiac troponin (≥10 times the 99th percentile upper reference limit) with supporting evidence of myocardial ischemia (ECG changes, new wall motion abnormalities, or angiographic findings)[3]

Results

Patient Demographics: The study included 600 patients, with a mean age of 63 years (range 45–82). Of these, 410 were male (68.3%), and 190 were female (31.7%).

Table 1 shows comorbidities such as Hypertension (65%), diabetes (50%), and hyperlipidemia (48%). The surgical procedures included CABG (360 patients (60%), valve surgery (180 patients (30%), and combined procedures (60 patients (10%).

This study's total number of PMI cases was 54 patients (9%). The CABG group had 30 360 cases (8.3%), the valve surgery group had 18 180 cases (10%), and the combined procedures group had 6 60 cases (10%).

Graph 4 describes the diagnostic methods used. Elevated cardiac troponins: all 54 cases (100%).

ECG changes: 40 cases (74%), including ST-segment elevation (18%), ST-segment depression (38%), and new-onset left bundle branch block (18%). Echocardiographic findings (new wall motion abnormalities): 32 cases (59%), as shown in Table 2.

Parameter PMI Group (n=54) Non-PMI Group (n=546)

Parameter	PMI Group (n=54)	Non-PMI Group (n=546)	Total Cohort (n=600)
Mean age (years)	66 ± 10	63 ± 12	63 ± 12
Male (%)	70.4%	68.1%	68.3%
Hypertension (%)	72.2%	64.6%	65.0%
Diabetes (%)	57.4%	49.6%	50.0%
Surgical Type: CABG (%)	55.6%	61.2%	60.0%
Surgical Type: Valve (%)	33.3%	29.7%	30.0%
Combined Procedures (%)	11.1%	9.1%	10.0%

Table 1: Patient Demographics and Surgical Distribution

Diagnostic Modality	PMI Cases (n=54)	Percentage (%)
Elevated Troponins	54	100%
ECG Changes	40	74%
ST-Segment Elevation	10	18%
ST-Segment Depression	21	38%
New LBBB	10	18%
Echocardiography (WMA)	32	59%

Table 2: Diagnostic Methods for PMI

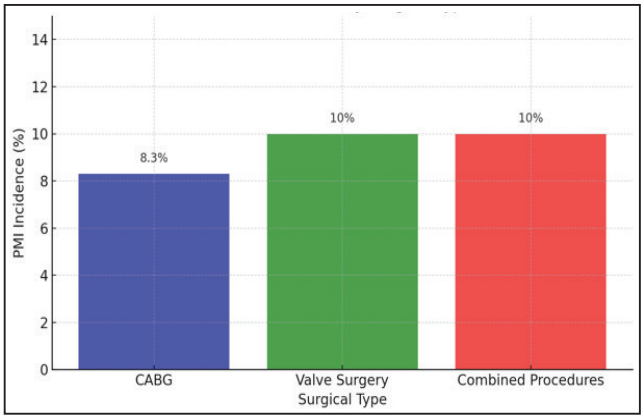
Management of PMI: 35 patients (65%) were managed with medical treatment alone. Two patients (4%) underwent coronary artery bypass re-intervention. IABP was placed in 15 patients (28%) of PMI cases. Graph 1 shows the incidence of PMI according to the surgical type performed.

IABP Usage in the entire Cohort: Total IABP usage: 30/600 patients (5%). 15/54 (28%) of PMI cases required IABP as treatment according to the indications as seen in Graph 2: Cardiogenic shock (67%) and refractory ischemia (33%).

Postoperative Outcomes: We used ICU stay as the leading indicator of postoperative outcomes in our patients and compared the 30-day mortality in each group, as seen in Graph 3.

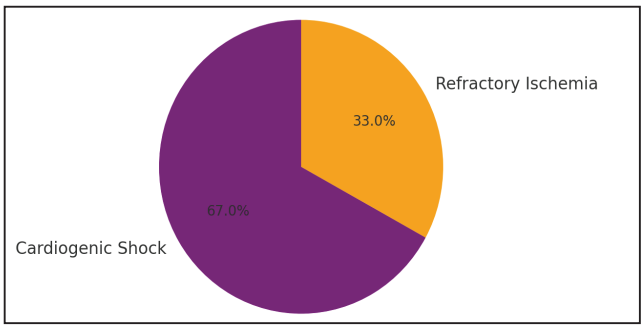
The ICU stay was significantly more extended in the PMI group (>3 days): 38 PMI patients (70%) vs. 120 non-PMI patients (22%). Graph 5 shows the duration of the ICU stay in the two groups.

30-day mortality was also significantly higher in the PMI group, 8/54 (14.8%), and in the non-PMI group, 10/546 (1.8%).



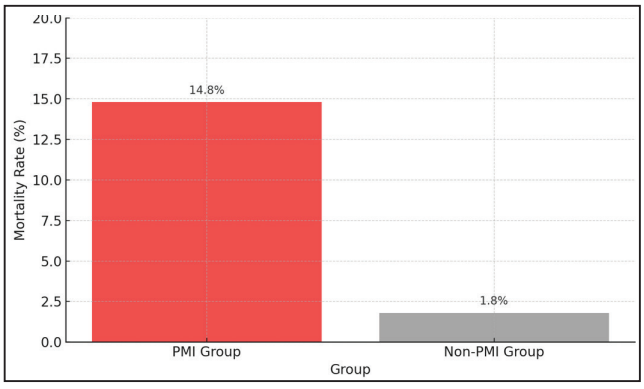
Graph 1: Incidence of PMI by Surgical Type

A bar chart compares PMI incidence across CABG, valve surgeries, and combined procedures.



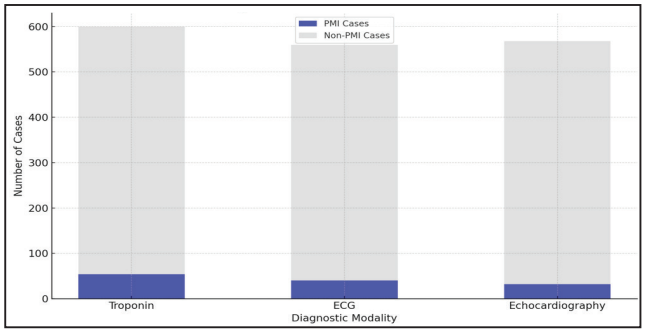
Graph 2: IABP Usage and Outcomes

Here is a pie chart showing the indications for IABP in PMI cases: cardiogenic shock (67%) and refractory ischemia (33%).

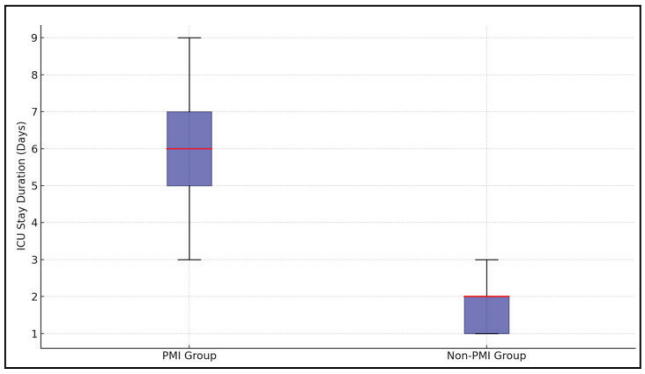


Graph 3: 30-Day Mortality Rates

A line graph comparing the mortality rates between PMI and non-PMI groups.



Graph 4: Distribution of Diagnostic Modalities



Graph 5: ICU Stay Duration

Discussion

PMI Incidence and Risk Factors: This study's observed 9% incidence of PMI aligns with the expected range reported in the literature (5–15%)[1, 2]. This variability can be attributed to differences in patient demographics, comorbidities, and surgical complexities across studies. In recent studies, the incidence of myocardial infarction has been reported to range from 0.3% to 9.8% after isolated CABG and from 0.7% to 11.8% after concomitant valvular surgery. The slightly higher PMI rates in valve surgeries (10%) and combined procedures (10%) compared to CABG (8.3%) underscore the impact of prolonged cardiopulmonary bypass (CPB) times and heightened myocardial vulnerability during these operations [4, 5].

Many factors may lead to acute PMI after cardiac surgery, and they differ by the type of surgical procedure performed, as seen in Figure 1.

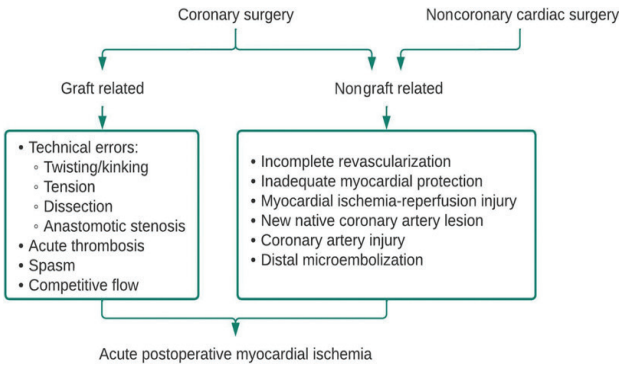


Figure 1. Mechanisms of postoperative myocardial ischemia after cardiac surgery.

Patients with comorbidities like diabetes (50%) and Hypertension (65%) demonstrated higher PMI risks, consistent with the role of systemic inflammation and microvascular dysfunction in ischemia [3, 6]. Identifying such risk factors preoperatively can guide preventive strategies, including enhanced myocardial protection techniques.

Diagnostic Challenges: Clinical diagnosis of acute PMI in patients undergoing cardiac surgery is challenging. The reasons for this are multifactorial: Sedation may mask ischemic symptoms; there is distracting pain from either sternotomy or thoracotomy incisions; and hemodynamics after extracorporeal circulation frequently require support with inotropic and vasoconstrictor infusions even in patients without myocardial injury. Diagnosis may be further confounded by other early postoperative complications such as tamponade due to pericardial effusions compromising myocardial function. In a patient with failure to wean from cardiopulmonary bypass, new or unexpectedly high requirements for vasoactive support or mechanical circulatory support (MCS), postcardiotomy shock, low cardiac output syndrome, or chest pain out of proportion to usual incisional pain, further evaluation for acute PMI is warranted. This study reaffirms the diagnostic utility of cardiac troponins, ECG, and echocardiography in detecting PMI. The universal troponin elevation in PMI patients emphasizes its role as a sensitive biomarker; however, its specificity remains limited due to potential postoperative elevations unrelated to ischemia [7].

Hence, integrating biomarkers with imaging modalities such as echocardiography and advanced ECG analysis enhances diagnostic accuracy. While echocardiography identified wall motion abnormalities in 59% of PMI cases, its limited sensitivity highlights the need for real-time perioperative imaging tools like transesophageal echocardiography (TEE). Future research could explore combining TEE with myocardial strain analysis to improve early ischemia detection.

Therapeutic Strategies: The predominance of medical management (65%) in PMI cases reflects the perioperative bleeding risks associated with interventions like PCI or repeat CABG [7]. PCI was not performed in any of the PMI cases because of their severity and the difficulty of transporting them to the hemodynamic operating room. However, careful multidisciplinary planning is essential.

The 28% utilization of IABP in PMI underscores its importance in managing cardiogenic shock and refractory ischemia [9, 10]. Despite controversies surrounding IABP efficacy, its mechanical circulatory support remains vital in hemodynamic stabilization during critical postoperative periods. Future studies could explore expanding the use of advanced mechanical support devices, such as extracorporeal membrane oxygenation (ECMO), for severe cases.

Outcome Analysis: The study's findings on ICU stays and mortality rates reveal the profound impact of PMI on postoperative recovery. Patients with PMI had a nearly eightfold increase in 30-day mortality compared to non-PMI patients (14.8% vs. 1.8%), emphasizing the urgency of preventive measures. Targeted perioperative optimization, such as beta-blockade and myocardial conditioning, could help mitigate such adverse outcomes.

Conclusion

PMI occurred in 9% of patients undergoing cardiac surgery in this cohort study, with significant impacts on morbidity and mortality. Troponin surveillance, multidisciplinary management, and timely interventions, including IABP placement, are essential to improve outcomes. Anesthesiologists play a crucial role in the early diagnosis and hemodynamic stabilization of PMI, emphasizing the need for vigilant perioperative care.

COI Statement: This paper has yet to be submitted in parallel, presented fully or partially at a meeting, podium, or congress, published, or submitted for consideration beforehand.

This research received no specific funding from public, commercial, or non-profit sectors. The authors declare that they, their relatives, or next of kin have no financial relationships with external companies that could be considered relevant or minor.

Disclosure: The authors declared no conflict of interest. No funding was received for this study.

Abbreviations

PMI - Postoperative myocardial infarction; IABP - Intra-Aortic Balloon Pump; MI - Myocardial Infarction; CABG - Coronary Artery Bypass Grafting; ICU – Intensive Care Unit; CPB - Cardiopulmonary Bypass; TEE - Transesophageal Echocardiography; PCI - Percutaneous Coronary Intervention;

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ORIGINAL ARTICLES

A Comprehensive Systematic Review of Etiology and Risk Factors of Surgical Site Infections

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Abstract

Introduction: Surgical wound infections (SWIs) remain a significant risk to patients due to their high morbidity and mortality rates. Moreover, they pose substantial economic challenges for both developing and developed countries. The global impact of these infections is staggering, with the World Health Organization (WHO) reporting that millions of patients worldwide are affected by hospital-acquired infections annually, with many succumbing to these infections.

This study aims to analyze the incidence of surgical site infections (SSIs) based on the type of surgical intervention, identify the most frequent causes of these infections, and explore effective management strategies. The findings of this study will provide valuable insights into the prevention and management of SSIs, thereby enlightening the medical community and empowering them to improve patient outcomes.

Material and Methods: This study, conducted with meticulous attention to detail, focuses on patients operated on in our clinic from January to October 2024. It will reflect the incidence of SSI according to the type of surgical intervention, the most frequent causes of these infections, and the way of their treatment.

Results: From January 2023 to June 2024, 788 patients were hospitalized, and 408 were operated on in the Surgery Department of the Clinical Hospital of Tetovo. Three hundred fifty were male, and 438 were female. The ages of the patients included in the study ranged from 21 to 81.

Most of the patients were operated on because of cholecystolithiasis, inguinal, ventral, and umbilical hernias, breast cancer, acute appendicitis, and neoplasia of the colon and ileus. From the total number of operated patients (408), the infection of operative wounds was recorded in 49, representing an incidence of 11.76 %.

Conclusion: The findings of this study underscore the serious global implications of SSIs, including increased morbidity and mortality rates and the strain on healthcare budgets. Therefore, the prevention and reduction of these infections should be a priority for all countries, irrespective of their economic status.

Keywords: surgical site infections (SSIs); incidence; risk factors;

Introduction

Nosocomial infections continue to present a significant risk to patients, not only due to their high morbidity and mortality rates but also because of the substantial economic burden they impose on healthcare systems in both developing and developed countries.[1]

The World Health Organization (WHO) reports that millions of patients are affected by hospital-acquired infections annually, with many fatalities resulting from these infections.[2] Concerns regarding bacteria in hospital

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environments causing operative wound infections were first raised in the late 19th century. [3]

Two prominent physicians of the time, the Englishman Joseph Lister and the Hungarian Ignaz Semmelweis hypothesized that bacteria circulating in hospital wards could contaminate patients' wounds.[4]

Both Lister and Semmelweis observed that the risk of puerperal sepsis in pregnant women was significantly higher when medical students who had been in autopsy rooms assisted in deliveries. To address this, they mandated rigorous handwashing with carbolic acid for all medical personnel involved in childbirth and thoroughly cleaning incision sites and wounds. This intervention significantly reduced the incidence of puerperal sepsis. Shortly thereafter, aseptic techniques during surgical interventions were widely adopted and became a mandatory standard in hospitals across Europe. [4, 5]

The introduction of antibiotics in the mid-20th century reduced hospital-acquired infections, particularly surgical wound infections. However, the indiscriminate use of antibiotics soon led to the emergence of multi-drug-resistant bacteria, commonly referred to as "superbugs," which remain a major global health challenge and jeopardize patient safety.[6]

The rise of antibiotic-resistant bacteria led to the establishment of specialized infection prevention teams, initially in the United States and England, and later as a global standard. Nurses have been instrumental in these efforts, playing a key role in infection prevention and control teams since 1959.[7]

For an infection to be classified as nosocomial, it must not be present at the time of hospital admission, and symptoms must appear at least 48 to 72 hours after admission. It is estimated that over 30% of hospital-acquired infections can be effectively prevented through adherence to established algorithms and protocols for infection control.[8]

While all hospitalized patients are at risk of nosocomial infections, the highest incidence is recorded in intensive care units and surgical departments. Pathogenic microorganisms, including bacteria, viruses, and fungi, cause these infections. Among bacterial causes, the most common gram-positive pathogens include *Streptococcus pneumoniae, Streptococcus pyogenes,* and *Clostridium difficile.* Among gram-negative bacteria, *Pseudomonas aeruginosa, Klebsiella pneumoniae, Acinetobacter spp.,* and *Escherichia coli* are the most frequently implicated.[9]

Aim of the study: This is a descriptive study that aims to show the incidence of nosocomial infections in the surgery department of the Clinical Hospital of Tetova. The most frequent causes of these infections, their sensitivity to antibiotics, and the treatment of patients with these infections will be the focus of this study.

Material and Methods:

The study included patients hospitalized in the Department of Surgery from January 2023 to 2024 for treatment. Of the total number of patients admitted to the surgery department in this time period (1088), 788 had surgical intervention due to some surgical disease.

Of the operated patients, 98 of them showed signs of infection of the operative wound. Material was taken from each of them with a swab stick for microbiological examination.

The type of surgical intervention, the patient's age and gender, and underactive complications in the sense of wound infection have been studied and analyzed for study.

At the same time, other disorders related to the patient's health condition and that may impact the risk of infection of operative wounds, such as the level of glucose in the blood, the level of hemoglobin, and the hematocrit before surgery, were taken into consideration to increase the value of this study.

The study excluded patients with existing infectious processes such as abscesses, fistulas, circumscribed or generalized peritonitis, or those who underwent dirty surgical interventions such as anorectal procedures.

All the necessary data for this study were taken from the patient's records and were carefully processed.

Results

Out of the 788 patients operated on in the period from January 2023 to June 2024, 350 were male, while 438 were female. The patients included in the study were from 21 to 81 years old. The surgical interventions performed have been different, but most of the patients were operated on for cholecystolithiasis, inguinal, ventral, and umbilical hernias, breast cancer, acute appendicitis, and neoplasia of the colon and ileus. (tab. 1)

Of the 408 patients operated on during this period, 49 had operative wound infections, representing an incidence of 11.76 %. The highest incidence of surgical wound infection is recorded in patients whose gastrointestinal tract integrity is broken, such as those with colorectal neoplasia, acute appendicitis, perforated ulcers, and mechanical ileus.

The data show that of the 14 patients operated on for acute appendicitis, three of them developed an infection of the operative wound, which represents an incidence of 21%. None of these patients had any co-morbidities and were not treated with therapy that would increase the risk of surgical wound infection.

Of the 11 patients operated on for colorectal cancer, infection of the surgical wound was recorded in four patients, which also represents the highest incidence of 36% in this study. All four of these patients have accompanying problems, such as one with diabetes and cardiorespiratory

	Age (years)												
Diagnosis	**20-30**		**31-40**		**41-50**		**51-60**		**61-70**		**>70**		**Total**
Inguinal hernias	9		23		31		38		14		8		**123**
	M	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	
	9	0	20	3	26	5	36	2	14	0	8	0	
Cholecystolithiasis	9		25		40		37		16		8		**136**
	M	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	
	2	7	3	22	5	35	3	34	2	14	1	7	
Incisional hernias	-		7		9		13		5		3		**37**
	M	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	
	-	-	1	6	2	4	4	9	2	12	3	5	
Appendicitis acuta	8		3		2		1		-		-		**14**
	M	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	
	3	5	1	2	1	2	1	-	-	-	-	-	
Ileus	-		1		1		2		2		2		**8**
	M	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	
Ca colorectal	-		-		-		2		5		4		**11**
	M	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	
	-	-	-	-	-	-	2	-	3	2	3	1	
Perforated gastroduodenal ulcer	-		1		2		1		1		-		**5**
	M	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	
	-	-	1	-	2	0	1	0	1	-	-	-	
Sigmoid diverticulosis	-		-		1		1		-		-		**2**
	M	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	
	-	-	-	-	1	-	1	-					
Ca of the breast	-		11		23		19		6		-		**69**
	M	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	
	-	-	-	11	-	23	-	19	-	6	-	-	

Table 1 Age and gender of the patients included in this study according to the performed surgical intervention

disease, the other with obesity and cardiovascular disease, and the third patient was previously treated with radiotherapy. One of the patients who operated on for colorectal cancer received fresh blood and plasma transfusions one day before the operation.

Of the patients with perforated gastroduodenal ulcers (5 patients), wound infection was seen only in one, thus marking an incidence of 20%.

Of the three patients operated on for sigmoid diverticulosis, sigmoid resection and terminal-terminal anastomosis were performed in two, while in another, a provisional colostomy was opened after sigmoid resection. Only one of these patients registered an infection of the operative wound, which marks an incidence of 33%.

Among the eight patients operated on due to mechanical ileus, the surgical wound infection was registered only in one (incidence of 12.5%). It should be mentioned that in no patient was the continuity of the TGI broken during the surgical intervention, and no one had any accompanying disease or received any therapy that could affect the increase in the risk of infection of the operative wound.

Patients operated on with so-called "clean operations" such as cholecystectomies and inguinal and incisional hernias have shown a much lower incidence of surgical wound infection. Thus, of the 137 patients operated on for Cholecystolithiasis, 16 had an operative wound infection, representing an incidence of 11.7%. Two of these patients had diabetes, four were overweight, and three patients had a reduced blood count but without the need for transfusions.

Of the 122 patients operated on for inguinal hernia, the infection of the surgical wound occurred only in 11 of them, representing an incidence of 8.2%. Two of these patients had diabetes, one overweight and another with cardiorespiratory problems and previously operated on for BPH.

In this period, a total of 38 patients with incisional hernia were operated on, and only 4 of them (10%) had surgical wound infection. Three patients were overweight, while one also suffered from poorly controlled diabetes.

Even in the group of patients operated on for breast cancer, in 8 cases out of a total of 69 operated patients, infection of the operative wound was observed, which marks an incidence of 11.6%.

The incidence of SSI according to surgical intervention is shown in Table 2

Diagnosis	Patients		SSI	
Inguinal hernias	**122**		**11**	
	M	**F**	**M**	**F**
	98	24	8	2
Cholecystolithiasis	138		16	
	M	**F**	**M**	**F**
	35	102	4	9
Incisional hernias	38		4	
	M	**F**	**M**	**F**
	11	26	1	3
Appendicitis acuta	14		3	
	M	**F**	**M**	**F**
	6	8	2	2
Ileus	8		1	
	M	**F**	**M**	**F**
	5	3	2	0
Ca colorectalis	11		4	
	M	**F**	**M**	**F**
	8	3	3	1
Perforated gastro-duodenal ulcer	5		1	
	M	**F**	**M**	**F**
	4	1	1	0
Sigmoid diverticulosis	3		1	
	M	**F**	**M**	**F**
	2	0	1	0
Ca of the breast	69		8	
	M	**F**	**M**	**F**
	0	69	0	8

Table 2. The incidence of SSI according to surgical intervention

Out of a total of 49 patients with operative wound infections, in 40 of them, the interventions were clean, while in 10 (20.8%), others were contaminated or dirty; this is because during the surgical intervention, there was a TGI opening, or damage, to this tract was the reason for the surgical intervention.

The infection of the operative wound was recorded in 49 patients during their hospital stay. In comparison, it was identified in 11 patients after discharge during routine follow-up appointments prescribed by the surgeon.

The most frequent causes of surgical wound infection were the bacteria S. aureus, isolated in 41.2% of patients, and E. coli in 32.5%. Other isolated bacteria were Pseudomonas aeruginosa (12%), Klebsiella (9%) (15%), Enterococcus spp (9%), and Streptococcus (8 %).

Discussion

This study focuses on the incidence of surgical wound infections (SWIs) in the General Surgery Clinic of Tetovo Clinical Hospital from January 2023 to 2024. Cases involving generalized peritonitis due to gastrointestinal (GI) tract lesions, proctological pathologies, and abscesses—whether superficial or in the abdominal cavity—were excluded from this analysis.

Numerous studies' data on surgical wound infections reveal significant variations in their incidence across countries. These differences are primarily influenced by factors such as adherence to infection prevention protocols, the knowledge, and training of medical personnel regarding prevention and treatment, the care and precision exercised by surgeons, the surgical techniques employed, the ventilation systems in operating theaters, and the sterilization and storage methods for surgical instruments and materials.

The incidence of SWIs observed in this study was 12%. Comparatively, other studies report varying rates of postoperative wound infections, with some demonstrating higher incidences, particularly in countries with lower socio-economic standards [10, 11, 12, 13, 14, 15]

Conversely, studies from higher-income countries often report lower infection rates, highlighting the disparity. This study observed aty.

There was a notable difference in SWI incidence between conventional and laparoscopic surgical studies, a finding corroborated by various other studies [16,17, 18, 19]

Factors contributing to an increased risk of surgical wound infections, such as diabetes, obesity, chronic anemia, longer operation duration, extended hospital stays, and postoperative complications, were also evident in this research and are similarly reported in the literature. [20, 21, 22].

Age is another factor influencing the risk of postoperative infections. This study found an increased incidence of SWIs in older patients, aligning with findings from other authors. Gender also plays a role; excluding breast surgeries (where all patients were women), a higher incidence of SWIs was observed in male patients. This gender-based difference is consistent with findings from several other study. [22, 23, 24, 25]

Microbiological cultures of swabs from infected wounds indicated a predominance of gram-positive bacteria, including *Staphylococcus aureus, Staphylococcus spp.,* and *Enterococcus spp. Escherichia coli, Pseudomonas aeruginosa,* and *Klebsiella spp.* were most frequently identified among gram-negative bacteria. Similar studies, particularly in developed countries, also report gram-positive bacteria as the primary causative agents of SWIs [26, 27]17,18, except in surgeries involving the large intestine, where gram-negative bacteria, especially *E. coli,* are more prevalent. [28, 29, 30, 31, 32]

The treatment of SWIs in this study involved thoroughly cleaning the surgical wounds daily and administering antibiotics based on microbiological culture results and antibiograms. However, the data highlight an alarming rise in antibiotic-resistant bacteria, particularly gram-negative bacteria resistant to third-generation cephalosporins such as ceftriaxone. This phenomenon is also widely reported in the literature and underscores the need for effective antibiotic stewardship. [33].

Conclusion

This study underscores the growing challenge of surgical site infections and their multifactorial nature. Prevention requires strict adherence to aseptic principles, proper sterilization, and awareness among medical personnel. Gram-positive bacteria, such as *S. aureus,* dominate most SSIs, while gram-negative bacteria are prevalent in GI tract surgeries.

Effective treatment includes aggressive wound management and antibiotic therapy guided by microbiological results. Future efforts should focus on establishing detailed etiological profiles to define preventive and therapeutic strategies, particularly in surgical departments.

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ORIGINAL ARTICLES

Redo Aortic Valve Replacement After Prior Transcatheter versus Surgical Aortic Valve Replacement: Insights from Western Experience

Arber Aliu*, Klodiana Durici, Ira Lazo, Altin Veshti

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Abstract

Introduction: The demand for reoperation on the aortic valve in Albania is rising, mirroring the increasing average age of the population and the subsequent rise in patients requiring aortic valve surgery. This trend underscores the need for this informative article, which aims to provide insights into the risks and outcomes of aortic valve reoperations, particularly in light of efforts by interventional cardiologists to expand the indications for TAVR to younger and lower-risk patients. Data from the Society of Thoracic Surgeons (STS) National Database reveal results that warrant attention, with concerns over reoperations after TAVR growing, mainly due to the uncertain feasibility of repeat TAVR.

This article presents a novel perspective on the risks associated with surgical aortic valve replacement (SAVR) after prior TAVR or SAVR. It underscores the urgent need to develop an optimal strategy for managing these patients and offers fresh insight.

Material and Methods: Our research, based on a comprehensive analysis of data from the Society of Thoracic Surgeons in the USA's 10-year database, included individuals who underwent bioprosthetic SAVR following prior TAVR and/or SAVR. Our analyses, which included total and isolated SAVR groups, focused on the primary outcome of operative mortality, ensuring the reliability and thoroughness of our study.

Results: The study included 31,106 patients who underwent SAVR. Among them, 1,126 had prior TAVR (TAVR-SAVR), 674 had undergone SAVR followed by TAVR and SAVR (SAVR-TAVR-SAVR), and 29,306 had undergone prior SAVR (SAVR-SAVR). Matched analysis for isolated SAVR cases showed a 1.74-fold higher operative mortality for TAVR-SAVR than SAVR-SAVR (P = 0.020). In our center, 5 cases have been performed in the last two years with excellent results, no losses, and operating times close to the first-time interventions.

Conclusions: This study's findings significantly contribute to the field. They could influence clinical practice, particularly for patients with longer life expectancies and anatomy unsuitable for TAVR. They suggest an initial SAVR approach may provide better results even in necessary surgical re-interventions on the aortic valve.

Keywords: TAVR, SAVR, Aortic Valve Reoperation

Introduction

Since being approved as an alternative to surgical aortic valve replacement, transcatheter aortic valve replacement (TAVR) has increased even in low-risk patients, but at the expense of surgical aortic valve replacement (SAVR). [1] The placement of TAVR remains unclear regarding its long-term effects, as the median age in clinical studies was 80 years. [2]

For patients undergoing valve replacement, we must first assess whether the patient's life expectancy exceeds the expected life expectancy of the prosthesis. [3]

Second, statistics on the long-term viability of TAVR and the prognosis for patients with failure TAVR valves remain unclear.[4]

The prevalence of endocarditis is comparable after SAVR and TAVR, but a limited number of patients with post-TAVR endocarditis had surgical intervention, highlighting

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this distinct trend. [5]

In patients with a 10-year life expectancy, structural valve degeneration, paravalvular leakage (PVL), and endocarditis should increase the likelihood of reintervention. [6]

What should SAVR or TAVR patients choose first? High-volume institutions may redo SAVR after de novo SAVR with the same mortality risk as primary SAVR. Unlike SAVR repair after TAVR, in individuals without adequate aortic root anatomy for redo-TAVR repair. [7]

This article illustrates the risk assessment of redoing SAVR after prior TAVR (TAVR-SAVR) versus SAVR. Reoperation is also performed in patients with a TAVR-to-SAVR (ViV) valve. This research compares the risk of TAVR-SAVR versus SAVR-SAVR.

Materials and Methods

The data for this study were obtained from the Society of Thoracic Surgeons National Database Participant File Search Program (STS) and analyzed at the investigators' institutions.

Patient Population

Data included all SAVR patients with previous aortic valve procedures. Data included the STS Adult Cardiac Surgery Database (2011-2021). The PUF data file had 48,220 patients. [7]

Prior patient procedures (TAVR and SAVR) were based on initial valve procedure, explant type, device, and urgent/emergent cause. Previous non-bioprosthetic valve (mechanical, homograft, autotransplant, unknown, or repair), endovascular procedures, emergency valve explant TAVR, unplanned SAVR, ventricular transplants/assistance devices, aortic root replacement, and non-aortic valve pathology were excluded. After exclusion, 29,306 patients had prior SAVR, and 1800 had prior TAVR. Patients were categorized according to previous TAVR, SAVR, or both.[7]

Results

Current trends in reoperation after TAVR and SAVR Of the 31,106 patients analyzed, 29,306 had a prior SAVR, 1,126 had a prior TAVR, and 674 had a prior SAVR plus TAVR.[7]

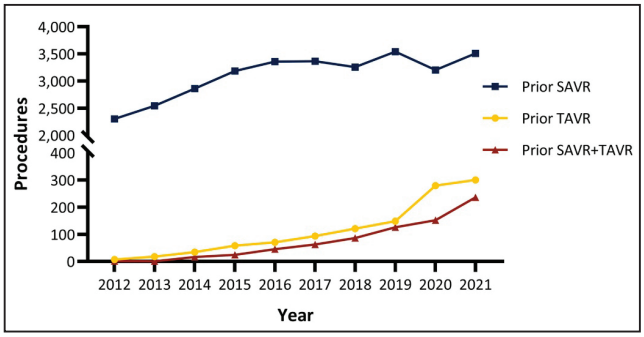

Figure 1. Shows trends over time for each group.[7]

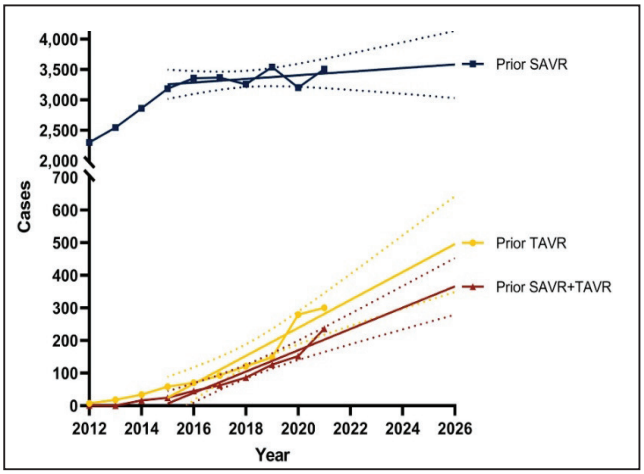

Figure 2. Shows historical trends and forecasts for 2026.[7]

Baseline and operative characteristics for Surgical Reinterventions after TAVR and SAVR

The TAVR-SAVR and SAVR-TAVR-SAVR groups were older and had higher comorbidities, multivalvular disease, and coronary artery disease. The SAVR-TAVR-SAVR group has a similar risk profile to the TAVR-SAVR and SAVR-SAVR groups, although no individual comparisons were made. The TAVR-SAVR group had the

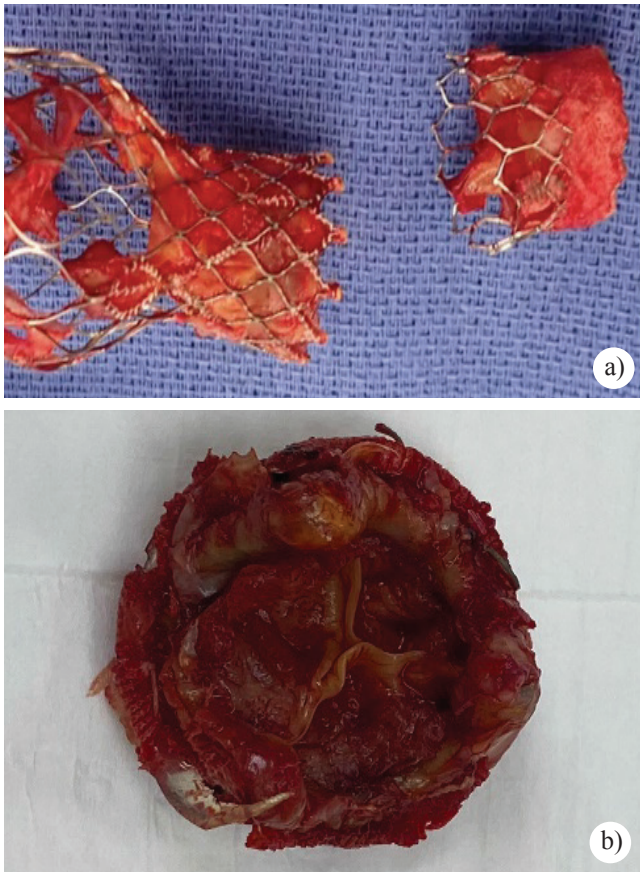

Figure 3: a) Explanted degenerated TAVI b) Explanted degenerated aortic bioprosthesis

oldest mean age at 74 years, followed by SAVR-TAVR-SAVR at 71 years and SAVR-SAVR at 67 years (P < 0.0001). Similar disparities were seen in the frequencies of insulin-dependent diabetes (15% vs. 13% vs. 9%; P < 0.0001) and moderate-to-severe chronic pulmonary disease (17% vs. 14% vs. 12%; P < 0.0001).[8, 9]

Unadjusted Results for Surgical Reinterventions after TAVR and SAVR

TAVR-SAVR patients had the highest operative mortality rate (17%), followed by SAVR-TAVR-SAVR patients (12%) and SAVR-SAVR patients (9%, P < 0.0001). [7]

The rates of severe morbidity for TAVR-SAVR, SAVR-TAVR-SAVR, and SAVR-SAVR were 37%, 31%, and 28%, respectively. SAVR-SAVR had lower component complications, length of stay, and readmission rates than TAVR-SAVR.[7]

Isolated SAVR subgroup analysis

Risk-adjusted analysis showed that TAVR-SAVR had more significant operative mortality (OR: 1.9) and greater morbidity (OR: 1.3) than SAVR-SAVR.[7]

TAVR-SAVR had 11.3% operative mortality compared with 6.7% for SAVR-SAVR (P = 0.020), corresponding to an OR of 1.7 (95% CI: 1.1–2.9). The risk of significant morbidity was similar in all groups (28% vs. 24%; P = 0.223). For patients with severe STS disease, the TAVR-SAVR group had a higher rate of salvage failure (32% vs. 16%; P = 0.008). TAVR-SAVR patients had more excellent rates of renal failure, longer intensive care unit stays, and fewer home discharges. [7, 8, 9]

Discussions

Although TAVR has higher valve reintervention rates than SAVR, previous TAVR/SAVR studies did not report them. In these studies, reintervention rates were calculated without including major risk events (ex, death) during follow-up, even though many patients died within 5 years.

In the NOTION (Nordic Aortic Valve Intervention) study, TAVR patients had 13.9% structural valve deterioration after 8 years, compared with 28.3% for SAVR patients (P = 0.0017). Despite the substantial difference in the rate of structural valve degradation, SAVR and TAVR had identical rates of bioprosthetic valve failure (valve-related mortality, reintervention, or degeneration).[10]

Landes et al. documented 212 redo-TAVRs in 37 centers with a frequency of 0.3% (212/63,876) in one of the most extensive data sets. Despite the positive results, this research did not exclude patients lacking adequate anatomy for redo-TAVR or patients without technical success.[11]

The international EXPLANTORREDO-TAVR registry reported clinical outcomes in 396 patients from 29 sites: 181 (46%) with reoperations and 215 (54%) with re-TAVR. This was the first study to show re-TAVR and reoperation across centers. [12, 13, 14]

In patients over 80 years of age, the American College of Cardiology/American Heart Association recommends transfemoral TAVR initially. [12]

Patients 65-80 should choose TAVR or SAVR after shared decision-making. [15, 16]

Many patients in the latter group will outlive their TAVR valves. The main question remains unsettled for patients with SAVR and TAVR options: "What is the optimal choice of the first valve?" Previous studies of the STS database showed increased mortality after reoperation after TAVR.

FinnValve, *Laakso, et al*. examined the incidence of PVL and the prognostic effect after TAVR. Small PVL by transthoracic echocardiography was associated with worse survival in this multicenter study. Transthoracic echocardiography may underestimate mild PVL, so we grade it from mild to moderate to severe. [17]

In this context, the results of this study provide data for decision-making regarding the patient's management throughout his life. The results demonstrate the importance of carefully evaluating concurrent cardiac pathologies and aortic root anatomy during the initial evaluation for TAVR.

Conclusions

This study highlighted the increased risk of reoperation in patients after TAVR compared to patients after SAVR, providing a crucial perspective for the initial choice of valves in lifelong treatment. The importance of TAVR in treating aortic stenosis has extended to lower-risk patients, leading to a significant projected increase in post-TAVR reoperations over the next decade. Increasing numbers of post-TAVR reoperations reflect an at-risk population high. The multidisciplinary team concept for TAVR remains vital. For patients with a longer life expectancy (especially over 10 years) and anatomy unsuitable for TAVR, an initial SAVR approach may provide better results even in necessary surgical re-interventions on the aortic valve. We emphasize that in our center, the number of mini-invasive interventions for aortic valve surgery is moving towards routine, reducing trauma and hospital stay with minimal mortality and morbidity, making TAVR competitive even for older and high-risk patients.

COI Statement: This paper has yet to be submitted in parallel, presented fully or partially at a meeting, podium, or congress, published, or submitted for consideration beforehand.

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Patient consent: The patient's consent was obtained for the publication of the case.

Abbreviation

TAVR - Transcatheter Aortic Valve Replacement; STS - Society of Thoracic Surgeons'; SAVR - Surgical Aortic Valve Replacement; PVL - Paravalvular Leakage; NOTION - Nordic Aortic Valve Intervention;

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OPEN ACCESS JOURNALS

REVIEW ARTICLES

Surgical Approaches for Aortic Root Aneurysm: A Comparative Analysis of the David and Yacoub Techniques

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Abstract

Introduction: This paper compares the David and Yacoub procedures for valve-sparing aortic root replacement, two leading techniques for treating aortic root aneurysms while preserving the native aortic valve. Both methods aim to avoid prosthetic valve replacement and the need for lifelong anticoagulation.

Material and Methods: We reviewed the technical nuances, clinical outcomes, and long-term durability of each technique, incorporating findings from recent and historical studies. Also, we'd like to present two case reports from our clinic showing the application of the David procedure.

Results: The David procedure involves complete excision of the aortic root and reimplantation of the native aortic valve within a Dacron graft. It offers superior long-term durability and lower reoperation rates, particularly in younger patients and those with connective tissue disorders. In contrast, the Yacoub procedure entails partial root resection and remodeling with preservation of the sinuses of Valsalva, making it a viable option for older patients or those with isolated root dilation.

Conclusions: Both the David and Yacoub procedures are advanced techniques for aortic root replacement, each with unique advantages and challenges. The David procedure, with its excellent durability, has consistently delivered successful outcomes. It is especially beneficial for younger patients and those with connective tissue disorders, supporting its role as a preferred approach for long-term outcomes in this population.

Keywords: Aortic root aneurysm, Valve-sparing aortic root replacement, David procedure, Yacoub procedure

Introduction

Aortic root replacement is a life-saving surgical procedure to manage life-threatening conditions, including aortic root aneurysms, aortic dissection, and aortic valve insufficiency. [1] Among these various surgical protocols created, two of the most influential for this specific surgery are the David and Jacoub procedures.[2] They both aim at preserving the patient's native aortic valve, which eliminates the use of prosthetic valve replacement and long-term anticoagulation therapy. [3]

We discuss the technical aspects and long-term outcomes of these procedures here. We specifically illustrate the practical application of the David procedure with two case reports performed at our clinic last year.

Case 1: *A 73-Year-Old Male with Aortic Root and Ascending Aorta Aneurysm*

A 73-year-old male presented in the emergency department with chest pain accompanied by exertional dyspnea and generalized weakness. He had a three-month history of the

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complaints above, which were progressively worsening.

An echocardiogram revealed an ascending aortic aneurysm. The aorta's angio-CT showed a bulging aortic bulb measuring 67 mm, ascending aorta 69 mm, aortic arch 38 mm, and thoracic aorta 28 mm. The heart exhibited enlarged dimensions and left atrial dilation. Coronary angiography was performed, and no stenosis was found in the coronary arteries.

The patient was transferred to the Cardiac Surgery Department for intervention. Preoperative echocardiography showed the left ventricle with an ejection fraction of 45-50%. The ascending aorta was dilated to around 69 mm, with a tricuspid aortic valve.

Moderate to severe aortic regurgitation and mild to moderate mitral regurgitation were noted. Right atrial dilation and mild tricuspid regurgitation were also reported, with a peak systolic pulmonary artery pressure of 50 mmHg. No pericardial effusion was observed. The patient's medical history was significant for hypertension and permanent atrial fibrillation.

Procedure: General anesthesia was induced, and a median sternotomy was performed to open the pericardium and expose the dilated root of the aorta and ascending aorta. The heart was cannulated, and extracorporeal circulation was initiated. The aorta was clamped. Anterograde arrest was achieved with blood cardioplegic solution directly into the coronary ostia. An insufficient aortic valve was noted, with smooth leaflets and no calcium. The ascending aorta and Valsalva sinuses were resected, and after that, the aortic valve and coronary buttons were isolated. The aortic root was freed from the surrounding structures, and a Dacron n.32 mm graft was fixed to the native aortic annulus with 12 polyester 2.0 sutures. According to the David procedure, the valve was reimplanted in the 32 prosthetic Dacron graft tube with three continuous polypropylene 5.0 sutures. Coronary buttons were reimplanted. A hydrostatic test was performed with cardioplegia without observing any bleeding areas and no aortic regurgitation. The distal anastomosis is carried out with continuous 4.0 polypropylene. The heart is then de-aired, and decannulation is completed. A pacemaker is placed in the right ventricle. The prosthesis is well-positioned. Decannulation is performed after protamine application, and the sternum and operative wound are closed.

Outcome: The patient had an uncomplicated postoperative recovery and was discharged on postoperative day 6. At follow-up, echocardiography showed a stable aortic root with well-preserved valve function.

Case 2: *A 50-Year-Old Male with an Isolated Aortic Root Aneurysm*

The patient presented to the emergency department with chest pain, dyspnea, and palpitations. He reported a history of these complaints for several months. On echocardiography, an aneurysm of the ascending aorta was noted.

He underwent a CT scan of the aorta, which showed an ascending aorta with aneurysmal dilation up to 5 cm. The arch was measured at 3.4 cm. The aorta at the sinuses of Valsalva measured 55 mm, and the aorta at the Sino-tubular junction measured 52 mm.

Mild to moderate aortic regurgitation was noted. The aorta showed normal contrast throughout the entire trajectory.

Coronary angiography was performed and showed no critical stenosis of the coronary arteries. The patient was transferred to the cardiac surgery department for further intervention.

Procedure: Given the patient's young age and the desire to preserve the native aortic valve, the David procedure was selected. The diseased aortic root was excised with

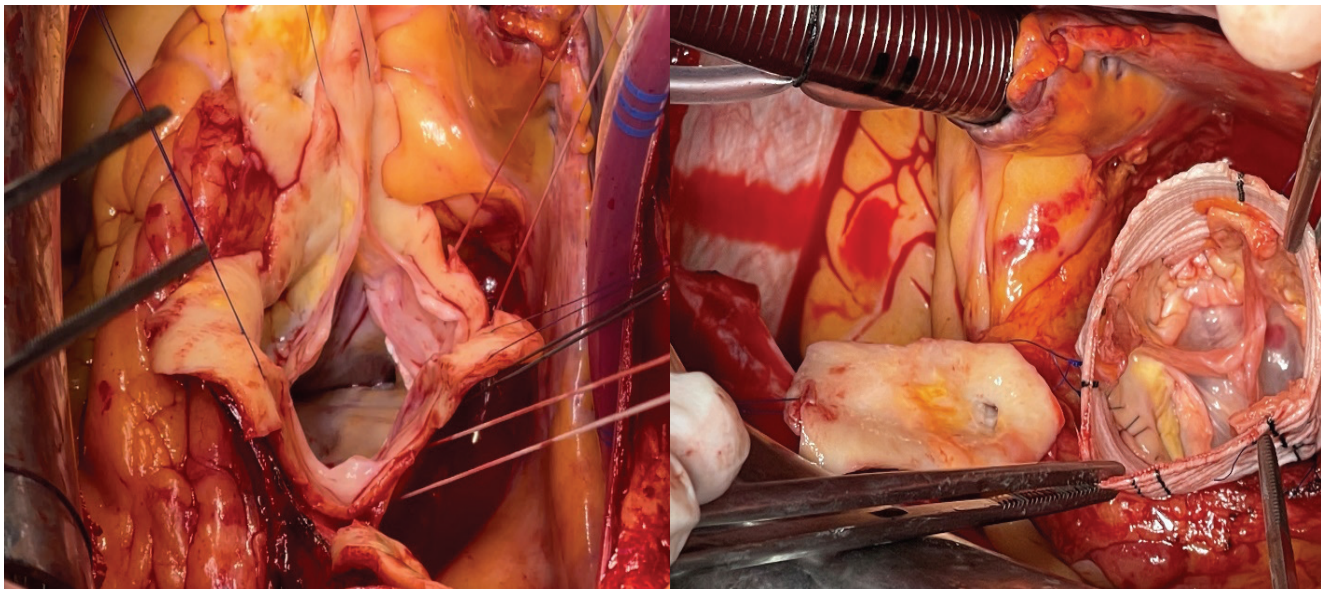

Figure 1. Aortic root excision and reimplantation of the aortic valve into the dacron tube

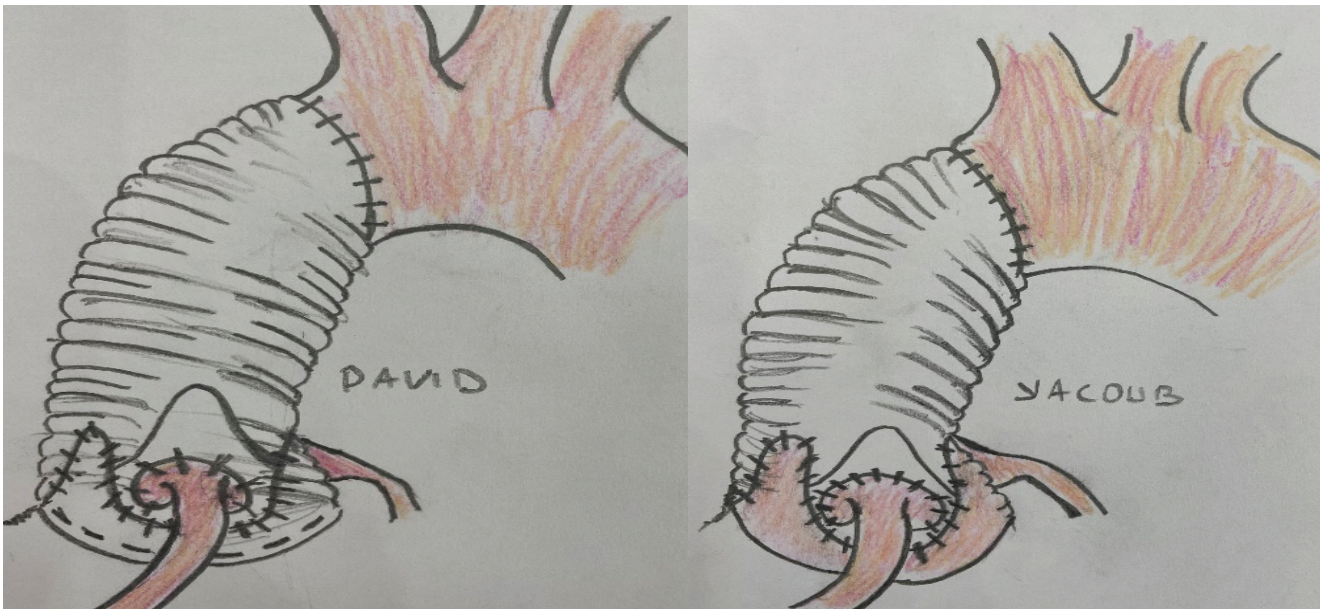

Figure 2. Schematic explanation of the different techniques

utmost care, and the aortic valve was reimplanted into a Dacron tube as described in the first case. The graft was meticulously tailored to support the aortic annulus, and the reconstruction was completed with excellent intraoperative valve competence.

Outcome: The patient's postoperative course was marked by an episode of atrial fibrillation converted into sinus rhythm by Cordarone infusion. He was discharged on the 7th postoperative day. Follow-up echocardiography showed a well-functioning aortic valve with no regurgitation and a stable aortic root diameter.

Discussion

The David Procedure: *Valve-Sparing Aortic Root Replacement: Reimplanting*

The David procedure, popularized by Dr. Tirone David in 1992, is a valve-sparing aortic root replacement procedure for patients with aneurysms of the aortic root associated with a functional but regurgitant aortic valve. [4, 5, 6]

The operation, which has been performed for more than 30 years, involves resection of the aneurysmatic or diseased segment of the aortic root while preserving the aortic valve leaflets.[4]

The aortic valve is reimplanted by carefully repositioning it inside a synthetic Dacron graft, which replaces the cut-out aortic root. The graft is fixed deeply in the aortic annulus to support it, avoiding annular dilatation and ensuring valve competence over the long term. It is tailored to fit the annulus individually. This procedure, by reconstructing the root around the native valve, restores the valve's competence, and regurgitation is prevented.[7]

Long-term studies have established the durability and effectiveness of the David procedure. In a seminal article by David et al., the 20-year survival was 80%, while freedom from reoperation was 92% [4]. Other authors, such as de *Kerchove et al.,* have corroborated these findings. Thus, the operation brought about excellent long-term valve function with meager rates of valve-related complications, even with bicuspid aortic valves [8]. Meanwhile, the role of getting the most perfect outcomes is enormous for the technical experience and patient-related characteristics.[8]

The Jacoub Procedure: *Remodeling of the Aortic Root: Remodeling*

Another innovative technique developed for reconfiguring the aortic root without damaging the aortic valve and aortic root structures, particularly the sinuses of Valsalva, is the Jacoub procedure.

The Jacoub procedure involves the partial excision of the aortic root, not the complete excision as in the David procedure, where aortic root excision is practically total. An artificial graft is sewn directly onto the remaining aortic wall. [10] It is cut out to fit around the native aortic valve, and thus, the essential valvular complex is preserved in its normal anatomical position and function. [10]

Preserving Valsalva's sinuses is one of the cardinal features of the Jacoub operation. This is important in maintaining physiological blood flow and valve dynamics. [10, 11] Also, it allows us to avoid the most extensive re-reconstruction needed in the David procedure.

Lansac's and other surgeons' modification of the original procedure by adding an external ring annuloplasty suggests that it could be an excellent option in patients with dilated aortic annulus to achieve valve competence and prevent dilatation in the future [12].

A study by Lenoir et al. compared reimplantation and remodeling with ring annuloplasty over more than 15

years in 142 patients, with a mean follow-up of 3.9 years (100% complete). They concluded that mid-term outcomes following remodeling or reimplantation were comparable and that implementing an extra-aortic ring annuloplasty effectively stabilizes annular dimensions [13, 14].

Despite the advantages and pitfalls of specific techniques, the outcome greatly depends on the surgeons' experience and skill. Reimplantation has a longer CPB time and aortic clamping time than remodeling, which results in longer learning curves for younger surgeons [15, 16].

The David and Jacoub procedures are entered under the preservation of the native aortic valve. However, they differ in supporting valve and aortic root reconstruction.

The reimplantation technique used in David's operation provides the most secure support to the hypothetically relatively unimpaired aortic annulus, which would prevent dilation in the future and provide physiological competence of the valve for an extended period. In contrast, we can retain the native anatomy of the aortic root through the Jacoub procedure, which may improve the physiological blood flow pattern and potentially reduce stress over the valve leaflets.

Although higher-quality studies with larger population sizes and more extended follow-up data are required for further analysis, the current meta-analysis indicates that patients who undergo reimplantation procedures have a significantly lower late mortality and reoperation rate than those who undergo remodeling procedures. However, no significant difference in early mortality or postoperative moderate to severe aortic regurgitation was exhibited between the two groups [17, 18].

Conclusion

David and Jacoub's procedures remain among the most advanced techniques of aortic root replacement. With varying advantages and corresponding challenges, the David procedure exhibits the solidest and longest-lasting valve durability, especially in younger patients and patient populations with associated connective tissue disorders. The Jacoub procedure is slightly less durable in the long term and offers a less invasive approach, with preservation of the native root anatomy; thus, it can be of value to some patient profiles. Ultimately, the decision to perform one procedure or the other depends on the team's experience and the patient's characteristics.

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REVIEW ARTICLES

Types of Road Traffic Accidents and Emergency Medical Care

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Abstract

Introduction: A traffic accident is when only material damage is caused to the vehicle and track environment, and there are no casualties. RTA represents a significant risk for morbidity and mortality in Kosovo, of which head injury and multiple-site injury increase injury severity.

The anatomical site, mechanism of injury, time to reach an initial health facility, time of the day, patient condition at ED, type of treatment given, GCS at admission, and days spent in the hospital were among independent predictors of management outcome. Targeted approaches to improving the care of the injured victims may improve outcomes.

Thus, the clinician should consider the clinical presentation of RTA and give due attention to the identified contributing factors in managing it. Law enforcers should also emphasize the identified types and mechanisms of accidents. The PubMed database was utilized for article selection, and papers were obtained and reviewed. The ATLS protocol has been developed to manage trauma patients systematically so as not to miss any condition that may kill the patient.

Conclusions: Triage is essential in managing accidental situations and strengthening the primary, secondary, and tertiary health system. To design clinical guidelines, algorithms, and triage protocols at the three levels of health care, all healthcare professionals should be educated and trained with continuing courses in triage, communication, and Basic Life Support -AED, ACLS, PHTLS, BTLS, and ATLS.

Keywords: Traffic accidents, Emergency, Types of automobile accidents, Clinical pattern, Management outcomes

Introduction

Traffic medicine is an interdisciplinary field that includes medicine, psychology, accident research, and vehicle type. Traffic medicine as a term has been used for 40 years by the International Association for Traffic Accident Medicine, founded in 1960 in San Remo, Italy. World Road Safety Health Day is marked on Apr 7, 2004, when hundreds of associations organize events to raise awareness of road traffic injuries as a global health problem. [1]

Traffic medicine is an integral part of the field of concern in forensic medicine because it concerns accidents with fatalities and survivors. Traffic is one of modern humanity's most important economic activities because the routes are the routes by which goods and orders are exchanged. Road traffic accidents are one of the world's leading causes of injuries and fatalities and, hence, represent an essential field of research that uses traffic accident analysis and prediction techniques to determine the key factors contributing to road traffic accidents. [2, 3]

Epidemiology – Causes. The number of road traffic deaths remains unacceptably high. A global estimate

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Photo 1. Traffic Medicine Symbol. The symbol of the International Association for Accident and Traffic Medicine (IAATM) was founded in 1960 in San Remo, Italy, with the new name renamed in 2000 by the (IAATM) as the International Traffic Medicine Association (ITMA).[7]

shows that about 1.35 million people die from preventable accidents, and 50 million are injured by road traffic accidents every year. Road traffic accident is the 8th leading cause of death among people of all ages, while it is the leading cause of death for the age group of 5-29 years. [4, 5]

In 2022, the NHTSA counted 42,795 fatalities in motor vehicle traffic crashes; that is 1.35 fatalities per 100 million vehicle miles traveled. Worldwide, approximately 16,000 people die each day as a result of injuries (5.8 million deaths per year), and projections for 2020 indicate that approximately 8.4 million deaths are expected per year. Six million car accidents occur each year in the United States. [6]

Statistical data concludes that the following are responsible for traffic accidents: inadequate human behavior in 85% of cases, condition of roads, and climatic conditions in about 10%, whereas technical releases with 5%.[8]

Figure 1. DRSABCD is a crucial first-aid action plan that can significantly impact emergencies.

Car accidents are scary, and Road traffic injuries are the leading cause of death for children and young adults aged 5-29 years. Approximately 1.35 million people die each year as a result of road traffic crashes. More than half of all road traffic deaths are among vulnerable road users: pedestrians, cyclists, and motorcyclists. 93% of the world's road fatalities occur in low- and middle-income countries, even though these countries have approximately 60% of the world's vehicles.[9]

Division of traffic accidents

- A traffic accident occurs when only material damage is caused to the vehicle, track, or environment, and no human casualties are reported.
- A traffic accident involves human victims and material damage. Rolling over a moving vehicle is an accidental event in which the car hits or tramples the pedestrian or passive participant in the traffic.
- Traffic accidents can involve both the active participant—the driver or pedestrian in motion—and the passive participant—the passenger in the vehicle or the calm pedestrian.
- We talk about human victims when there are injured or dead participants in the traffic accident, active or passive participants in the traffic.
- We talk about injury or trauma when, in a traffic accident, the entirety of the human body is violated in one or more places. [10, 11]

Types of automobile accidents

Traffic accidents can be divided into several types: loss of control, head-on vehicle collision, vehicle rollover, head-on vehicle accident, multiple collision, unilateral, side, and single collision.

- ***Loss of control*** is most often the leading cause for any driver involved in a traffic accident, which can be caused by illnesses that prompt this reaction to begin, but it depends on the type of car accident that is taking place.

- ***Head-on vehicle collision.*** The driver is driving on the road, and suddenly, another vehicle traveling in the opposite direction comes towards your car due to losing control and colliding head-on with the other vehicle.
- ***Rolling the vehicle.*** Passengers can be ejected when a car, truck, or bus slides off the road or into an abyss or rolls over many times. Unfortunately, there is no time to react immediately, and as a result of the vehicle rolling, the injured may have serious injuries, endangering the lives of the victims. When drivers and passengers are wearing seat belts, survival is significantly increased.
- ***Head-on vehicle accident.*** One of the most dangerous collisions can be when a vehicle collides head-on. But often, this "T" effect occurs on the driver's side of the car, who can suffer broken bones and brain concussions, which can be fatal because these crashes are usually sudden and unavoidable.
- ***Multiple collision vehicle accidents.*** Another highly vulnerable traffic accident is a multi-vehicle crash involving three or more vehicles in a chain of events from a single event, the accidents of which can be associated with minor and serious injuries.
- ***Head-on vehicle accident.*** One of the most dangerous collisions can be when a vehicle collides head-on. But often, this "T" effect occurs on the driver's side of the car, who can suffer broken bones and brain concussions, which can be fatal because these collisions are usually unexpected and unavoidable.
- ***Multiple collision vehicle accidents.*** Another highly vulnerable traffic accident is a multi-vehicle crash involving three or more vehicles in a chain of events from a single event, the accidents of which can be associated with minor and serious injuries.
- ***Vehicle accident with one-sided collision.*** Driving next to another vehicle is quite dangerous if the driver is on a country road or highway. Any distraction from the other driver can cause them to drift out of their lane, resulting in injury.
- ***Vehicle accidents with side-impact collisions.*** When a vehicle is broad-sided (struck sideways by the front of the other driver), it is known as a side-impact collision. **T**his type of car accident most often occurs at an intersection, but to avoid collisions, slow down when approaching the intersection—whether you have a green light or not.
- ***Vehicle accident*** - alone in the vehicle. A car accident involves a vehicle, but that does not mean its driver is always at fault. It is generally caused when a single driver reacts by swerving to avoid hitting something, perhaps an animal or the driver hitting an oak tree, concrete pillar, tree, or utility pole. In these cases, the weather is often a factor that can present unavoidable risks in road traffic. [12]

Management. Before the patient is received at the emergency department, emergency medical services (EMS) provide the hospital with a list of information about the patient. This list includes the patient's mechanism of injury, vital signs, age and sex, and apparent injuries [13, 14]. The advantage of this early warning is that it notifies additional personnel, assures resources are available, and prepares for anticipated procedures and blood transfusions **[**15].

DRSABCD Action Plan

The Royal Life Saving DRSABCD Action Plan is vital in assessing whether a casualty has any life-threatening conditions and if any immediate first aid is necessary. The DRSABCD emergency action plan involves seven steps:

Photo 2. Kosovo Police Service, Kosovo Fire Brigade, SHME 112, Emergency Clinic.

Thus, the Advanced Trauma Life Support (ATLS) protocols put forth a systematic approach to treating trauma patients [16]. The most crucial element of the ATLS protocol is the initial investigation. It is organized based on the lethality of the injuries, from most to least lethal. It is also practical in cases of limited personnel, as it simplifies priorities. Thus, any injury found can be dealt with before moving on to the next step [17]. Primary investigation is split into five core steps: airway examination and protection, breathing and ventilation, circulation examination, disability evaluation, and exposure.

Road traffic accidents are a leading cause of injury and death worldwide, especially in the younger population. [3,18, 19]

Fig 2. The first step of first aid is to preserve the victim's health, treat, stabilize, and transport with medical care to the hospital.

The injury depends on the mechanism of the accident, as specific injuries are associated with particular Accidents. The primary goal in managing these patients is to ensure

that they do not suffer from life-threatening conditions and that, if they do, they are handled swiftly and appropriately. The Advanced Trauma Life Support protocol has been developed to approach trauma patients and manage them accordingly and systematically. [17]

These protocols have helped physicians save countless patients who were afflicted with injuries from traumatic events.[16]

The work aims to summarize the best available evidence on interventions that can reduce road traffic injuries.

Objectives to: Demonstrate the ability to assess and manage emergency airway, breathing, and circulation. Use a defibrillator and administer appropriate therapy. Formulate a list of possible diagnoses and prioritize the assessment elements. Develop a disposition plan after stabilization in the emergency department. Prevent death. Avoid aggravating injuries. Relieve pain and anxiety. Facilitate the arrival of EMS 112 Teams.

Material and Methods

A rapid evidence synthesis approach adapted from the SURE Rapid Response Service was applied to search, appraise, and summarize the best available evidence on effective intervention in reducing road traffic injury. We found 15 articles through a search of different databases mentioned above. After screening for the titles and abstracts of the articles, four of them that satisfy the inclusion criteria were included in the final review. To answer the question under review, we searched for relevant studies from databases, including PubMed and the Cochrane Library [20, 21, 22]

Review findings. Based on our search, we identified systematic review, meta-summary, meta-analysis, and review. Then, we appraised and graded the methodological quality of systematic reviews that are deemed to be highly relevant using AMSTAR 2. [10]

Discussion

Road traffic crashes occur on all continents and in every country. Every year, they take the lives of more than a million people and incapacitate many millions more. Pedestrians, users of non-motorized vehicles – including bicycles, rickshaws, and carts – and motorcyclists in low-income and middle-income countries carry a large proportion of the global burden of road traffic death and serious injury. The elderly, children, and people with disabilities are particularly vulnerable. [2, 6. 19]

Each country should prepare a multisectoral road safety strategy involving agencies concerned with transport, health, education, law enforcement, and other relevant sectors. The strategy should also be multidisciplinary, involving road safety scientists, engineers, urban and regional planners, health professionals, and others. The identified interventions to reduce road traffic accidents were [2]

Legislation and enforcement, Public Awareness/ Education, Speed Control/ rumble strips. Each country needs a lead agency on road safety, with the authority and responsibility to make decisions, control resources, and coordinate efforts by all government sectors – including health, transport, education, and the police. This agency should have adequate finances for road safety and be publicly accountable for its actions. National efforts will be boosted if one or more well-known political leaders can actively champion the cause of road safety. [10]

Specific actions are needed to prevent road traffic crashes and minimize their consequences. These actions should be based on sound evidence and analysis of road traffic injuries, be culturally appropriate and tested locally, and form part of the national strategy to address the problem of road crashes. Road traffic crashes are predictable and, therefore, preventable. To combat the problem, though, close coordination and collaboration across many sectors and disciplines must be achieved using a holistic and integrated approach. While many interventions can save lives and limbs, political will and commitment are essential; more can be achieved with them. [2, 3]

The time to act is now. Road users everywhere deserve better and safer road travel. The mobilization of governments and relevant institutions, especially civil associations, aims to reduce traffic injuries, disability, and mortality in road accidents. Each government will implement stricter measures to reduce road traffic injuries through health promotion campaigns, consolidating the injury surveillance system, and mobilizing different sectors at all levels of society.

The governments of most countries welcome the report of the World Health Organization and the World Bank on the prevention of road traffic injuries, respecting the implementation of the recommendations to the fullest extent possible. Road accidents are considered one of the three main public health problems in every country of the world. This worrying global problem makes us aware that effective and sustainable prevention of injuries and deaths in road traffic can only be achieved through coordinated multisectoral cooperation. To prevent fatal road accidents in the country, healthcare professionals and citizens must know how to provide first aid and basic care and how to treat a road accident victim at the scene. [5, 6]

Knowing the basics of first aid and basic care will undoubtedly help buy time to save the lives of road traffic accident victims.

The mobilization of the Government of the Republic of Kosovo, together with all actors, and a firm long-term policy can affect the prevention and monitoring of road traffic accidents. However, there is still more to do in this direction; however, at least through nationwide policies and strategies, we can influence the reduction of road traffic deaths by 20%. [12, 14]

But one thing is now clear: the mentalities must be changed, and together, we will manage to win this collective and individual fight to save the lives of victims of road traffic accidents. To address this critical problem, the Government of the Republic of Kosovo should create a Road Safety Operations Center or advance or strengthen it, where different sectors of the country can be involved, such as government agencies, non-governmental associations, and society. Civil society manages and monitors road traffic accidents through policies and a nationwide strategy to reduce road traffic accidents. This center should have taken many initiatives to prevent injuries, disability, and mortality in road traffic through awareness campaigns for the country's general population. The motto for the prevention of injuries and deaths in road traffic is "Do not drink alcohol, do not take drugs while driving. It kills you," which should be considered as a campaign to encourage motorists as well as motorcyclists to wear safety helmets while driving.[12]

Conclusions.

Triage is essential in managing accidental situations and strengthening the primary, secondary, and tertiary health system. To design clinical guidelines, algorithms, and triage protocols at the three levels of health care, all healthcare professionals should be educated and trained with continuing courses in triage, communication, and Basic Life Support -AED, ACLS, PHTLS, BTLS, and ATLS.

Recommendations

Triage is an essential component in managing accidental situations, and it institutionally supports the advancement and strengthening of the health system at the primary, secondary, and tertiary levels.

To design clinical guidelines, algorithms, and triage protocols at the three levels of health care.

All healthcare professionals should be educated and trained through continuing courses in triage, communication, Basic Life Support (AED), ACLS, PHTLS, BTLS, and ATLS.

If the following recommendations are to be successful, they should be addressed across a wide range of sectors and disciplines. However, they should be treated as flexible guidelines for adapting to local conditions and capacities.

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OPEN ACCESS JOURNALS

REVIEW ARTICLES

Selection of Prosthesis in Aortic Valve Surgery: Short Review and Trend in our Practice in 10 Years

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Abstract

Introduction: In our country, the predominant condition treated in aortic valve surgery in its early stages was aortic valve disease of rheumatic origin, primarily in patients under the age of 60. In recent decades, due to lifestyle changes, increased average lifespan, and a shift in surgical treatment concepts among the elderly, there has been a noticeable trend towards atherosclerotic aortic valve disease treated surgically. This condition poses challenges in selecting the type of prosthesis for surgical replacement—either bioprosthetic or mechanical. The replacement of the aortic valve, aside from its undeniable benefits for patients, also introduces various complications, such as bleeding related to anticoagulation, thromboembolism, prosthetic endocarditis, and structural degeneration of the prosthesis. These complications vary between the two main groups of prostheses: bioprosthetic and mechanical. In this context, we are confronted with the challenge of selecting the type of prosthesis suitable for each patient.

This paper presents current issues regarding selecting aortic valve prostheses, considering factors related to the prosthesis and the patient. We will also discuss the trends in prosthesis usage in our country over the past decade.

Materials and Methods: We reviewed the types of mechanical and bioprosthetic valves used over the past ten years at our clinic, the Cardiac Surgery Service of the University Hospital Center "Mother Teresa." We consulted articles, studies, and guidelines for managing heart valve diseases from European and American cardiology associations.

Conclusion: The choice of prosthesis for aortic valve replacement remains a current issue, involving considerations of patient-related and prosthesis-related factors. The decision is based on guidelines recommendations, surgical team judgment, and patient preference, following a detailed explanation of the benefits and risks associated with each type of prosthesis.

Keywords: aortic valve surgery, aortic valve, mechanical prosthesis, bioprosthetic prosthesis.

Introduction

According to the European Heart Survey, 28% of patients undergoing valve surgery have had previous valve surgery and are subjected to reintervention. Complications related to the prosthesis are a significant cause of reintervention. Hence, choosing a prosthesis during implantation and caring for patients with valve prostheses are crucial in preventing complications [1].

Aortic valve surgery is our country's most critical part of valve surgery. The predominant condition treated in aortic valve surgery in its early stages was aortic valve disease of rheumatic origin, primarily in patients under the age of 60. In recent decades, due to lifestyle changes, increased average lifespan, and a shift in surgical treatment concepts among the elderly, there has been a noticeable trend towards atherosclerotic aortic valve disease treated surgically. This condition poses challenges in selecting the type of prosthesis for surgical replacement—either bioprosthetic or mechanical. The replacement of the aortic valve, aside from its undeniable benefits for patients, also introduces various complications, such as bleeding related to anticoagulation, thromboembolism,

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prosthetic endocarditis, and structural degeneration of the prosthesis. These complications vary between the two main groups of prostheses: bioprosthetic and mechanical. In this context, we are confronted with the challenge of selecting the type of prosthesis suitable for each patient.

Materials and Methods:

We presented the mechanical and bioprosthetic valve types in numbers and percentages used over the past ten years at our clinic, the Cardiac Surgery Service of the University Hospital "Mother Teresa." We reviewed articles and studies on different types of valves and guidelines for managing heart valve diseases from European and American cardiology associations.

Results:

We reviewed patients operated on in our clinic from 2014 to 2023. The patients were analyzed in total and by year. From 2014 to 2023, we have seen a consistent growth of biological aortic prosthesis implantation compared to mechanical prosthesis. The graphic lines that show the use of the prosthesis intersect in 2021. In 2023, the number of biological aortic prostheses was higher than that of mechanical prostheses.

The overall trend of different studies and the guidelines recommendations favors biological prosthesis use.

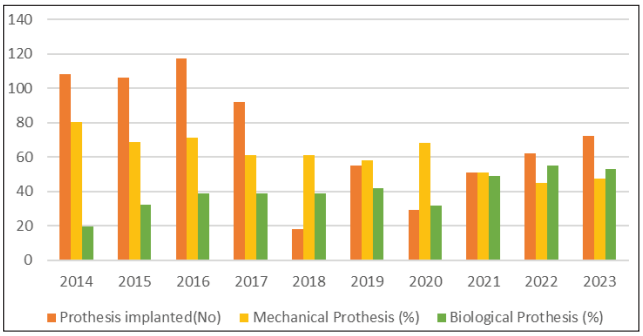

Table 1. Aortic valve prosthesis from 2014-2023

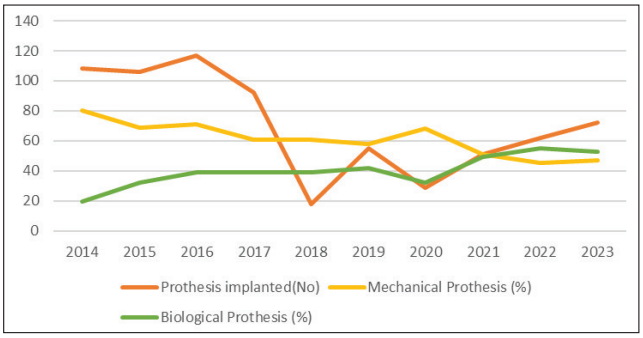

Table 2. Aortic valve prosthesis from 2014-2023

Discussion

Despite continuous improvement in the technology of manufacturing these artificial aortic valve prostheses, the so-called "ideal prosthesis" has not yet been achieved. This ideal prosthesis would have an excellent hemodynamic profile, durability without requiring anticoagulation, ease of implantation, and cost-effectiveness. In these conditions, despite the complications they entail, surgeons are mostly compelled to choose between standard bioprosthetic and

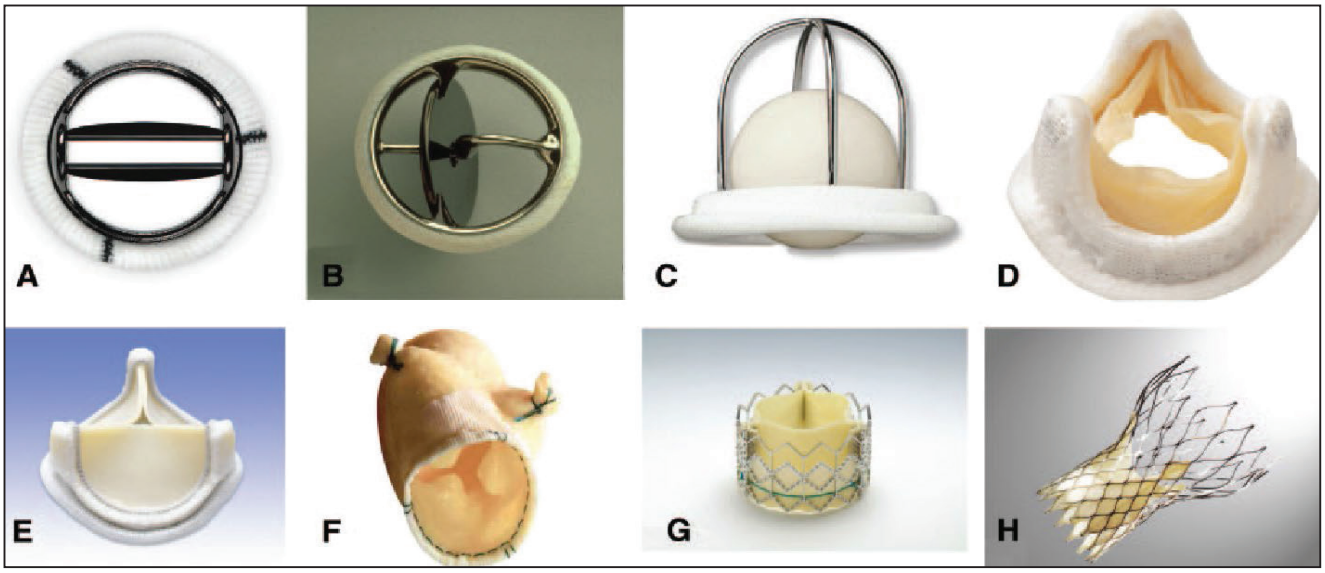

Figure 1. Different types of prosthetic valves.
A, Bileaflet mechanical valve (St Jude); B, monoleaflet mechanical valve (Medtronic Hall); C, caged ball valve (Starr-Edwards); D, stented porcine bioprosthesis (Medtronic Mosaic); E, stented pericardial bioprosthesis (Carpentier-Edwards Magna); F, stentless porcine bioprosthesis (Medtronic Freestyle); G, percutaneous bioprosthesis expanded over a balloon (Edwards Sapien); H, self-expandable percutaneous bioprosthesis (CoreValve). (Circulation2009; 119:1034-1048. Prosthetic Heart Valves: Selection of the Optimal Prosthesis and Long-Term Management. Philippe Pibarot and Jean G. Dumesnil)

mechanical prostheses. Figure 1 illustrates the various types of prostheses, generally highlighting the selection between single or double discs for mechanical and stented for bioprosthetic valves.

Factors influencing the choice of prosthesis are grouped into two categories: those related to the prosthesis and the patient [2, 3]. Regarding factors related to the prosthesis, the benefits and risks of each type of prosthesis are considered. Mechanical and biological prostheses have specific benefits and risks. Mechanical prostheses are durable, which is advantageous when selecting this type for implantation. However, complications, bleeding, and thromboembolism related to anticoagulation remain the most frequent.

On the other hand, biological prostheses do not require anticoagulation, but their main issue is structural degeneration, leading to reoperation [4, 5, 6, 7]. The Edinburgh Heart Valve Trial (EHVT) [8] and the Veterans Affairs Trial (VA) [9] are the most extensive randomized studies comparing mechanical and biological prostheses. Surgeons generally base their decisions on these studies. In these trials, 65 years is the limit for the type of prosthesis that should be used. Above this age, the risk of bleeding due to anticoagulation is significantly higher for mechanical prostheses than younger ones. In contrast, the likelihood of structural degeneration for biological prostheses increases notably under this age.

In our clinic, we primarily adhere to the guidelines of the European Society of Cardiology, considering the types of biological prostheses we have used. According to these guidelines, the upper age limit has been 65 years [10]. Over the years, there has been a trend towards lowering this age limit.

Bartus et al. [11], in a series of 9616 patients, concluded that in recent years, there has been a significant increase in the implantation of biological prostheses even in younger age groups than 65 years, with excellent outcomes in follow-up and lower probability of reintervention. Recent assessments [12,13] have shown the potential for more extended durability of modern biological prostheses and a global trend towards choosing this type for ages younger than 65. Biological prostheses manufactured with the latest technologies may last longer, thus compromising the primary reason for using mechanical prostheses, which is to prevent valve reinterventions. However, the same could also apply to mechanically improved prostheses [14], reducing the need for high international normalized ratio (INR) anticoagulation. It is also known that patients with excellent INR monitoring have a significantly lower probability of bleeding or thromboembolic events.

There is a clear increasing trend in the use of biological prostheses. Brown et al. analyzed the results for 108,687 patients undergoing isolated aortic valve surgery from 1997 to 2006. Year after year, there has been an increase in the use of biological prostheses (BP).

In 1997, BP was implanted in 43.6% of cases compared to 49.9% for mechanical prostheses (PM). By 2007, these numbers shifted significantly, with 78.4% of cases receiving BP and only 20.5% PM (p=0.000001) [15]. This trend is reflected in Table 3.

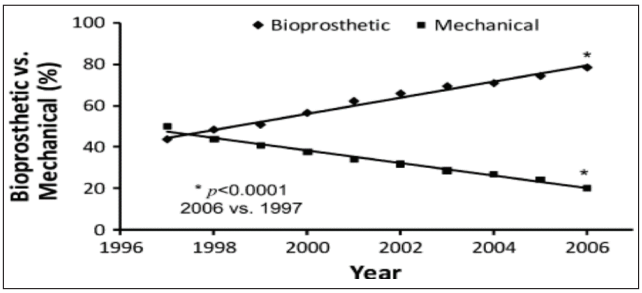

Table 3 Data according to Bioprosthetic vs Mechanical prosthesis (J Thorac Cardiovasc Surg 2009; 137:82-90. Brown et al.)

The trend towards increased use of biological prostheses is also reflected in the guidelines of the European Society of Cardiology for 2021, which lowered the age limit for implantation of mechanical prostheses to under 60 [16]. In addition, the American College of Cardiology lowers the age for mechanical prosthesis implantation even further to 50 [17].

In our country, biological prostheses are being used more than mechanical ones. The graphs above present (see results) data collected on the type of prostheses implanted for patients undergoing aortic valve surgery in our country during the period 2014-2023. There is a clear trend towards increased use of biological prostheses year after year.

Besides age, which remains a crucial factor, we must recognize other factors that do not necessarily change over time. Another significant factor after age is gender, mainly linked to physiological life stages, family planning, and pregnancy. Biological prostheses are recommended for women of childbearing age based on specific studies [18, 19] or general guidelines. Other important factors include the number of previous cardiac surgeries or the need for lifelong anticoagulation, where mechanical prostheses are recommended [19, 20, 21]. Shuli Silberman et al. [21] emphasize social and infrastructural factors that rigorously affect the ability or willingness to follow anticoagulation therapy. Recommendations lean towards choosing biological prostheses in conditions with difficulties adequately monitoring anticoagulation.

Under these circumstances, it seems reasonable to favor the choice of a biological prosthesis for patients who do not require lifelong anticoagulation, for patients over 60-65 years old, for women who wish to remain pregnant, and for patients with monitoring difficulties or contraindications to anticoagulation. On the other hand, mechanical prostheses should be reserved for younger patients, chronic users of anticoagulants, and patients who have undergone reinterventions. In guideline practices, decision-making always focuses more on the patient's own decision after understanding explanations regarding the benefits and risks of each type of prosthesis.

The decision to implant a mechanical or biological prosthesis has been a persistent challenge for patients and

surgeons. Despite having a longer lifespan, mechanical prostheses require lifelong anticoagulation to prevent complications such as thromboembolic events and hemorrhages. Conversely, biological prostheses do not require long-term anticoagulation but have a higher incidence of valve structural degeneration leading to reintervention. Balancing risks and benefits is a challenge that must be personalized for each patient.

Conclusions:

The choice of prosthesis in aortic valve replacement remains a current issue. The process considers factors related to the patient and the prosthesis. In recent decades, there has been an increase in the use of bioprosthetic valves compared to mechanical ones, even in our practice. The decision is based on guideline recommendations, the judgment of the surgical team, and the patient's preference after receiving comprehensive explanations regarding the benefits and risks associated with each type of prosthesis.

COI Statement: This paper has yet to be submitted in parallel, presented fully or partially at a meeting, podium, or congress, published, or submitted for consideration beforehand.

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OPEN ACCESS JOURNALS

REVIEW ARTICLES

Basic Medical Emergency Treatment for Maxillofacial Injuries

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Abstract

Introduction: Maxillofacial trauma presents unique challenges due to the complex anatomy of the face, encompassing vital structures. Beyond physical injuries, these cases significantly impact a patient's appearance and function, necessitating a multidisciplinary approach.

Challenges: Maxillofacial trauma often co-occurs with other injuries, particularly head, chest, and extremity trauma. This increases complexity, with head injuries observed in 7.6-8.9% of facial fracture cases, frequently associated with lower Glasgow Coma Scores. Cervical spine injuries and airway obstruction are significant concerns.

Management: While trauma management has significantly improved mortality rates, maxillofacial injuries in polytrauma patients remain a challenge. Their proximity to the brain, spine, and airway necessitates modifications to standard ABC assessments. These modifications often incorporate DRSABCDE, a comprehensive evaluation that includes airway clearance with C-spine control, breathing, ventilation, oxygenation, circulation, disability-neurologic status, exposure-environment, and body temperature. Each component of DRSABCDE is crucial in the initial management of maxillofacial trauma.

Conclusion: Continuous education and training in triage, communication, and advanced life support (e.g., BLS-AED, ACLS, PHTLS, BTLS, ATLS) are crucial and empowering for healthcare professionals managing maxillofacial trauma in polytrauma patients. This ongoing learning equips them with the necessary skills and knowledge to handle these complex cases effectively.

Keywords: Maxillofacial injuries, airway management, trauma, polytrauma, emergency care, facial fractures.

Introduction

Maxillofacial injuries are a not unusual presentation in emergency departments, ranging from uncomplicated nasal fractures to complicated facial disfigurements. Coping with these injuries poses full-size demanding situations due to the noticeably vascular nature of the place, its involvement in upper airway features, and its proximity to cranial and cervical systems, which are often concomitantly affected. [1, 2]

In contrast to non-maxillofacial trauma, where standardized protocols for airway, respiratory, and circulatory (ABC) control are nicely established, dealing with maxillofacial injuries frequently calls for specialized considerations. Those issues are necessary because of the specific challenges posed by the location's noticeably vascular nature, its involvement in higher airway function, and its proximity to cranial and cervical structures, which might be regularly concomitantly affected.

This evaluation specializes in the initial control of these sufferers, specifically addressing challenges associated with airway protection, cervical spine stabilization, and circulatory support while highlighting controversies and complexities in care.

Maxillofacial accidents can contain superficial lacerations, smooth tissue damage, or fractures and can

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coexist with accidents to the pinnacle, chest, abdomen, cervical spine, or extremities [4].

Head injuries are often the most extreme and call for early interest. The superiority of head injuries in instances of maxillofacial trauma is stated to range between 7.6% and 8.9%, with the hazard growing as the number of facial fractures rises and focus degrees decrease. The Glasgow Coma Scale (GCS) is a precious device for assessing the severity of those injuries.[5]

Maxillofacial trauma is an essential situation that may independently pose existence-threatening dangers or exacerbate the consequences of related accidents. Physicians must examine the affected person promptly, determine the minimum fasting time (MFT), and become aware of extra pathologies to ensure timely and decisive intervention. A multidisciplinary technique isn't simply frequently necessary however vital to deal with the complexities of such cases, making every healthcare professional a valued a part of the team. [6, 7]

The aetiology of maxillofacial injury? The leading reasons for maxillofacial fractures internationally include street site visitors' injuries, falls, assaults, firearm accidents, and sports activities or industrial injuries. Significantly, over 60% of sufferers with maxillofacial trauma (MF trauma) revel in a couple of injuries, often accompanied by way of vast risks of airway compromise.[8]

Injuries related to MF trauma often include the head, face, cervical backbone, and eyes. While nasal and mandibular fractures are the most usually determined accidents in emergency departments, mid-facial and zygomatic fractures are more prevalent in specialized trauma centers. [8]

Patients with extreme facial trauma regularly present with multisystem trauma, contributing to the complexity of their control.

Key associated risks encompass:

- *Airway compromise*: found in approximately 60% of severe cases.
- *Concurrent mind injuries:* taking place in 20–50% of cases.
- Cervical spine injuries: observed in 1–4% of instances.
- *Blindness:* mentioned in zero.5–three% of instances.[9]

Maxillofacial trauma can result from various aetiologies, along with motor car accidents, interpersonal violence, household accidents, athletic activities, animal assaults, business incidents, and gunshot wounds. Knowing those reasons and dangers is vital for developing effective emergency and trauma care control strategies.[10]

Signs and symptoms of Maxillofacial injuries

Maxillofacial accidents can come with several symptoms, including:

- *Altered facial sensation:* Numbness or tingling in affected areas.
- *Deformity or asymmetry:* visible misalignment or distortion of facial functions.
- *Impaired nasal respiratory:* caused by swelling, bleeding, or structural damage.
- *Diplopia* (double vision): as a result of orbital accidents.
- *Missing teeth:* A signal of dental trauma regularly associated with facial accidents.
- *Swelling or bruising* around the eyes: [11]

This can cause imaginative and prescient disturbances or brief impairment. These signs and symptoms require a set-off assessment to decide the harm volume and appropriate control techniques. This proactive technique is critical in coping with maxillofacial trauma efficaciously.[12]

Diagnosis and Emergency Care of Maxillofacial Trauma

Diagnosis: Computed tomography (CT) is the gold general imaging modality for comparing facial trauma. It allows specific visualization of bone and smooth tissues, permitting correct evaluation of the accidents. Excessive or complicated injuries can also require facial reconstruction surgical treatment for the most efficient, functional, and aesthetic consequences. [13]

Emergency Care;

Initial Eye examination: the primary evaluation of maxillofacial injuries ought to consist of a thorough eye examination, assessing:

- Visual acuity.
- Pupillary light reflexes.
- Ocular movements.

Any acute discount in visual acuity warrants a direct referral to an ophthalmologist or maxillofacial healthcare professional for specialized care. [14]

Initial Airway assessment:

A scientific looking, listening, and feeling approach is essential to becoming aware of airway obstructions and assuming complications. Airway management in unconscious trauma sufferers needs to encompass cervical spine safety. High-velocity trauma involving the mandible often disrupts swallowing due to pain and impaired reflex modulation, which may compromise airway clearance. [15]

General Assessment:

The primary evaluation of maxillofacial accidents should prioritize identifying life-threatening conditions. Related accidents, which include cervical spine fractures and widespread head trauma, have to be cautiously evaluated. Following the standard Airway, respiratory, and Flow (ABC) protocol, instant and suitable management ought to be implemented. [16]

History and Treatment of Maxillofacial Trauma

The primary assessment of maxillofacial injuries should prioritize identifying life-threatening conditions. Focusing on:

- Mechanism of injury and any related lack of recognition.
- Visual disturbances, together with impaired eye movement.

- Hearing problems such as vertigo or tinnitus.
- Presence of discharge from the ears or nostril, including blood or cerebrospinal fluid (CSF).
- Nasal respiration problems.
- Ability to bite down without pain and normal alignment of the teeth.
- Any facial numbness or tingling sensations. [17]

Treatment

Surgical intervention is warranted if the injury impairs everyday characteristics3 or consequences in significant deformity. The primary objectives of treatment consist of:

- Controlling bleeding and making sure of a clear airway.
- Treating fractures and stabilizing bone segments.
- Minimizing scarring when viable.
- Preventing complications including double vision, sunken eyes, or cheekbones.
- Identifying and addressing related injuries.

Treatment should commence promptly if the patient is solid and has no neck fracture. [18]

Initial Hospital Care and Usage of the ATLS System:

- A: Airway management with cervical spine protection.
- B: Breathing and ventilation assessment.
- C: Circulation and hemorrhage control.
- D: Evaluation of neurologic disability.
- E: Exposure and environment control.

Regular reassessment is essential to ensure patient balance and development of care. [19]

Algorithm for Trauma Management:

1. *Primary Survey*: Follow the ABCDEs of trauma care.
2. *Resuscitation:* Stabilize vital signs and initiate immediate interventions.
3. *Secondary Survey:* Conduct a thorough head-to-toe evaluation, including the Glasgow Coma Scale (GCS) assessment.
4. *Definitive Care:* Address all identified injuries and implement long-term management strategies. [19, 20]

Management stages for Trauma patients

A. Pre-hospital phase

- Notify the receiving hospital earlier than the trauma patient's arrival.
- Transport of the trauma patients to the nearest, most appropriate facility.

B. In-Hospital Phase

- Implement advanced planning to handle trauma upon arrival.
- Establish protocols for summoning extra clinical assistance as wanted.
- Ensure transfer agreements with verified trauma facilities are in place.
- Take precautions to save you from the spread of infectious illnesses. [21]

Emergency management of Maxillofacial Trauma

Airway Control

- Maintain the airway using chin lift, jaw thrust, and oropharyngeal suctioning techniques
- Manually strengthen the tongue beforehand, even while preserving cervical backbone immobilization.

Key considerations for airway control:

- Risk of the tongue falling back and obstructing the airway
- Presence of blood clots in the mouth or throat.
- Fractured tooth or damaged dental fillings.
- Dentures or different capability obstructions.

Haemorrhage Control

- Manage soft tissue lacerations effectively.
- Provide support for bone fragments and practice brief immobilization as needed.
- Control pain and prevent infections, specifically in instances of compound fractures.
- Initiate fluid resuscitation directly.

Managing mechanical asphyxia:

- D: Dislocation or fractures of the jaws.
- O: Obstruction due to tissue or overseas bodies.
- ok: Soft tissue lacerations functioning as a valve at some stage in inhalation, compromising the airway.
- S: Airway stenosis.
- A: Aspiration of blood clots, fractured teeth, or other foreign objects.

Breathing

Without airway compromise, the focal point shifts to evaluating respiration function.

Keep in mind the six number one reasons for respiratory compromise:

1. Upper airway obstruction.
2. Tension pneumothorax.
3. Open pneumothorax.
4. Flail chest.
5. Massive hemothorax.
6. Cardiac tamponade. [5, 11]

Cervical spine protection

The ATLS principle emphasizes that trauma above the clavicle necessitates a high suspicion of cervical backbone damage. Therefore, sufferers with maxillofacial or craniofacial trauma have to be managed with:

- Apply a cervical spine collar until clinical and radiological clearance.
- Comprehensive neurological examination, including cranial nerve evaluation.
- Assessment for cerebrospinal fluid (CSF) rhinorrhoea. [22]

Hemorrhage control

- Insert large-bore IV strains to update fluid loss and rule out hidden bleeding in the thorax, stomach, or vital organs.
- Assess circulation by monitoring blood volume, cardiac output, cognizance level, skin color, and pulse.

Specific strategies for maxillofacial bleeding:

- *Apply direct pressure* while avoiding blind clamping of wounds.
- Perform ligation or electrocauterization with good enough visualization to prevent nerve injury.
- For *nasal bleeding*, utilize anterior or posterior nasal packing.
- Address pharyngeal bleeding by packing around the endotracheal tube and suturing soft tissues.

Disability (Neurological status)

Evaluating the opportunity for brain damage is critical in trauma cases. A decrease in the patient's level of consciousness may indicate a primary brain injury and is assessed through:

- *Pupil size and reactivity.*
- *Responsiveness:* whether or not the patient is alert, responds to verbal stimuli, reacts most effectively to pain, or is unresponsive.

The Glasgow Coma Scale (GCS) is a treasured scientific device for monitoring neurological reputation following head trauma.

- *A GCS score of 15* reflects a patient who's alert, cooperative, and responsive in motor, verbal, and eye responses.
- *A GCS score of 8 or less* indicates severe cranial trauma. [12, 16, 18]

Complications of Maxillofacial Injuries

Maxillofacial trauma can result in numerous complications, along with:

- Permanent facial deformities and scarring.
- Chronic sinusitis.
- Nerve injury causes loss of sensation, movement, vision, or impairments in aroma and taste.
- Malocclusion (misalignment of the teeth).

Other possible complications include:

- Bleeding.
- Uneven facial symmetry.
- Infections.
- Neurological problems affecting the brain and nervous system.
- Numbness or facial weakness.
- Vision loss or double vision. [23]

Prevention of Maxillofacial injuries

Preventive measures can considerably lessen the danger of maxillofacial trauma:

- *Seat Belts and Airbags:* These are established to decrease accidents and fatalities in motor vehicle injuries.
- *Enforcement* of consequences for alcohol and drug abuse while driving.
- *Speed* reduction for motor vehicles.
- *Helmet use:* Reduces the threat of cranial trauma by eighty percent and offers a sixty percent protective impact for top and mid-facial injuries.
- *Plastic splints* for facial safety. [24]

This study aimed to evaluate a complete literature for accurate analysis, emergency management, and hospital treatment in maxillofacial trauma.

The objectives protected:

- Establishing guidelines to aid decision-making processes in emergency care.
- Identifying the aetiologies of maxillofacial trauma cases presenting to the ED.
- Assessing associated comorbidities to improve overall management strategies.

Materials and Methods

This article highlights the typical medical and radiographic findings in maxillofacial injuries that require professional intervention. It identifies and discusses the signs and symptoms necessitating instantaneous treatment in detail.

A rapid proof synthesis technique, tailored from the positive fast response service, was hired to go looking, appraise, and summarize the fine to be had evidence on interventions to reduce street visitor accidents.

Literature search:

- a systematic seek changed into finished throughout multiple databases, including PubMed and the Cochrane Library.
- 4 of the thirteen articles recognized met the inclusion standards after very well screening titles and abstracts.

Review and Appraisal:

- Systematic critiques, meta-analyses, and different relevant studies were assessed.
- The AMSTAR tool changed into used to appraise and grade the methodological first-class of the systematic reviews deemed reasonably applicable to the research question.

Review Findings

The review synthesized evidence from systematic reviews, meta-summaries, and meta-analyses, offering insights into effective interventions for managing maxillofacial injuries and reducing road traffic injuries. This process ensures that the findings are based on high-quality evidence and can inform clinical practice.

Discussion

The human face performs a vital role as the point of interest of interaction, and accidents to the maxillofacial (MF) location extensively affect a person's physical, functional, and economic well-being. Such injuries can result in extreme morbidity, lack of features, and long-term disabilities.

The primary purpose of treating MF bone fractures is to repair the mechanical integrity of the bone and recover normal muscular function, such as chewing [5].

Following advanced Trauma life support (ATLS) standards, the initial evaluation of MF damage sufferers should prioritize preserving airway patency, a crucial component in managing trauma patients. Airway compromise can result from tongue obstruction, bleeding inside the oropharyngeal cavity, foreign bodies, or fractures. In these cases, endotracheal intubation remains the desired method for securing the airway. In instances wherein intubation isn't always feasible, cricothyroidotomy can be performed, especially in comatose patients [3].

Several studies have investigated styles and elements related to facial fractures. Our look at the mean age of members to be 41.1 ± 18.0 years, without a vast correlation between age and fractures. Fracture occurrence appears more intently connected to trauma severity as opposed to age. Older individuals are susceptible to falls because of comorbidities like osteoporosis, whereas more youthful human beings are more frequently worried about motor vehicle injuries or physical assaults.

Studies from Turkey highlight that three 1% of trauma sufferers admitted to the emergency room had an alcohol consumption, with alcohol consumption related to extra intense accidents [25]. Regularly with earlier research, our findings imply that people elderly 19–30 years are the most affected by MF trauma, with more youthful patients extra liable to avenue traffic accidents and attacks. At the same time, falls are greater accepted among older individuals.

In our analysis, falls accounted for 42.9% of female injuries, while attacks were the leading cause of injuries in adult males (47.1%). This gender-based difference underscores the need for tailor-made preventive techniques.

Most patients supplied to emergency departments with MF trauma are controlled using plastic surgeons, with treatment varying based on the nature and severity of the harm. Each MF trauma case should be approached for my part, and consultation with a skilled plastic doctor has to no longer be on time, irrespective of whether surgical treatment is essential [26].

Maxillofacial injuries, particularly the ones concerning a couple of fractures, may be lifestyles-threatening, requiring spark-off, unique remedy. As MF trauma instances become increasingly more unusual, adherence to ATLS protocols at some point in the preliminary control segment is essential. Following airway and hemorrhage control, a thorough evaluation of imaginative and prescient facial skeletal mobility and meticulous documentation of findings is necessary.

The number one survey of trauma sufferers, guided by ATLS protocols, includes opinions on airway clearance with cervical spine control, respiration, air flow, neurological popularity, exposure, and body temperature (DRSABCDE). This method provides a dependent framework for handling complex trauma instances [27].

MF trauma poses enormous risks due to its lifestyles-threatening nature and the capability for associated accidents. Early diagnosis, timely intervention, and suitable control of each MF injury and other systemic traumas can significantly lessen morbidity and mortality [26].

Conclusion

Continuous schooling and schooling in triage, communique, and advanced life aid (e.g., BLS-AED, ACLS, PHTLS, BTLS, ATLS) are essential and empowering for healthcare experts dealing with maxillofacial trauma in polytrauma sufferers. This ongoing getting-to-know equips them with the necessary talents and knowledge to address these complicated instances efficaciously.

COI Statement: This paper has yet to be submitted in parallel, presented fully or partially at a meeting, podium, or congress, published, or submitted for consideration beforehand.

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REVIEW ARTICLES

Oligodendrocyte Injury in Multiple Sclerosis

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Abstract

Introduction: Multiple sclerosis (MS) is a chronic autoimmune disorder of the central nervous system (CNS), marked by inflammation, demyelination, and significant oligodendrocyte injury. This disease arises from a complex interplay of genetic predispositions and environmental triggers that drive immune-mediated damage to oligodendrocytes and myelin proteins.

This research paper explores the multifaceted aspects of oligodendrocyte injury in MS, ranging from underlying pathophysiological mechanisms to potential therapeutic interventions and translational implications for clinical practice.

Oligodendrocyte damage in MS occurs via multiple mechanisms, including metabolic stress, oxidative damage, and cytokine-induced apoptosis, mainly mediated by interferon-gamma (IFN-γ) signaling. This process exacerbates neuroinflammation and contributes to disease progression. Emerging therapeutic strategies, such as targeting metabolic pathways, reducing oxidative stress, and enhancing autophagy, have demonstrated potential in preclinical studies. Furthermore, stem cell therapies are being explored for their ability to regenerate oligodendrocytes and restore myelin integrity.

Conclusions: The intricate interplay among oligodendrocyte injury, demyelination, and neuroinflammation is central to multiple sclerosis (MS) pathogenesis. Oligodendrocytes safeguard myelin in the CNS, facing challenges from immune attacks to metabolic stress. Understanding oligodendrocyte dysfunction is vital for targeted therapies that suppress immune damage and promote remyelination and CNS repair. MS's etiology,

Keywords: Multiple sclerosis, oligodendrocytes, neuroinflammation, neurodegeneration, demyelination, immune system, apoptosis, cellular metabolism.

Introduction

Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system (CNS) characterized by demyelination, inflammation, and neurodegeneration[6]. It affects over 2.3million people worldwide[7], leading to significant disability and reduced quality of life. The hallmark pathological feature of MS is the destruction of myelin sheaths, primarily by immune-mediated mechanisms targeting oligodendrocytes[8], the cells responsible for myelin synthesis and maintenance. This introduction section will provide an overview of MS epidemiology, clinical manifestations, and the central role of oligodendrocyte injury in disease pathogenesis.

The clinical course of MS is highly variable, ranging from relapsing-remitting to progressive forms, each with unique clinical manifestations and disease progression patterns. Despite advancements in understanding MS pathophysiology and therapeutic interventions, significant challenges remain in managing disease progression and improving long-term patient outcomes.

The central pathological feature of MS is the destruction of myelin, the protective sheath surrounding axons in the CNS[9], leading to impaired nerve conduction and neurological dysfunction. Oligodendrocytes, the myelin-producing cells of the CNS, play a pivotal role in maintaining myelin integrity and neuronal function.[10]

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However, in MS, oligodendrocytes become targets of autoimmune attacks, resulting in their injury, apoptosis, and demyelination.[10] This dysregulated immune response, characterized by infiltrating immune cells into the CNS and activating pro-inflammatory pathways, contributes to the heterogeneous clinical presentation and disease progression observed in MS patients.[11]

Understanding the intricate interplay between immune dysregulation, oligodendrocyte injury, and neuroinflammation is essential for developing targeted therapies that modulate disease activity, preserve neuronal function, and promote remyelination.

This research paper explores the multifaceted aspects of oligodendrocyte injury in MS, ranging from underlying pathophysiological mechanisms to potential therapeutic interventions and translational implications for clinical practice.

Methodologies

This review employed a combination of narrative and critical review methodologies to explore the multifaceted aspects of multiple sclerosis (MS) and oligodendrocyte injury. The narrative review approach was utilized to provide a qualitative summary and interpretation of the existing literature on MS epidemiology, clinical manifestations, etiology, immune dysregulation, and the central role of oligodendrocytes in disease pathogenesis. This narrative approach presented a comprehensive overview of the topic, integrating various theories, mechanisms, and therapeutic strategies related to MS and oligodendrocyte dysfunction.

Additionally, a critical review methodology was applied to analyze the literature's strengths and weaknesses, identify gaps in knowledge, and evaluate the complexities of MS etiology and oligodendrocyte injury. This critical analysis encompassed discussions on the heterogeneity of MS phenotypes, the impact of genetic and environmental factors, and the challenges in developing targeted therapies for MS patients. Emphasis was placed on assessing the quality of evidence, addressing conflicting viewpoints, and highlighting areas for future research and advancements in the field.

The integration of narrative and critical review methodologies allowed for a comprehensive exploration of the literature, providing insights into the diverse aspects of MS pathophysiology, oligodendrocyte function, immune responses, and therapeutic interventions. This approach facilitated a nuanced understanding of the complexities surrounding MS and oligodendrocyte injury, contributing to the broader discourse on neurological disorders and therapeutic strategies.

Etiology

The etiology of MS is multifactorial, involving a complex interplay of genetic, environmental, and immunological factors. Genetic susceptibility, particularly within the major histocompatibility complex (MHC) region, predisposes individuals to MS[12]. Environmental triggers such as viral infections, vitamin D deficiency, and smoking can also influence disease risk[13]. This section will delve into the various factors contributing to MS development and the mechanisms by which they interact to initiate and propagate disease pathology.

Multiple sclerosis (MS) is widely recognized as an autoimmune disorder with a complex etiology influenced by genetic, environmental, and immunological factors. [14]Genetic susceptibility plays a significant role in MS, as evidenced by familial clustering and genome-wide association studies (GWAS) identifying susceptibility loci within the MHC region, specifically the HLA-DRB1 gene[15]. Variants in other genes, such as those involved in immune regulation (e.g., IL2RA, CD40), vitamin D metabolism (e.g., CYP27B1), and myelin biology (e.g., MOG, MAG), also contribute to MS risk and pathogenesis. [16]

Environmental factors further modulate MS risk and disease course. Viral infections, particularly Epstein-Barr virus (EBV) and human herpesvirus 6 (HHV-6), have been implicated in MS pathogenesis, possibly triggering aberrant immune responses and promoting autoimmunity[17]. Low vitamin D levels, commonly observed in MS patients, are associated with increased disease susceptibility and severity, possibly due to its immunomodulatory effects and role in regulating T-cell responses.[16] Other environmental factors, such as smoking, diet, and exposure to pollutants, may also contribute to MS risk and disease progression.[18]

The immunological basis of MS centers on dysregulated immune responses targeting CNS antigens, particularly myelin proteins such as myelin essential protein (MBP), proteolipid protein (PLP), and myelin oligodendrocyte glycoprotein (MOG)[19]. Autoreactive T cells, primarily of the CD4+ Th1 and Th17 subsets, infiltrate the CNS and initiate inflammatory cascades, leading to oligodendrocyte injury, demyelination, and neuroinflammation.[20]

B cells, plasma cells, and innate immune cells (e.g., macrophages, microglia) also contribute to MS pathology through antibody production, cytokine release[21], and phagocytosis of myelin debris.

The complex interplay between genetic predisposition, environmental triggers, and immune dysregulation shapes the heterogeneity of MS phenotypes, including relapsing-remitting MS (RRMS), secondary progressive MS (SPMS), and primary progressive MS (PPMS)[22]. Understanding the etiological factors driving MS pathogenesis is crucial for identifying biomarkers of disease activity, predicting disease progression, and developing targeted therapeutic strategies tailored to individual patient profiles. Ongoing research efforts, including large-scale genomic studies, environmental epidemiology investigations, and immunological studies, continue to elucidate the multifactorial nature of MS etiology and inform precision medicine approaches for improved patient outcomes[23].

Role of Interferon-Gamma Signaling

Interferon-gamma (IFN-γ) is a key cytokine implicated in MS pathogenesis[24]. It modulates immune responses and directly impacts oligodendrocyte function and survival. This section will discuss the role of IFN-γ signaling in promoting oligodendrocyte injury, exacerbating neuroinflammation, and modulating the disease course in MS and experimental models.

Interferon-gamma (IFN-γ) is a pro-inflammatory cytokine produced by activated T cells, natural killer (NK) cells, and macrophages, playing a central role in immune responses and inflammation[25]. In multiple sclerosis (MS), IFN-γ drives neuroinflammation, promotes oligodendrocyte injury, and modulates disease progression. The effects of IFN-γ signaling in MS pathology involve direct and indirect mechanisms that impact CNS homeostasis and immune regulation.[2]

IFN-γ can induce oligodendrocyte apoptosis and inhibit myelin gene expression, impairing myelin production and maintenance[26].

IFN-γ-mediated signaling pathways, including Janus kinase-signal transducer and activator of transcription (JAK-STAT) and mitogen-activated protein kinase (MAPK) pathways, regulate gene expression profiles in oligodendrocytes, influencing cell survival, differentiation, and myelin synthesis.[27]

Chronic exposure to IFN-γ in MS lesions contributes to oligodendrocyte dysfunction and demyelination, exacerbating neurological deficits in affected individuals. [13]

Indirectly, IFN-γ modulates immune responses and neuroinflammation in the CNS microenvironment. It enhances antigen presentation by microglia and macrophages, promotes T-cell activation and differentiation, and amplifies pro-inflammatory cytokine production, including interleukin-1 beta (IL-1β), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α)[13].

The sustained inflammatory milieu driven by IFN-γ contributes to tissue damage, axonal injury, and glial activation, further propagating neurodegeneration and disease progression in MS. [28]Experimental studies using animal models of MS, such as experimental autoimmune encephalomyelitis (EAE), have demonstrated the critical role of IFN-γ signaling in driving disease pathogenesis and severity[29].

Blockade of IFN-γ or its downstream signaling pathways has shown therapeutic efficacy in ameliorating EAE symptoms, reducing CNS inflammation, and preserving myelin integrity[30]. However, the clinical translation of IFN-γ-targeted therapies in MS patients has been challenging, highlighting the complexity of immune regulation and the need for personalized treatment approaches.

The dynamic interplay between IFN-γ signaling, immune dysregulation, and oligodendrocyte injury underscores the importance of understanding cytokine-mediated pathways in MS pathophysiology. Targeting IFN-γ and its downstream effectors represents a potential therapeutic strategy for modulating neuroinflammation, preserving oligodendrocyte function, and promoting remyelination in MS.[31]

Future research efforts to unravel the intricacies of IFN-γ signaling in CNS immune responses and disease progression will contribute to advancing precision medicine approaches for MS patients.

Heterogeneity of Oligodendrocyte Injury

Oligodendrocyte injury in MS exhibits heterogeneity across disease stages, lesion types, and CNS regions.[32]

Acute inflammatory demyelination leads to rapid oligodendrocyte death and myelin breakdown, while chronic demyelinated lesions may show ongoing oligodendrocyte loss alongside attempts at remyelination[33]. This section will explore the diverse patterns of oligodendrocyte injury observed in MS pathology, including differences in lesion activity, remyelination capacity, and clinical implications.

Oligodendrocyte injury in multiple sclerosis (MS) is characterized by its heterogeneous nature, encompassing a spectrum of pathological changes that vary across disease stages, lesion types, and CNS regions[34]. This heterogeneity contributes to the diverse clinical manifestations and disease courses observed in MS patients, ranging from relapsing-remitting to progressive forms of the disease.[35]

Acute inflammatory demyelination represents one aspect of oligodendrocyte injury in MS, characterized by rapid myelin breakdown and oligodendrocyte death in active lesions.[36]Immune-mediated attacks, primarily driven by autoreactive T cells and pro-inflammatory cytokines, destroy myelin sheaths and subsequent axonal injury.[37] The acute demyelination phase is associated with clinical relapses and neurological deficits, reflecting the focal nature of inflammatory activity within the CNS.[38]

Chronic demyelinated lesions exhibit distinct features of oligodendrocyte injury, characterized by ongoing tissue damage, gliosis, and remyelination attempts.[39]

In chronically demyelinated areas, oligodendrocyte loss may persist despite reduced inflammatory activity, leading to persistent axonal dysfunction and neurodegeneration. [40] The balance between demyelination and remyelination processes influences disease progression and clinical outcomes in MS patients.[41]

The heterogeneity of oligodendrocyte injury extends beyond lesion activity to include variations in remyelination capacity and regenerative potential.[42] Some MS lesions demonstrate robust remyelination by recruiting oligodendrocyte precursor cells (OPCs) and successful myelin repair, contributing to functional recovery and neurological preservation.[42] In contrast, other lesions exhibit limited remyelination and chronic demyelination, resulting in progressive disability and neurologic impairment.[42]

The clinical implications of oligodendrocyte injury heterogeneity in MS underscore the need for personalized treatment strategies that target specific disease mechanisms and stages. Biomarkers of lesion activity, remyelination status, and neurodegeneration can aid in disease monitoring and therapeutic decision-making, optimizing patient outcomes and treatment responses.[43] Future research efforts focused on understanding the factors influencing oligodendrocyte injury heterogeneity and promoting regenerative processes will contribute to advancing precision medicine approaches for MS patients.[44]

Regeneration and Repair Strategies

Promoting oligodendrocyte regeneration and myelin repair is a primary therapeutic goal in MS research. This section will review current strategies to enhance remyelination, such as promoting oligodendrocyte precursor cell differentiation, modulating myelin regulatory factors, and targeting inhibitory factors in the CNS microenvironment. Emerging regenerative approaches, including stem cell therapies and gene editing techniques, will also be discussed, as they can potentially restore myelin integrity in MS patients.

Oligodendrocyte regeneration and myelin repair are crucial aspects of disease modification in multiple sclerosis (MS), aiming to restore neuronal function and preserve CNS integrity. Current therapeutic strategies for enhancing remyelination encompass a range of approaches targeting oligodendrocyte precursor cells (OPCs), myelin regulatory factors, and inhibitory factors within the CNS microenvironment.[45]

Promoting OPC differentiation into mature oligodendrocytes represents a key strategy for enhancing remyelination in MS lesionsSkaper[46]

OPCs are abundant in the adult CNS[47] and can differentiate into myelinating oligodendrocytes[48] in response to demyelinating stimuli. Promoting OPC recruitment, proliferation, and differentiation through growth factors (e.g., brain-derived neurotrophic factor, insulin-like growth factor-1), small molecules (e.g., retinoids, thyroid hormones), and epigenetic modulators (e.g., histone deacetylase inhibitors) can stimulate remyelination and improve neurological outcomes in preclinical models.[49]

Modulating myelin regulatory factors, such as myelin-associated inhibitors and signaling pathways, represents another approach for promoting oligodendrocyte regeneration and myelin repair in MS. [50]

Inhibitory factors, such as Nogo-A, myelin-associated glycoprotein (MAG), and oligodendrocyte myelin glycoprotein (OMgp), limit axonal regeneration and remyelination in MS lesions.[51] Targeting these inhibitors using monoclonal antibodies, decoy receptors, or small molecule inhibitors can overcome growth inhibition and facilitate axonal remyelination.[52]

In addition to promoting oligodendrocyte regeneration, targeting inhibitory factors in the CNS microenvironment is critical for enhancing remyelination in MS.[53]The inflammatory milieu in MS lesions, characterized by pro-inflammatory cytokines, chemokines, and reactive oxygen species (ROS), creates a hostile environment for oligodendrocyte survival and myelin repair.[21]

Anti-inflammatory agents, antioxidants, and immunomodulatory therapies can mitigate neuroinflammation, reduce oxidative stress, and create a permissive environment for remyelination processes[54]

Emerging regenerative approaches, including stem cell therapies, hold promise for restoring myelin integrity and promoting functional recovery in MS patients.[55]

Stem cell-based therapies offer potential remyelinating cells and neuroprotective factors, such as mesenchymal stem cell transplantation, neural stem cell grafts, and induced pluripotent stem cells (iPSCs) [56]. Gene editing technologies, such as CRISPR-Cas9, enable targeted modifications of oligodendrocyte genes involved in myelin synthesis, repair, and regeneration.[57]

Despite the progress in regenerative strategies for MS, challenges remain in translating preclinical findings into effective clinical therapies. Optimizing cell delivery, ensuring long-term safety and efficacy, and addressing immune-mediated responses to transplanted cells are ongoing areas of research and development. Integrating regenerative approaches with immunomodulatory therapies and neuroprotective strategies represents a comprehensive approach to enhancing remyelination and improving outcomes in MS patients.

Immunomodulatory Therapies

Immunomodulatory therapies represent the cornerstone of MS treatment, aiming to suppress autoimmune attacks while preserving oligodendrocyte function and promoting repair processes. This section will overview current disease-modifying therapies (DMTs), including interferon-beta, glatiramer acetate, and monoclonal antibodies targeting immune cells or cytokines. The role of immunomodulatory agents in mitigating oligodendrocyte injury and supporting remyelination will be examined, along with emerging immunotherapeutic strategies under investigation.

Immunomodulatory therapies are crucial in managing disease activity, reducing relapses, and slowing disease progression in multiple sclerosis (MS) patients. These therapies target immune system components involved in autoimmune responses against oligodendrocytes and myelin, aiming to suppress inflammation, modulate immune cell function, and promote CNS repair processes.[58]

Interferon-beta (IFN-β) is one of the first-line immunomodulatory therapies approved for relapsing-remitting MS (RRMS).[59] It exerts anti-inflammatory effects by inhibiting pro-inflammatory cytokine production, enhancing anti-inflammatory cytokines, and modulating immune cell activation and migration.[60] IFN-β therapies reduce relapse rates, delay disease progression, and have a favorable safety profile in MS patients, making them widely used in clinical practice.[60]

Glatiramer acetate is another immunomodulatory agent approved for RRMS, acting as a synthetic polypeptide that mimics myelinantigens.[60] Glatiramer acetate modulates immune responses by inducing regulatory T cells, shifting the immune balance toward an anti-inflammatory state, and reducing autoimmune attacks against oligodendrocytes.[61] It is well-tolerated, with efficacy in reducing relapse rates and MRI lesion burden in MS patients.[61]

Monoclonal antibodies targeting immune cells or cytokines represent a more targeted approach to immunomodulation in MS.[62]

Natalizumab, a monoclonal antibody against α4-integrin, inhibits immune cell migration into the CNS, reducing inflammatory infiltrates and relapse rates in RRMS patients.[63] Alemtuzumab, targeting CD52 on lymphocytes, depletes autoreactive T and B cells, leading to sustained remission and disease stabilization in RRMS and active SPMS patients.[64]

Emerging immunotherapeutic strategies focus on modulating specific immune pathways implicated in MS pathogenesis. Siponimod, a selective sphingosine-1-phosphate receptor modulator, regulates lymphocyte trafficking and CNS inflammation, reducing relapses and disability progression in SPMS patients.[65] Ocrelizumab, targeting CD20 on B cells, depletes peripheral B cells and inhibits their migration into the CNS, reducing relapse rates and disability progression in RRMS and PPMS patients.[66]

Combination therapies combining immunomodulatory agents with regenerative or neuroprotective approaches hold promise for optimizing MS treatment outcomes. Integrating disease-modifying therapies (DMTs) with remyelination-promoting strategies, such as OPC-targeted therapies or neurotrophic factors, may enhance CNS repair processes and improve long-term neurological function in MS patients.[67]

Dynamic Interactions within the Glial-Axonal Unit

The glial-axonal unit represents a complex network of interactions between oligodendrocytes, astrocytes, microglia, and neurons. It plays a crucial role in maintaining CNS homeostasis[68] and responding to pathological insults. This section will explore the dynamic interactions within the glial-axonal unit in the context of MS, highlighting bidirectional signaling pathways, trophic support mechanisms, and dysregulation contributing to neuroinflammation and neurodegeneration.

The glial-axonal unit is a fundamental component of CNS function, encompassing oligodendrocytes responsible for myelin synthesis and maintenance, astrocytes providing metabolic and trophic support, microglia mediating immune surveillance and responses, and neurons transmitting electrical signals and neurotransmitters[21]

Interactions within this unit are tightly regulated under normal conditions but become dysregulated in neurological disorders like multiple sclerosis (MS).[69]

Oligodendrocytes play a central role in the glial-axonal unit by ensheathing axons with myelin, facilitating rapid signal transmission, and providing metabolic support to neurons.[70]

Loss of oligodendrocytes and demyelination disrupts axonal integrity, leading to conduction deficits and neurodegeneration in MS lesions. Oligodendrocyte dysfunction triggers a cascade of events, including astrocyte activation, microglial response, and neuronal stress, contributing to disease progression.[10]

Astrocytes, the most abundant glial cells in the CNS[71], interact closely with oligodendrocytes and neurons, modulating synaptic function, neurotransmitter clearance, and metabolic support. Reactive astrocytes in MS lesions exhibit gliosis, characterized by hypertrophy, increased glial fibrillary acidic protein (GFAP) expression, and altered neurotrophic factor secretion[10]. These changes can have neuroprotective and neurotoxic effects, influencing disease outcomes and neuronal survival in MS.[72]

Microglia, the resident immune cells of the CNS733], play a dual role in the glial-axonal unit by surveilling the microenvironment, phagocytosing cellular debris, and modulating immune responses. In MS, activated microglia/macrophages infiltrate lesions, release pro-inflammatory cytokines, and contribute to oligodendrocyte injury and demyelination.[21]activation is a hallmark of neuroinflammation in MS pathology[74], driving disease activity and exacerbating neuronal damage.

Neurons within the glial-axonal unit communicate bidirectionally with glial cells, modulating myelin maintenance, synaptic plasticity, and neurotransmitter release.[75]

Axonal signals regulate oligodendrocyte differentiation and myelination, while myelin-derived signals influence axonal integrity and neuronal survival.[70]Dysregulation of axo-glial signaling pathways in MS disrupts these interactions, leading to synaptic dysfunction, axonal degeneration, and functional deficits.

Understanding the dynamic interactions within the glial-axonal unit is essential for elucidating disease mechanisms and developing targeted therapies for MS. Strategies aimed at restoring glial-axonal communication, promoting remyelination, and preserving neuronal function hold promise for improving clinical outcomes and enhancing quality of life for MS patients. Future research on unraveling the intricacies of glial-neuronal interactions and their modulation in disease states will pave the way for personalized and effective treatments in MS management.

Translational Implications and Future Directions

Translating essential research findings into clinical applications and therapeutic interventions is critical to advancing MS management. This section will discuss the translational implications of research on oligodendrocyte injury in MS, including biomarker development, drug

discovery, regenerative therapies, and personalized medicine approaches. Future directions and challenges in MS research and treatment will also be explored, highlighting the need for collaborative efforts and innovative strategies to address the complexities of the disease.

Translational research in multiple sclerosis (MS) bridges the gap between fundamental discoveries in disease mechanisms and developing effective therapies for patients. Key translational implications of research on oligodendrocyte injury in MS include the following areas:

1. *Biomarker Development:* Identifying reliable biomarkers of disease activity, progression, and treatment response is crucial for optimizing patient management and clinical trial outcomes. Biomarkers related to oligodendrocyte dysfunction, myelin integrity, and neuroinflammation can provide insights into disease pathophysiology and aid in monitoring treatment efficacy.[76]
2. *Drug Discovery and Development*: Drug discovery efforts in MS focus on targeting specific pathways involved in oligodendrocyte injury, demyelination, and remyelination [77].
3. *Regenerative Therapies:* Stem cell-based therapies, regenerative medicine approaches, and myelin repair strategies hold promise for restoring oligodendrocyte function and myelin integrity in MS patients.[78] Clinical trials evaluating cell transplantation, gene editing techniques, and remyelination-promoting factors are ongoing to assess their safety and efficacy in treating MS-related disability.[78]
4. *Personalized Medicine Approaches:* Tailoring treatment strategies based on disease subtype, genetic profile, biomarker status, and patient-specific factors is essential for optimizing therapeutic outcomes in MS.[10] Precision medicine approaches aim to deliver targeted therapies, minimize treatment-related risks, and improve long-term prognosis for individuals with MS.[10] Future directions in MS research and treatment involve multidisciplinary collaborations, innovative technologies, and patient-centered care models.

Discussion

The complex interplay among oligodendrocyte injury, demyelination, and neuroinflammation is fundamental to understanding MS pathogenesis and developing targeted therapies. Navigating the vast MS literature required meticulous review to avoid information overload and ensure a comprehensive grasp of the subject. Synthesizing diverse study designs and methodologies posed challenges, necessitating scrutiny to extract reliable evidence. The evolving nature of MS research demanded continuous updates to incorporate emerging trends and discoveries. Despite challenges, this research strives to contribute meaningfully to MS understanding and management, improving patient outcomes by addressing oligodendrocyte injury comprehensively.

Conclusions

The intricate interplay among oligodendrocyte injury, demyelination, and neuroinflammation is central to multiple sclerosis (MS) pathogenesis. Oligodendrocytes safeguard myelin in the CNS, facing challenges from immune attacks to metabolic stress. Understanding oligodendrocyte dysfunction is vital for targeted therapies that suppress immune damage and promote remyelination and CNS repair. MS's etiology, involving genetic and environmental factors, contributes to heterogeneous oligodendrocyte injury and diverse clinical MS presentations, each posing unique treatment challenges. While immunomodulatory therapies like interferon-beta and monoclonal antibodies have reduced relapse rates, they fall short of addressing oligodendrocyte injury and fostering long-term remyelination.

Emerging regenerative approaches, including stem cell and gene editing therapies, promise to halt disease progression, repair myelin, and enhance MS patient outcomes. The intricate interactions within the glial-axonal unit, encompassing oligodendrocytes, astrocytes, microglia, and neurons, are crucial for CNS homeostasis. Dysregulation leads to neuroinflammation, neurodegeneration, and functional deficits, necessitating comprehensive approaches targeting immune modulation and CNS repair. Bridging research to clinical applications and personalized therapies demands collaboration, innovative technologies, and patient-centered care models. Biomarker development, drug discovery, regenerative therapies, and personalized medicine are key to optimizing MS management and enhancing patient quality of life.

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Abbreviation

MS - Multiple Sclerosis; CNS - Central Nervous System; IFN-γ - Interferon-gamma; MHC - Major Histocompatibility Complex; GWAS - Genome-Wide Association Studies;MOG - Myelin Oligodendrocyte Glycoprotein; RRMS - Relapsing-Remitting Multiple Sclerosis;SPMS - Secondary Progressive Multiple Sclerosis; PPMS - Primary Progressive Multiple Sclerosis; JAK-STAT -Janus Kinase-Signal Transducer and Activator of Transcription; MAPK - Mitogen-Activated Protein Kinase; IL-1β - Interleukin-1 beta; IL-6 - Interleukin-6; TNF-α -Tumor Necrosis Factor-alpha; EAE - Experimental Autoimmune Encephalomyelitis; OPCs - Oligodendrocyte Precursor Cells; OMgp - Oligodendrocyte Myelin glycoprotein; ROS - Reactive Oxygen Species.

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REVIEW ARTICLES

Minimally Invasive Mitral Valve Surgery: Initial One-team Experience and Short Review

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Abstract

Introduction: Minimally invasive mitral valve surgery (MIMVS) is now a widely accepted and more frequently utilized method for patients needing mitral valve surgery. The promoted advantages are less trauma, less bleeding, less pain, and fewer wound infections, allowing faster postoperative and decreased healthcare costs.

Material and Methods: This is a single-center retrospective study. We have collected the records of patients who underwent MIMVS by one team at the Cardiac Surgery Service, UHC" Mother Theresa" Hospital. The patients' data regarding demographic, preoperative, operative, and postoperative variables were collected from the medical records in the hospital. All statistical analyses were performed using IBM SPSS version 24.0 software (SPSS, Inc., Chicago, IL, USA).

Results: Surgical technique includes mitral valve repair or replacement through right lateral mini-thoracotomy, through a small 5-7cm incision in the 4th–5th right intercostal space under direct vision Seldinger technique under transesophageal echocardiogram guidance is used for cannulation, first 3 cases of MIMVS was performed with two venous cannulas – one percutaneous jugular cannula and femoral one, 8 cases underwent single two-stage femoral venous cannulation for venous drainage, femoral arterial cannulation and vacuum assisted cardiopulmonary bypass (CPB).

Conclusion: Minimal-invasive mitral valve surgery is as safe as the standard approach and allows faster recovery with a shorter length of hospitalization, resulting in decreased healthcare costs. We need a more extensive study to confirm the other advantages, but minimal-invasive should be pushed to become a standard approach for mitral valve surgery. An adequate learning curve is mandatory for all the operative teams to achieve all the benefits for the patients.

Keywords: Mitral valve surgery, minimally invasive mitral valve procedures, right lateral Mini thoracotomy.

Introduction:

Since 1996, when Carpentier performed the first video-assisted minimally invasive mitral valve surgery (MIMVS) through a mini-thoracotomy [1], a minimally invasive approach for mitral valve surgery has become an increasing trend. In the past decades, right mini-thoracotomy became a standard mitral valve repair and replacement approach in many centers. Approximately 1 in 3 isolated mitral operations in North America are performed via a less invasive, sternal-sparing approach.[2] Compared to traditional approaches, the potential advantages of MIMVS include decreased postoperative pain levels, faster recovery time, reduced necessity for blood product transfusions, and better cosmetic outcomes compared to mitral valve surgery performed via sternotomy. There were numerous technological developments, such as the methodology of canulation, clamps, and port access, to achieve the best results today [3, 4, 5]. Despite the mentioned benefits, minimally invasive mitral valve surgery was criticized mainly because it is technically more complex and requires a long learning curve that may negatively affect the results of standard surgery. We will present the initial experience of one team using the right mini-thoracotomy with the primary

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goal of making the mini-thoracotomy approach a standard technique. In addition, we will provide a short overview of MIMVS based on recent literature.

Surgical technique: The right mini-thoracotomy (RMT) approach is performed through a small 5-7cm right lateral sub-mammary incision, usually on the 4th or 5th intercostal space. The installation of CPB is realized through percutaneous jugular vein cannulation and open right femoral vein, both under trans-esophageal echocardiography (TEE). The arterial route of canulation used was the open right femoral artery.

There are different techniques to occlude the aorta and protect the heart. We use a transthoracic clamp (TTC). Using the TTC technique, the aorta is occluded through a transthoracic direct clamp inserted through an additional port or the working incision. The antegrade warm blood cardioplegia is delivered through a standard cardioplegia cannula secured with purse-string sutures in the ascending aorta. With the heart arrested on cardiopulmonary bypass, the left atrium is opened adjacent to the interatrial groove. The view of the left atrium and mitral valve is generally sufficient to repair or replace the mitral valve. Upon completion of the mitral procedure, the left atrium is closed in a standard fashion. De-airing of the heart is achieved. Any residual air on the echo can be aspirated through the aortic root vent. The aortic cross-clamp is removed once the heart is well de-aired on echo. The patient is gradually weaned from cardiopulmonary bypass after the placement of pacemaker wires on the anterior surface of the heart. Only one pleural drain is placed. The wound is closed as usual. (fig.1)

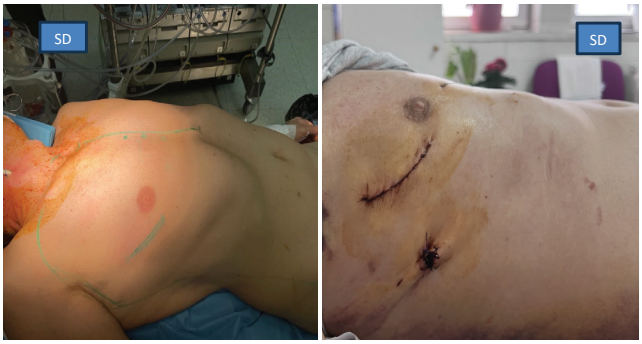

Figure 1. Dumani S: Photos before incision and after intervention

Materials and Methods:

This is a single-center retrospective study. We reviewed the records of all patients who underwent MIMVS by one team at the Cardiac Surgery Service of UHC "Mother Theresa" between May 2022 and April 2024. The patients' information regarding demographic, preoperative, operative, and postoperative variables was collected from the medical records in the hospital. All statistical analyses were performed using IBM SPSS version 24.0 software (SPSS, Inc., Chicago, IL, USA). Categorical variables are summarized with frequencies and percentages. Normally distributed variables were reported as mean ±standard deviation, and non-normally distributed variables were reported as median with range. The endpoints of our study include early mortality, significant postoperative complications, and postoperative time-related outcomes and recovery. We also will provide an overview of the recent literature about MIMVS.

Results:

The mean age (±SD) of cases is 61 years (±8), with a minimum age of 46 and a maximum age of 73.

Among 11 patients, 54.4% are male, 45.5% are female, 54.5% were diagnosed with severe mitral regurgitation, and 18.2% had mixed pathology mitral valve.

The majority of patients, precisely 90.9% (10), correspond to the class I of heart failure, while only 9.1% (1) belong to the class II of heart failure.

The echocardiographic data are presented in Table 2, which lists the risk factors for the patient's conditions, such as hypertension, diabetes mellitus, dyslipidemia, and smoking. Hypertension is the most common risk factor, followed by dyslipidemia and smoking. Almost all patients had preserved left ventricular function, with an average value of EF 60% (±6), a minimum of 47%, and a maximum of 65%.

Most patients (54.5%) underwent minimally invasive mitral valve replacement (MIMVR). Mitral valve repair, including annuloplasty, P2 resection, and "Alfieri suture," is performed in 5 patients. Regarding the CPB and aortic clamp time, the mean (±SD) time of CPB is 128 (±32) minutes with a minimum of 87 minutes and a maximum of 212 minutes. The mean (±SD) time of the aortic clamp is

Demographic data		Count	%	Mean(±SD)	Minimum	Maximum
Sex	Female	5	45.5 %			
	Male	6	54.5 %			
Age				61(±8)	46	73

Table 1: Demographic data of the patients. (Sex and age)

Preoperative data		**Count**	**%**	**Mean(±SD)**	**Min.**	**Max.**
Diagnosis	Mitral regurgitation	6	54.5%			
	Mitral stenosis	1	9.1%			
	Rheumatic mitral disease	1	9.1%			
	Mitral endocarditis	1	9.1%			
	Steno-insufficiency mitral valve	2	18.2%			
NYHA	I	1	9.1%			
	II	10	90.9%			
EF %				60(±6)	47	65
Left Atrium(mm)				45(±6)	39	54
Pulmonary systolic Pressure(mmHg)				37(±8)	23	45
Thickness Posterior Wall(mm)				10(±1)	8	11
Thickness Septum (mm)				11(±1)	9	13
Tele diastolic Diameter(mm)				51(±7)	39	68
Tele systolic Diameter(mm)				38(±3)	32	44
Mitral annulus Calcification	No	7	63.6%			
	Yes	4	36.4%			
Euroscore				1.27(±1)	1.04	1.41
Risk factors	Hypertension	10	91%			
	Diabetes Mellitus	1	9%			
	Dyslipidemia	6	55%			
	Smoking	4	36%			

Table 2: Preoperative data of the patients presented as number/ percentage or mean(±SD) and echo graphic data.

Operative data		**Count**	**%**	**Mean(±SD)**	**Min.**	**Max.**
CPB time, min				128(±32)	87	212
Aortic clamp time(min)				95(±24)	62	142
Intervention	Annuloplasty with Edwards ring and P2 resection	4	36.4%			
	Mitral repair, according to Alfieri	1	9.1%			
	Mitral replacement (MIMVR)	6	54.5%			
P2 Resection	No	7	63.6%			
	Yes	4	36.4%			
	None	5	45.5%			
Prosthetic Valve type	Bioprosthetic (SJM Epic Supra Valve)	1	9.1%			
	Mechanical valves (SJM Masters)	5	45.5%			

Table 3: Operative data of the patients presented as number/ percentage (type of intervention, p2 resection, prosthetic valve type) or mean(±SD) (CPB time, AC). CPB time- cardiopulmonary bypass time; AC- aortic clamp; MIMVR- minimally invasive mitral valve replacement.

Postoperative data		Count	%	Mean(±SD)	Min.	Max.
ICU(hours)				30(±11)	27	46
Hospitalization (days)				12 (±8)	7	30
Postoperative hospitalization (days)				8(±5)	5	18
Respiratory Assistance time (hours)				8(±4)	6	14
Postoperative complications	Pulmonary dysfunction	1	6.7%			
	Renal insufficiency	1	6.7%			
	Hemorrhage	2	13.3%			
	New Atrial fibrillation	2	22.3%			
	Infection	1	6.7%			
	Perceptual disorders	2	13.3%			
	Exitus	1	9.1%			

Table 4: Postoperative data of the patients presented as number/ percentage (postoperative complications) or mean (±SD), ICU- intensive care unit

95(±24) minutes, with a minimum of 62 and a maximum of 142 minutes.

One patient died due to a massive hemorrhage because of an atrioventricular sulcus rupture. The remaining patients received intensive care in the ICU for an average of 30 hours (±11). They stayed hospitalized for 5 to 18 days after the intervention, with an average hospital stay of 8 days (±5), and the respiratory assistance time ranged from 6 to 14 hours, averaging 8(±4) hours. The recovery early after the intervention, two to three days after the intervention, was notably much easier than the patient who underwent a standard sternotomy. Based on the analyzed data, the average overall hospitalization time was 12 (±8) days.

Discussion

Minimally invasive mitral valve surgery (MIMVS) was initiated in the middle 1990s, but systematic adoption of the technique has been limited. MIMVS has become a treatment for many patients with MV surgery: in the United States, its use has increased from 11.9% in 2004 to 20.1% in 2008, and in Germany, from 13.1% in 2004 to 45.2% in 2013 and more than 50% in 2017[6].

Skepticism about using MIMVS, even the increasing trend, derives from the fact that this approach is technically more complex, requires a long learning curve, and may negatively influence the standard approach results. We will represent some of the studies and meta-analyses according to the results, polemics, and complications of MIMVS.

The most challenging aspect of the surgical complexity is the possible development of serious complications associated with peripheral cannulation: retrograde aortic dissection is a rare but life-threatening complication that may arise from this cannulation method. Heart-Port World Wide Registry reported aortic dissection in 11 of 610 patients undergoing Port-Access surgery, which was superior to the incidence of aortic dissection after conventional cardiac surgeries [7].

Safety of the surgical technique: In 1998, Mohr et al. [4] published a preliminary study revealing severe complications in a series of 51 patients who underwent minimally invasive surgeries. The hospital mortality rate was 9.8%, the transient ischemic attack rate was 7%, acute retrograde aortic dissection was reported in 3.9% of patients, and 5.8% of patients required reoperation for para-valvular leakage. Aortic dissection events were probably caused by the guide wire transit that created an intimal tear, increased by the retrograde flow that led to a complete vessel dissection. The rate of these complications at the early stage of their experience was related to the limited surgeon and team expertise. The same team published several reports in the following years with excellent long-term results, a low rate of complications, and drastically decreased conversion to sternotomy [8]. After these initial studies, the efficacy and safety of the minimally invasive approach were evaluated with a few randomized trials and several meta-analyses or propensity score-matched investigations.

In 2005, Dogan and colleagues [9] published the first prospective randomized study about the video-assisted Port-Access technique, comparing it to standard surgery: in this study, the Port-Access technique was reported to be more time-consuming, even if the differences were not statistically relevant. The CPB and cross-clamp time were similar. A significant result was that no patient demonstrated clinical evidence of myocardial ischemia, indicating a similar quality of myocardial protection in both techniques. Furthermore, no permanent neurologic deficit was described. Before this study, Schneider and colleagues [10] had reported a similar experience, not observing significant differences in the stroke rates between patients undergoing Port Access or conventional surgery. It is essential to point out that before randomization, the surgical team had minimal experience with the minimally invasive port access technique, and some of the technical problems reported in these series may be attributed to the learning curve.

Neurological events: Gammie and coauthors [11], with their analysis of the STS database, reported a markedly higher rate of permanent perioperative stroke in patients who underwent minimally invasive surgeries compared to the conventional sternotomy group. Supplementary analyses demonstrated that patients who underwent MIVS without aortic occlusion were at higher risk of stroke (on beating- or fibrillating-heart); meanwhile, femoral cannulation was not independently related to increased risk of stroke. In addition, in 2011, a meta-analysis (Cheng et al.) including [12] comparative studies compared MIMVS clinical outcomes and resource utilization to conventional open mitral valve surgery. They reported that the 30-day risk of stroke (2.1% vs. 1.2%) and aortic dissection/injury (0.2% vs. 0%) were significantly increased for MIMVS compared to the standard procedure. The minimally invasive method increased cross-clamp, cardiopulmonary bypass, and procedure times. Still, ventilation time and length of stay in the intensive care unit and hospital were reduced.

In 2014, a systematic review and meta-analysis [13] by Sunderman et al. investigated more than 20.000 patients who underwent MV surgery from 45 different studies. An important outcome was that stroke rate (1.7% vs 1.6%) and all-cause mortality up to 30 days were similar in MIMVS and classic MV surgery. In contrast to the precedent-cited studies, specifically the meta-analysis by Grammie and Cheng and colleagues, [11, 12] this report showed that the MIMVS group of patients did not have an increased stroke rate compared with the conventional surgery. The initial negative results probably resulted from the learning curve in the centers involved in the earliest reports. In our study group, we did not have stroke events, but we had longer operative time, which is logically related to the fact that it is just the beginning of the experience. Nevertheless, this does not give the impression of predicting a negative clinical impact.

Bleeding, Transfusion, and revision for hemorrhage: A reduction in postoperative hemorrhage and transfusion requirements has been suggested as a potential advantage of minimally invasive valve surgery. This benefit is essential given the significant morbidity and mortality associated with transfusions. Smaller incisions should theoretically reduce postoperative bleeding, and transfusion requirements should be revised for bleeding. There is no significant difference in blood losses, blood product transfusions, or chest tube drainage [8, 14, 15, 16] despite longer CPB times that disfavor MIMVS. In a prospective, randomized trial, Dogan et al. [9] found a significant decrease in postoperative chest tube output in the mini group compared with the entire sternotomy group.

The right mini-thoracotomy was associated with 51% fewer blood products than a conventional sternotomy [17]. In addition, Cohn et al. confirm that patients undergoing minimally invasive valve surgery are transfused 1.8 units less than a traditional cohort [18]. In our group, we had two revisions for bleeding. One of them was the disruption of the atrioventricular sulcus, which resulted in fatalities, and we think that is unrelated to the approach. The group is small, and we will focus more on this topic in the future.

Atrial Fibrillation: It has been suggested that a less traumatic surgical approach would be a less potent trigger of postoperative AF. Meta-analysis of four eligible studies showed no significant difference between minimally invasive and sternotomy approaches. Asher et al. [19] addressed this question in a cohort of 100 patients having elective primary minimally invasive MV surgery compared with a control group undergoing conventional sternotomy. They found a similar prevalence of postoperative AF using either method. There are lots of reports that support a lower incidence of AF related to MIMVS. Some clinical outcomes, including atrial fibrillation, were significantly improved with MIMVS [12]. Postoperative new AF was inferior in the MIMVS group, probably related to reduced right atrial manipulation [13]. The PAIR registry reported a 10% incidence of new-onset AF with the port access technique, which is lower than expected for sternotomy [19]. In our group, we had only two patients who had a new onset of atrial fibrillation.

Wound infections: The incidence of wound infections and septic complications is lower with a thoracotomy than with a median sternotomy. Grossi et al., in a case-control study, reported a decreased incidence of wound complications [17]. Thirty-five studies, two randomized controlled trials, and 33 nonrandomized studies suggest that mini-MVS may be associated with decreased bleeding, blood product transfusion, atrial fibrillation, and sternal wound infection [12].

Pain, quality of life, and recovery time: Compared with a complete sternotomy, thoracotomy incisions are associated with less pain, discomfort, and postoperative analgesics [15]. Cohn's data show less pain in the hospital and after discharge, less analgesic usage, greater patient satisfaction, and a return to regular activity 4.8 weeks ahead of sternotomy patients [18]. Cheng et al., in an extensive review, reported that between several clinical outcomes, the time of postoperative recovery was significantly improved with MIMVS in terms of time to return to regular activity and scar cosmetic results [12]. Even though our group was small, almost all patients were more satisfied than those with standard sternotomy, and the postoperative activation was much more accessible.

Hospital Stay and Costs: The minimally invasive approach significantly reduced mean and median hospitalization costs, consistent with the observed difference in hospitalization duration between the groups. In addition, patients undergoing MIMVS had faster rates for independent ambulation and time to independent sit-to-stand activity [15,17,20]. Some reported benefits of MIMVS include decreased intensive care unit and total hospital length of stay, faster physical rehabilitation, and decreased overall hospital resource use [21].

Mortality: Several comparative mini vs complete sternotomy studies evaluating mortality showed no significant difference between minimally invasive and conventional approaches [15, 19, 21, 22, 23, 24]. Mihaljevic et al. compared 474 minimally invasive mitral operations (mostly lower sternotomy and right parasternal) with 337 median sternotomy procedures. The perioperative mortality was 0.2% for the minimally invasive group, and this is compared favorably with 0.3% in the sternotomy patients. However, the MIMVS patients were found to be a lower-risk group (better ejection fraction, more repairs, less symptomatic), and no attempt was made to adjust for these differences [23].

Furthermore, Grossi et al. matched 100 consecutive patients undergoing minimal invasive aortic and mitral valve surgery over a 2.5-year period (through either a 3rd or 4th interspace incision) to patients having the same valve surgery via a sternotomy [24]. They demonstrated no significant difference in hospital mortality (3.7% versus 3.4%) between groups, even though mean CPB times were 30 min longer in the minimally invasive group.

It is essential to remember that adopting a new surgical technique requires a learning curve, so if this point is not considered, the results are only partially realistic. Casselman et al. [25] defined the learning curve at 50 consecutive MIVS cases, finding favorable outcome data associated with MIMVS. The 30-day mortality rate of a series of 500 patients was 1.4%, the primary stroke rate was only 0.8%, and no aortic dissections occurred. These results significantly contrast with the precedent literature, and the main reason for these differences is that only in this study were surgeons fully experienced with minimally invasive mitral valve surgery (at least 100 patients operated with this technique). Later, in 2018, a multicenter propensity-matched study [26] of 1278 patients from England proved no difference between MIVS and sternotomy regarding early and late outcomes out to 8 years.

Conclusions:

MIMVS has been proven to be a safe alternative to the conventional complete sternotomy approach with low perioperative morbidity and short-term mortality. Reported benefits of MIMVS include decreased postoperative pain, improved postoperative respiratory function, reduced surgical trauma, and greater patient satisfaction. The operative team must have An adequate learning curve to achieve all patient benefits.

COI Statement: This paper has yet to be submitted in parallel, presented fully or partially at a meeting, podium, or congress, published, or submitted for consideration beforehand.

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CASE REPORTS

Traumatic Asphyxia due to Automobile Accident. A Case Report

Elona Markeci*, Admir Mustafa

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Abstract

Introduction: Traumatic Asphyxia is probably much more common than the surgical literature shows and should always be kept in mind as a possible complication of injuries of the thorax and /or upper abdomen. Traumatic Asphyxia or Perthe's syndrome is a result of a sudden and severe trauma of the thorax and /or upper abdomen. We report a case of traumatic Asphyxia due to an automobilistic accident.

Our patient is a 62-year-old male who was brought to the emergency room due to thorax trauma related to a bicycle accident. He got under a van from one side, and while the shaft of the van rotated, it pulled and crushed the patient between the body of the van and the shaft. There was no direct trauma history on the face and neck area of the patient. In our case, we found associated injuries such as a fracture of the right 7th rib, displaced fracture of the right tibia, and bilateral pulmonary contusion.

In our case, supportive therapy and specific treatment for the right tibial fracture were performed.

Conclusion: Perthes syndrome should be considered in patients presenting with the associated ecchymoses mask with cutaneous petechial hemorrhages and subconjunctival bleeding as a complication of compression of the thorax. The outcome is variable depending on the severity and duration of compression. When characteristic findings of traumatic Asphyxia are detected in traumatic patients, other organ pathologies should be quickly eliminated, and supportive therapy should be initiated. If any other organ pathology is detected, treatment for the detected pathology should be administered because the prognosis of patients with timely and effective treatment is considerably good.

Keywords: Trauma, Traumatic Asphyxia, Injury

Introduction

Traumatic Asphyxia is characterized by cyanosis, subconjunctival hemorrhage, and petechiae triad on the head–neck area, so-called Perthes syndrome. Approximately 170 years ago, Oliver reported the first clinical cases diagnosed as traumatic Asphyxia. [1] A sudden and severe trauma of the thorax and /or upper abdomen was typically the cause of this syndrome. Mainly, Perthes syndrome is caused by a motorcycle accident. The most common injuries that accompany Perthes syndrome are pulmonary contusion, hemothorax, and pneumothorax. [2] In this case report, a male patient with traumatic Asphyxia due to a bicycle accident was discussed.

Case Report

In this case report, a 62-year-old male patient who was brought to the emergency room due to thorax trauma related to a bicycle accident was discussed. From the anamnesis of the patient, it was concluded that he got under a van from one side, and while the shaft of the van rotated, it pulled and crushed the patient between the body of the van and the shaft. The patient fainted soon afterward. There was no direct trauma history on the face and neck area of the patient. The patient was treated for hypertension, and he was stable under medication. Pulses were 80 /min, and tension arterial was 123/75 mm/Hg in the patient's physical examination. Except for these, cardiovascular system examination was

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regular. The electrocardiogram was monitored as usual. Glasgow's Coma Score was 15. Distinct cyanotic, edematous, and multiple petechiae were present on the patient's face, neck, and upper thorax areas. Bilateral subconjunctival hemorrhage was detected. Subconjunctival hemorrhage of the patient is presented in Figure 1

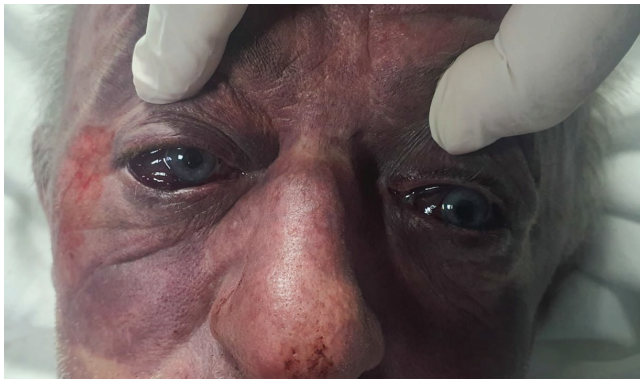


Figure 1. Subconjunctival hemorrhage

Distinct cyanotic, edematous, and multiple petechiae, which were present on the face, neck, and upper thorax of the patient, are presented in Figure 2.

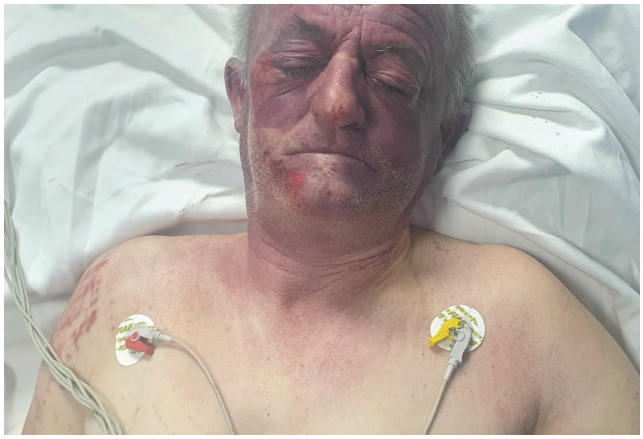


Figure 2. Shows distinct cyanotic, edematous, and multiple petechiae present on the face, neck, and upper thorax,

Pupillary isochoric and bilateral light reflexes were reactive during the patient's neurological examination. Respiratory movements were present in both hemithorax. Distal pulses of both upper extremities were palpable. There was a 20x40 cm dermabrasion area in the right tibial region, and findings like deformation and pathological movement in the right tibia were found in the upper 1/3. Hemoglobin count was normal, WBC count was 10,5K/uL, and platelet count was normal.CK count was 1040 U/L, CK-MB bioch count was 100.0 U/L, and Troponin-I count was 19.3 ng/L. Arterial blood gas analysis was compatible with respiratory acidosis. The hemoglobin value of the patient dropped inexplicably to 12.4 g/dl during the patient's followup. Minimally changed coagulation parameters were recorded PT 124%, INR 0.88, and aPTT 21.3 ne sec.

The patient was quickly evaluated with a full-body CT Scan, thyrocervical CT angiography, and direct graphics. In direct graphics, a displaced fracture was monitored in the right tibia upper 1/3. In thorax CT, on the left, a more apparent and widespread bilateral pulmonary contusion and a fracture of the right 7th rib were detected. Thorax CT image of the patient is presented in Figure 3.

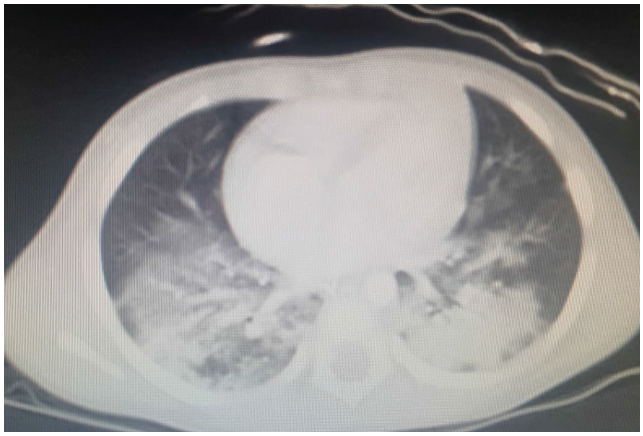


Figure 3. Bilateral pulmonary contusion on CT –Scan

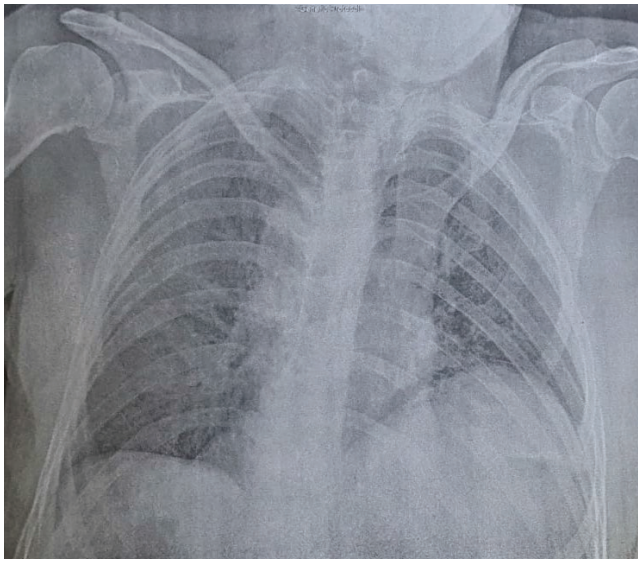


Figure 4 Geography of the thorax

Edema and hemorrhage were not detected in brain and spinal tomography. Vascular lesions were not monitored in thoracic-cervical CT angiography. The Abdomen CT image was standard.

No abnormal findings were encountered funduscopically during an eye examination. The patient was followed in the intensive care unit. Blood gas values in the intensive care unit (5L/min, under oxygen with 100%mask)were PaCo2 40,50 mmHg, PaO2 149.90 Ph 7,36 intravenous bolus of methylprednisolone (30mg/kg) methylprednisolone infusion of 5.4 mg/kg per hour for 24 hours. Fluid and electrolyte replacement and oxygen support with a mask were performed on the patient. Surgery was performed for the fracture in the right tibia (Figure 5, 6a, 6b). Mechanical

ventilation was not necessary during the followup. No complications arose during treatment. The length of the hospital stay was 16 days.

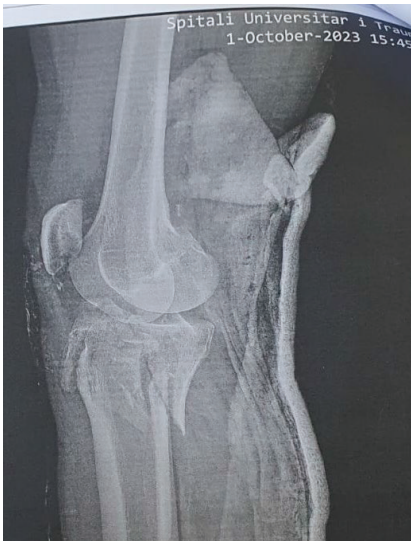
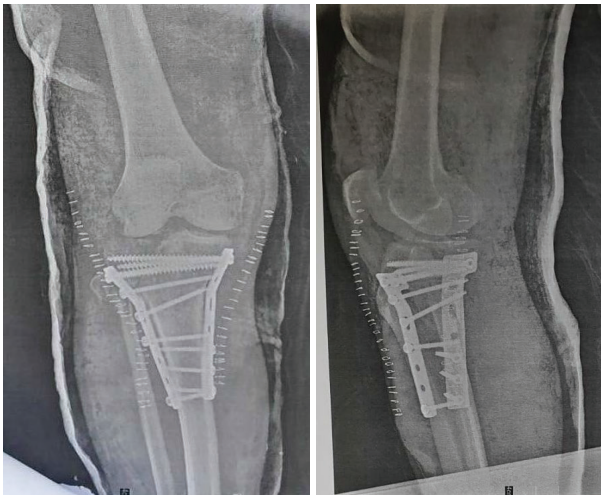


Figure 5. Right tibial fracture.



Figures 6a and 6b show A-P and L-L radiography after surgery.

At the control, after 1 month from discharge from the hospital, the patient presented with no more signs of subconjunctival hemorrhage, as in Figure 7

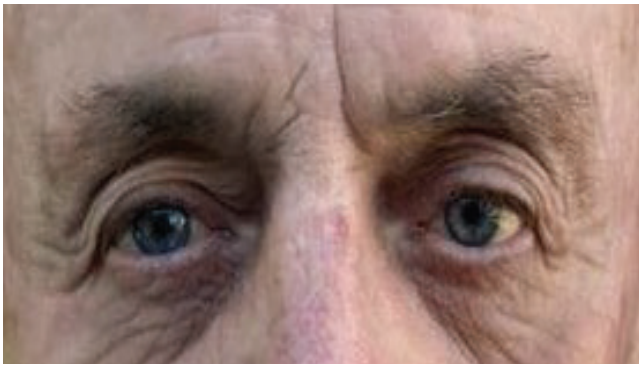


Figure 7. Shows no signs of subconjunctival hemorrhages after one month of discharge from the hospital.

Discussion

D'Angers was the first to describe Perthes syndrome in 1837. A clinical trial involving cervicofacial cyanosis, cutaneous petechiae, and subconjunctival hemorrhage following thoracoabdominal compression. [3]

In France's and Germany's literature were reported findings in autopsied people and similar cases related to traumatic Asphyxia, but no definition was made. [4]

In 1900, Perthes proposed a physiopathological mechanism including an abrupt rise in superior vena cava pressure during compressive chest trauma, and he observed cases diagnosed with mental confusion, hyperpyrexia, hemoptysis, tachypnea, and contusion pneumonia and cases diagnosed subsequently with progressing petechial bleeding in mucosal membranes, epistaxis, hematemesis and rectal bleeding, esophageal hematoma, albuminuria, microscopic hematuria, paraplegia, peripheral nerve damage, amnesia, and convulsion were monitored and for the first time it was described with the presently known term 'Traumatic Asphyxia '[5]

Traumatic Asphyxia is a rare condition presenting with cervicofacial cyanosis and edema, petechial and subconjunctival hemorrhages of the face, neck, and upper chest that usually occurs due to a compressive force to the thoracoabdominal region but has also been associated with asthma paroxysmal coughing, protracted vomiting and jugular venous occlusion [1, 6].

Factors implicated in developing these striking physical characteristics include thoracoabdominal compression after deep inspiration against a closed glottis, which results in venous hypertension in the valveless cervicofacial venous system [7].

Alternatively, increased airway pressure may cause the compressor to obliterate the inferior vena cava to protect the body's lower part. In the literature, it is reported that traumatic Asphyxia might develop during a 2-5 min (average) compression period [9]. Although most cases are seen as a result of motorcycle accidents, other causes include heavy machines /furniture crashes and, rarely, deep-sea diving, epileptic seizures, difficult delivery, and asthmatic attacks [10].

Senoglu et al. [8] presented a 4-year-old child developing traumatic Asphyxia associated with intramedullary spinal cord hemorrhage followed by thoracal compression. They said that it is essential for clinicians to be aware of the spinal cord hemorrhage that can be accompanied by traumatic Asphyxia and treated with steroids immediately after the trauma without radiological evidence.

Problems relating to other organ injuries can clinically be accompanied in patients with traumatic Asphyxia.[11] In our case, a generalized bilateral pulmonary contusion that is more distinct in the left and a fracture of the 7th rib were detected.

Although Perthes syndrome is seen rarely in the clinics, only 205 cases are reported; in the paper by Olusina et al. [10], they stated that as a result of an autopsy performed

on 10 out of 14 people who died during a social event, in 60% traumatic Asphyxia was detected.

The prognosis of Perthes syndrome is variable. Jobe et al. show that if Chest compression is more significant than 10 min, associated injuries are associated with poor prognosis. [3]

In other cases, traumatic Asphyxia has a good prognosis, and the management of these patients was done by giving oxygen and elevating the head to 30^0, which is called supportive treatment and is usually sufficient. [11]

However, specific treatment may be necessary to address associated injuries. In our case, supportive therapy was administered, and specific treatment was provided for the right tibial fracture. Furthermore, no additional surgical interventions were required to manage other organ pathologies, and no complications were encountered during follow-up appointments.

In conclusion, Perthes syndrome should be considered in patients presenting with the associated ecchymotic mask with cutaneous petechial hemorrhages and subconjunctival bleeding as a complication of compression of the thorax. The outcome is variable depending on the severity and duration of compression. When characteristic findings of traumatic Asphyxia are detected in traumatic patients, other organ pathologies should be quickly eliminated, and supportive therapy should be initiated. If any other organ pathology is detected, treatment for the detected pathology should be administered because the prognosis of patients with timely and effective treatment is considerably good.

COI Statement: This paper has yet to be submitted in parallel, presented fully or partially at a meeting, podium, or congress, published, or submitted for consideration beforehand.

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Patient consent: The patient's consent was obtained for the publication of the case.

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CASE REPORTS

Clinical Management and Surgical Outcomes of Wandering Spleen with Splenic Torsion in Pediatric Patients: A Case Report

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Abstract

Introduction: Wandering Spleen is a rare condition in which the splenic ligaments are abnormally loose or absent. This makes the Spleen more mobile and increases the risk of torsion.

This case report outlines the clinical presentation and management of a 10-year-old female patient who presented at our clinic with acute abdominal pain, vomiting episodes, and a severe fever. Imaging tests, such as abdominal ultrasonography and computed tomography, confirmed the diagnosis of splenic torsion by showing a hemorrhagic infarction and a large spleen. We performed a splenectomy to remove the damaged organ, a partial omental resection to remove the dead tissue and removed the mesenteric lymph nodes for further pathological examination.

After the surgical procedure, the intensive care unit carefully observed the patient and treated her with intravenous electrolyte replacement, broad-spectrum antibiotics, pain management, and measures to prevent thrombosis.

This case highlights the critical need for early diagnosis and timely surgical intervention in cases of wandering Spleen to prevent serious complications, including splenic infarction. By presenting this case, we seek to elevate awareness of wandering Spleen among healthcare professionals, mainly within pediatric groups. We emphasize the importance of timely diagnosis and appropriate management to optimize patient outcomes.

Conclusion: Early detection and prompt intervention are crucial in preventing severe complications in pediatric patients. This case emphasizes the necessity of rapid diagnosis and increased awareness in clinical practice. Due to the Spleen's impaired viability, a splenectomy was required. Following surgery, we provided comprehensive monitoring and pharmaceutical assistance to control pain, prevent infection, and maintain nutritional stability.

Keywords: Wandering Spleen, splenic torsion, pediatric surgery, splenectomy, acute abdomen

Introduction

Wandering Spleen, or hypermobile Spleen, occurs when the suspensory ligaments elongate or grow abnormally. It's an uncommon clinical condition primarily affecting children, but the incidence peaks in adult females of reproductive age. Because of its rarity and diverse presentation patterns, clinicians have found it challenging to diagnose and treat. [1]

Unrelated reasons often lead to the accidental detection of a wandering spleen during imaging. However, it may cause symptoms if the Spleen's vascular pedicle twists (torsion), resulting in an infarction, or if the Spleen compresses surrounding organs in its new position. Once

Original article, no submission or publication in advance or in parallel

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detected, surgical treatment is usually required, either through splenopexy, which fixes the Spleen in its usual position, or splenectomy, which entails removing the Spleen based on its mobility and condition. [2]

Individuals aged 20 to 40 may also develop the disease due to ligamentous support laxity resulting from splenomegaly or pregnancy. Approximately 15% of children with wandering Spleen are asymptomatic, whereas 55% experience stomach discomfort, and 90% have a palpable mass outside the left upper quadrant. In 64% of pediatric wandering spleens, torsion causes complications. Splenic torsion often occurs in a clockwise direction and can lead to vascular congestion, infarction, or even splenic gangrene. [3]

Case Presentation

A 10-year-old female patient presented to our clinic with symptoms of an acute abdomen. She presented with stomach pain lasting 4 to 5 days, two episodes of vomiting, and a fever of 39.5°C one day before admission.

Upon examination, she indicated discomfort in the left upper quadrant, abdominal distension, and symptoms of peritonitis. Vital signs suggested tachycardia and hypotension, necessitating an urgent examination. Laboratory studies showed elevated white blood cell counts and inflammatory markers, indicating the possibility of an acute abdominal process. A CT scan of the abdomen with contrast confirmed the diagnosis of splenic torsion, which revealed hemorrhagic infarction and significant splenomegaly (Figure 3).

The patient underwent extensive preoperative preparation, which included the placement of a nasogastric tube and urine catheter. The surgeon performed a median laparotomy under general anesthesia. Intraoperative examinations revealed a twisted spleen with necrosis (Figure 4). The surgery included a splenectomy to remove the affected organ, a partial omental resection of necrotic tissue, and an excision of mesenteric lymph nodes for pathological investigation. We inserted an intra-abdominal drain for postoperative monitoring.

According to histopathological examination, the removed spleen tissue showed clear evidence of infarction, consistent with splenic torsion. The infarcted tissue looked like areas of bleeding and clotting in the splenic parenchyma, as well as widespread necrosis and damage to the splenic architecture (Fig. 1a, Fig. 1b).

We saw ischemic changes like cell death and loss of standard splenic tissue structure with hematoxylin and eosin (HE) staining at low magnification (Fig. 1a, HE x100) and high magnification (Fig. 1b, HE x200). Furthermore, histological examination of the omental fat tissue revealed notable inflammatory changes, including bleeding regions and noticeable fat necrosis (Fig. 2). These results suggested localized tissue damage brought on by ischemia and torsion. Pathological examination of the mesenteric lymph nodes that were removed during surgery showed no signs of infection or cancer, which further supports the limited nature of the inflammatory process.

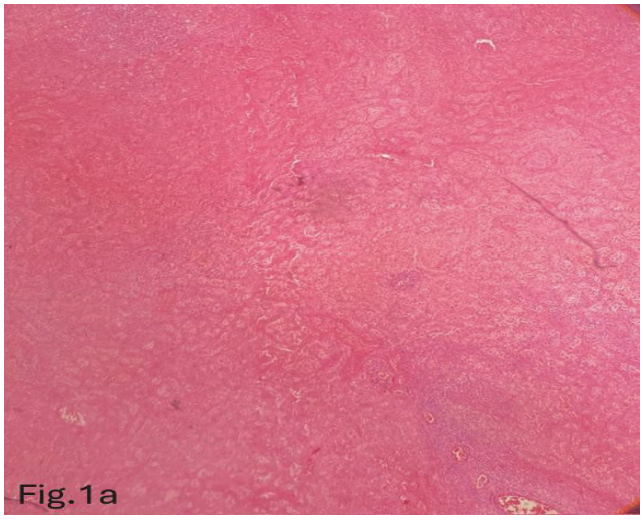

Figure 1a. Microscopic view of splenic infarct HE x100

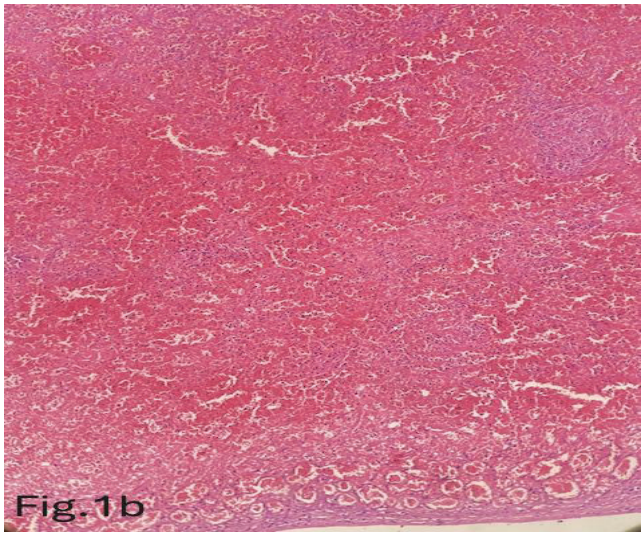

Figure 1b. Microscopic view of splenic infarct HE x200

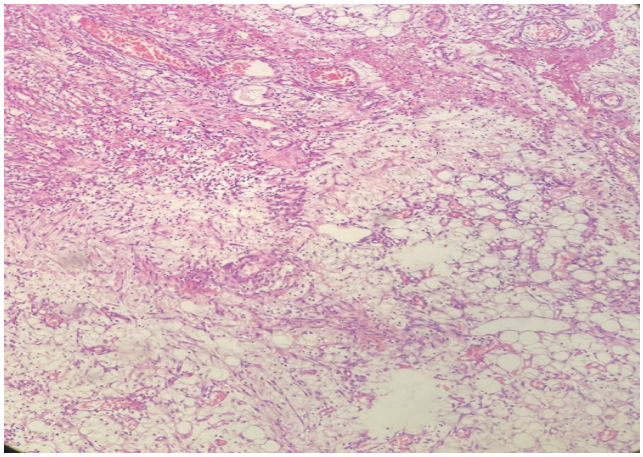

Figure 2. Omental fat tissue showed inflammation, fat necrosis, and hemorrhage.

The intensive care unit closely monitored the patient after surgery. On the first day after surgery, she was hemodynamically stable, spontaneously breathing, and her vital signs were within normal ranges.

We managed the condition with parenteral electrolyte replacement, antibiotics, gastric-protecting medications, analgesics, and thromboprophylaxis therapy. The patient remained stable for the next few days, and routine blood tests and an abdominal ultrasound were performed on the second day. On the sixth day, the patient was moved to the general ward and continued to receive IV antibiotics and analgesics.

As her condition stabilized, we began her oral intake to ensure proper nutrition and hydration for recuperation. Throughout her stay, we continuously monitored her vital signs (heart rate, blood pressure, and respiratory status). We checked her blood counts regularly to assess her response to therapy. We intended these procedures to manage her increased platelet counts and aid her recovery correctly.

By post-splenectomy treatment standards, we scheduled her vaccination against encapsulated pathogens such as Pneumococcus, Haemophilus influenza type B, and Meningococcus. The surgical team, nursing staff, and pediatric specialists worked collaboratively throughout her recuperation to ensure her stability and progress.

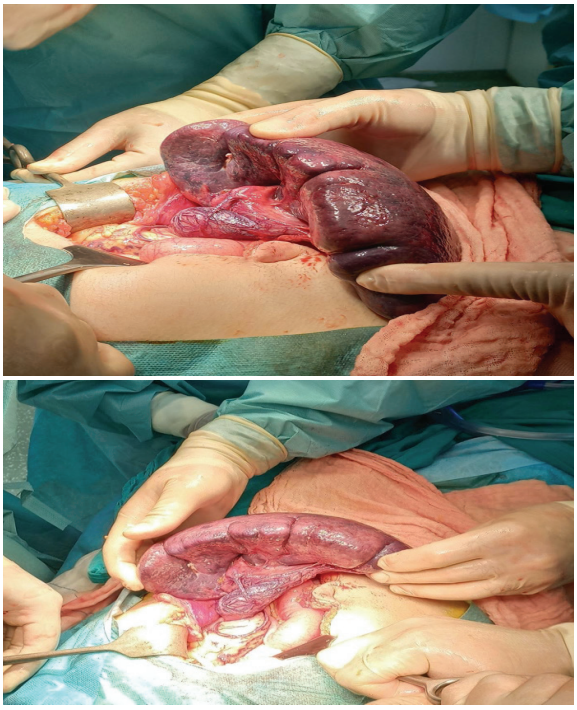

Figure 4. Surgical procedure: Splenectomy with partial omental resection and mesenteric lymph node excision

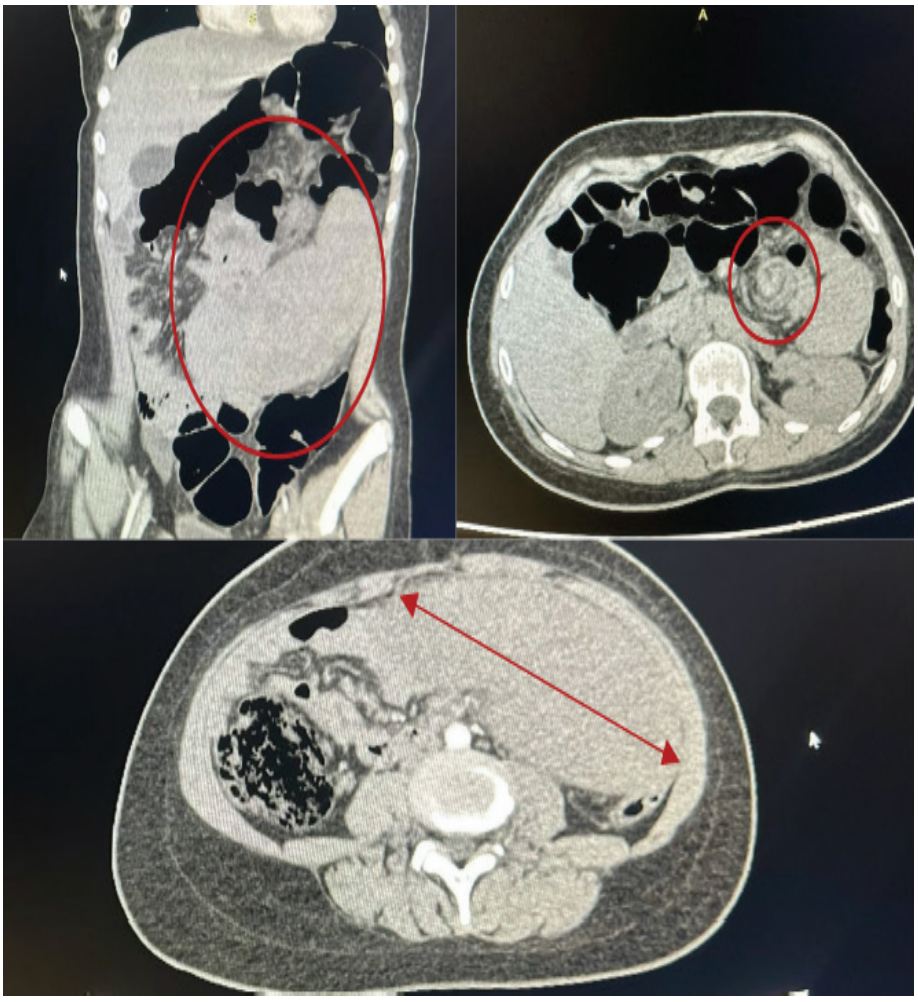

Figure 3. CT image of splenic torsion with hemorrhagic infarction and splenomegaly

Discussion

Wandering Spleen can be identified by laxity or lack of splenic ligaments, resulting in more significant movement and increasing the risk of torsion, hypoperfusion, thrombosis, or necrosis. The cause may be congenital, usually due to incorrect mesogastrium development, or acquired as a result of splenomegaly, trauma, or pregnancy. The incidence is low, with less than 500 instances documented, with peaks in children under 10 and people aged 20 to 40, particularly females. [4]

Trauma and connective tissue conditions can weaken or damage the suspensory ligaments, contributing to acquired WS. On the other hand, congenital etiology is thought to be the most common cause of WS, especially in children. This means that one or more ligaments were not present or developed correctly, which makes the Spleen move around a lot. This is related to inadequate union of the mesogastric and posterior abdominal walls during the second month of pregnancy. [5] The Spleen

can then move to several locations in the abdomen or pelvis, resulting in a complicated clinical condition.[6]

Abdominal ultrasonography (US) and computed tomography (CT) are essential imaging modalities for detecting WS and giving important preoperative information. Early detection of complications such as splenic torsion or infarction is critical to preventing symptom progression. [7, 8]

There are two surgical alternatives for the WS approach: splenopexy and splenectomy. The viability of the Spleen is the most critical factor in selecting the correct type of therapy. Splenopexy is performed in uncomplicated cases by suturing the spleen capsule to the left upper quadrant of the abdomen and creating a posterolateral extra peritoneal pocket at the 12th rib level.

Other procedures include dislocating the splenic flexure of the colon and suturing the stomach's more significant curvature to the anterior abdominal wall. Recently, there have been descriptions of using a polyglycolic mesh as a "snood" to anchor the Spleen. Despite complications such as sepsis and a high mortality rate, if the splenic blood supply is not restored after manual detorsion (non-viable Spleen), splenectomy is essential. On the other hand, there is a high recurrence rate after splenectomy. [9]

When a wandering spleen is found after surgery for other reasons, splenopexy or splenectomy should be discussed. Complex cases like infarction, hypersplenism, substantial size, or splenic vein thrombosis typically necessitate splenectomy, while mild cases may benefit from splenopexy. Although laparoscopic procedures are currently considered the highest standard, open approaches are still possible for splenopexy and splenectomy. [10]

This case is consistent with the results of other pediatric reports of wandering spleens, in which torsion and subsequent infarction are frequent complications. In contrast to specific instances in which splenopexy is feasible, our patient necessitated a splenectomy as a result of the extensive infarction and non-viable Spleen.

The literature frequently links wandering spleens (WS) to serious consequences such as splenic torsion, infarction, rupture, and gangrene. Although less severe, chronic or intermittent torsion can cause splenic congestion and mass effects. Delaying treatment can lead to problems such as bleeding and infection, often necessitating a splenectomy.

Early detection by imaging methods, such as CECT displaying the "whirl sign," is essential to avoid these potentially fatal consequences. [11] Significant surgery frequently results in thrombocytosis, which prompts early intervention and raises concerns about thrombotic events.

In this particular case, our patient experienced postoperative complications such as thrombocytosis and an increased platelet count, which raised concerns about potential thrombotic complications, given her recent surgery. Pediatric hematology specialists advised beginning antiaggregatory medication with aspirin to address this.

This strategy aims to lower the danger of thrombus formation by suppressing platelet aggregation, improving vascular health, and maintaining patient safety during healing. We chose aspirin because of its well-established safety profile in pediatric patients and its ability to reduce platelet aggregation effectively.

We set up a comprehensive medication plan to provide our patients with the necessary support. We administered 100 mg of acetylsalicylic acid once daily to relieve inflammation and pain. To prevent constipation, we administered bisacodyl 10 mg as needed. To alleviate fever and agony, we administered 500 mg of paracetamol every six hours.

We injected 50 ml of 20% albumin intravenously to maintain plasma volume. Parenteral feeding with a 500-mL ampule of 5% amino acids provided the necessary nutrients. To avoid nausea and vomiting, we gave 4 mg of ondansetron intravenously in 2 ml of ondansetron and 100 ml of 0.9% NaCl. To reduce stomach acid, we injected 40 mg of pantoprazole intravenously in 100 mL of 0.9% NaCl.

For pain relief and fever management, we administered 50 mg of Tramadol intravenously twice daily and 1 g of metamizole sodium in 2 ml thrice daily. We also administered metronidazole 500 mg in 100 ml three times a day to prevent infections and cefotaxime 1,000 mg intravenously thrice daily for broad-spectrum protection. We injected 1,000 cc of sodium chloride (0.9% solution) and glucose to restore fluids and address nutritional needs.

Conclusion

Early detection and prompt intervention are crucial in preventing severe complications in pediatric patients. This case emphasizes the necessity of rapid diagnosis and increased awareness in clinical practice. Due to the Spleen's impaired viability, surgical intervention, namely a splenectomy, was required in this case. Following surgery, we provided comprehensive monitoring and pharmaceutical assistance to control pain, prevent infection, and maintain nutritional stability. This case illustrates the necessity of awareness of wandering spleens, especially in juvenile populations, and quick surgical surgery to reduce potential complications and assist patient recovery.

COI Statement: This paper has yet to be submitted in parallel, presented fully or partially at a meeting, podium, or congress, published, or submitted for consideration beforehand.

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OPEN ACCESS JOURNALS

CASE REPORTS

Gastric MALT Lymphoma with Giant Ulcer from Untreated H. pylori: Role of Endoscopic Biopsy – A Case Report

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Abstract

Introduction: Gastric mucosa-associated lymphoid tissue (MALT) lymphoma is a rare extranodal non-Hodgkin lymphoma strongly linked to Helicobacter pylori infection. It often presents with nonspecific symptoms like dyspepsia, nausea, and epigastric pain and can mimic other gastric pathologies, such as peptic ulcers or gastric cancer.

This case report is significant as it highlights the importance of thorough biopsy procedures in diagnosing gastric MALT lymphoma. The patient presented with complaints of dyspepsia, nausea, and epigastralgia and had a giant ulcer on endoscopy. Only after biopsies with a large number of samples (over 10) from both normal and abnormal mucosa the diagnosis of MALT lymphoma was established and reconfirmed after immunohistochemistry. The presence of Helicobacter pylori was detected, and after its eradication treatment, the ulcer was more minor and improved from Forrest II-c to III. This case underscores the potential for a wrong diagnosis (undiagnosed MALT-Lymphoma) if biopsy samples are not comprehensive. It also emphasizes the need for suspicion of gastric MALT-Lymphoma and the necessity of more invasive tissue biopsy, such as EUS-FNA, EMR, and ESD, when suspicion persists.

Conclusion: Early diagnosis of gastric MALT lymphoma requires multiple biopsy samples during the initial endoscopy to prevent false negatives. Immunohistochemistry is essential for confirmation, and advanced techniques like EUS-FNA, EMR, or ESD play a significant role when suspicion persists. Timely H. pylori eradication can lead to ulcer healing and better outcomes. Proper endoscopist training is critical to reduce diagnostic delays.

Keywords: Gastric MALT lymphoma, Helicobacter pylori, giant gastric ulcer, endoscopic biopsy, immunohistochemistry.

Introduction

MALT lymphoma, a subtype of indolent B-cell non-Hodgkin lymphoma, arises from extranodal sites due to the malignant transformation of B lymphocytes, primarily triggered by infections or autoimmune processes [1].

Although they can exist in different organs, such as the salivary gland, thyroid gland, breast, lung, bladder, skin, and orbit, MALT lymphomas are most frequently detected in the gastrointestinal tract [2]. The most commonly affected organ is the stomach, where MALT lymphoma is incontrovertibly associated with chronic gastritis induced by a microbial pathogen, Helicobacter pylori [3].

Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) of the stomach is a rare entity with an estimated incidence of 0.41/100,000/year [4]. This subtype of non-Hodgkin lymphoma accounts for 50% of primary gastric lymphomas (PGL), which are estimated to represent 2-8% of all stomach malignancies [5].

A gastric MALT-lymphoma is typically a low-grade B-cell neoplasia. Most cases are associated with Helicobacter pylori (H. pylori) [6]. Therefore, line therapy in the early stages eradicates H. pylori. In advanced

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stages, radiotherapy, chemotherapy, immunotherapy, or combination chemoimmunotherapy is recommended [7, 8]

The incidence of gastric MALT lymphoma is increasing, but the diagnosis is difficult [9]. Most patients are asymptomatic or complain of nonspecific symptoms [9].

Gastric MALT lymphoma has variable endoscopic appearance, including erosion, erythema, discoloration, atrophy, ulcer, and subepithelial lesion [10]. Because its endoscopic features are variable and nonspecific, the possibility of this condition may be overlooked [9].

An endoscopic forceps biopsy is the primary diagnostic test, but false negative results are possible [9]. Therefore, clinical suspicion and jumbo biopsy are essential for accurate diagnosis [10].

Here, we report a case of gastric MALT lymphoma diagnosed by biopsy with large numbers of samples (over 10) collected from both normal and abnormal mucosae.

Case description:

A 69-year-old female with a history of chronic gastritis and no previous significant medical conditions presented at the outpatient gastro-enterology clinic with persistent complaints of indigestion, nausea, and epigastralgy. Physical examination showed no pathological signs. The blood routine test showed moderate anemia (Hemoglobulin 9.3 mg/L).

The fecal routine test and occult blood test were regular. The blood biochemistry test, tumor markers, and the urine routine test were all in normal ranges. Gastroscopy identifies in the antral region a giant ulcer **(Forrest II-C)**, with irregular lips of the dirty base which occupies a large part of the antral region, with extension from angulus ventriculi to the pyloric sphincter by occupying a considerable part of it. These endoscopic Findings, particularly the size and location of the ulcer, were indicative of a potential malignancy and prompted a comprehensive biopsy (biopsy with large numbers of samples was taken -over 10).

The biopsy showed atypical lymphocytes and gastric lymphoma of non-Hodgkin was suspected. The stool antigen test for Helicobacter Pylori was positive. CT scan identified irregular thickening of the antrum wall and Para-aortal Sinister Lymphonodes with a diameter up to 6 mm diameter but no metastases. Immunohistochemistry of morphological and immune-phenotypical data compliant with the lymphoproliferative disease of the B cell lymphoma (malt lymphoma). Chronic gastritis in the active phase is also present. Neoplastic cells: CD20 positive, positive CD3, CK AE/AE3 negative. Cytokeratin 7 negatives. CD 117 negative. (Figures 4, 5, 6, 7)

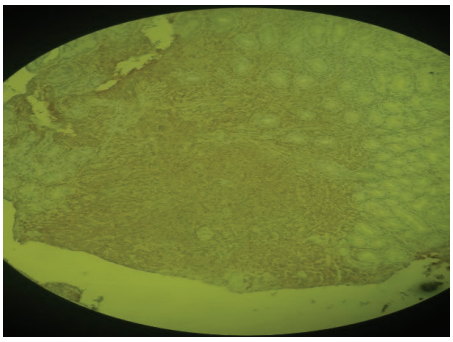

Figure 4 - CD20 positive

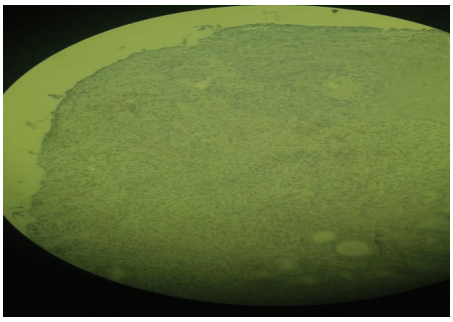

Figure 5 - CD3 Positive

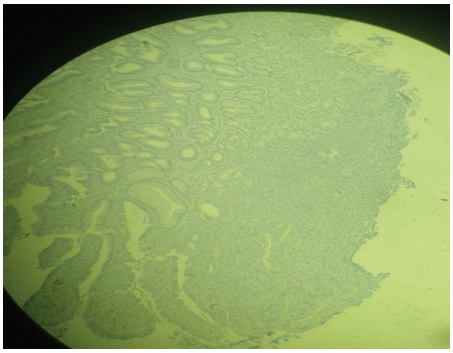

Figure 6 - Cytokeratin 7 Negative

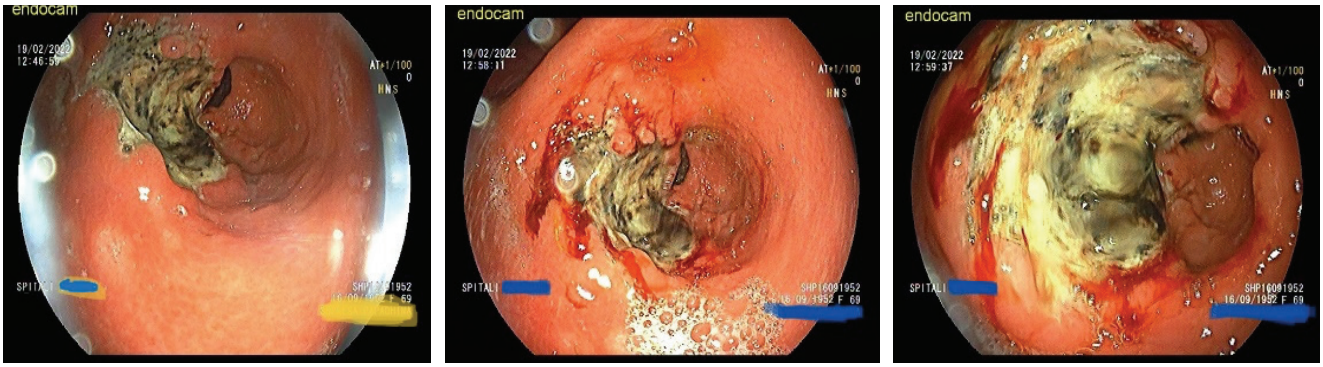

Figure 1, 2, 3: Endoscopic imaging of MALT Lymphoma presenting as a giant ulcer

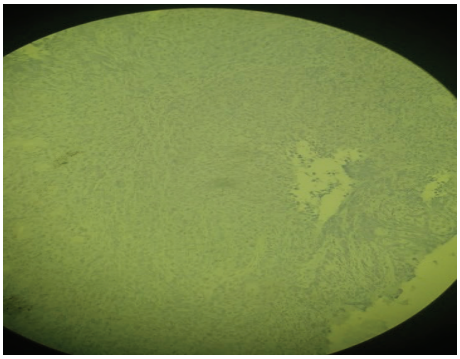

Figure 7 - CD 113 Negative

Eradication therapy with Pylera (bismuth/metronidazole/tetracycline) 4x3 tablets/day for 10 days and double dose PPI was started. The patient is re-examined endoscopically after 2 months in another clinic, concealing the diagnosis, and the endoscopic view shows an ulcer **(Forrest III)** half the previous size, with more regular edges, which is described as benign and 3-4 biopsy samples are taken (Figure 8)

After the biopsy result, only inflammation of the gastric mucosa is described without other suspicious cells. The patient continues to be treated with PPIs, but after another 2 months, the endoscopic re-examination shows the same appearance of the ulcer without any improvement. This time, the patient decides to indicate the immunohistochemical diagnosis and jumbo forceps are used, taking several biopsy samples that are more significant than 10. After the biopsy result is released, the diagnosis of MALT lymphoma is reconfirmed.

Discussion

As we can see in this case, symptoms of gastric MALT lymphoma range from vague dyspepsia and discomfort in the upper abdominal region to epigastralgia and vomitus [11]. Endoscopic appearance can vary from hyperemic gastric mucosa and mucosal petechial hemorrhages to multiple erosions or nodular patterns [8]. Zullo et al. proposed an endoscopic classification of gastric MALT lymphoma in 2014 (table 1) [5]. According to this proposed classification, our case is presented as an ulcerative type.

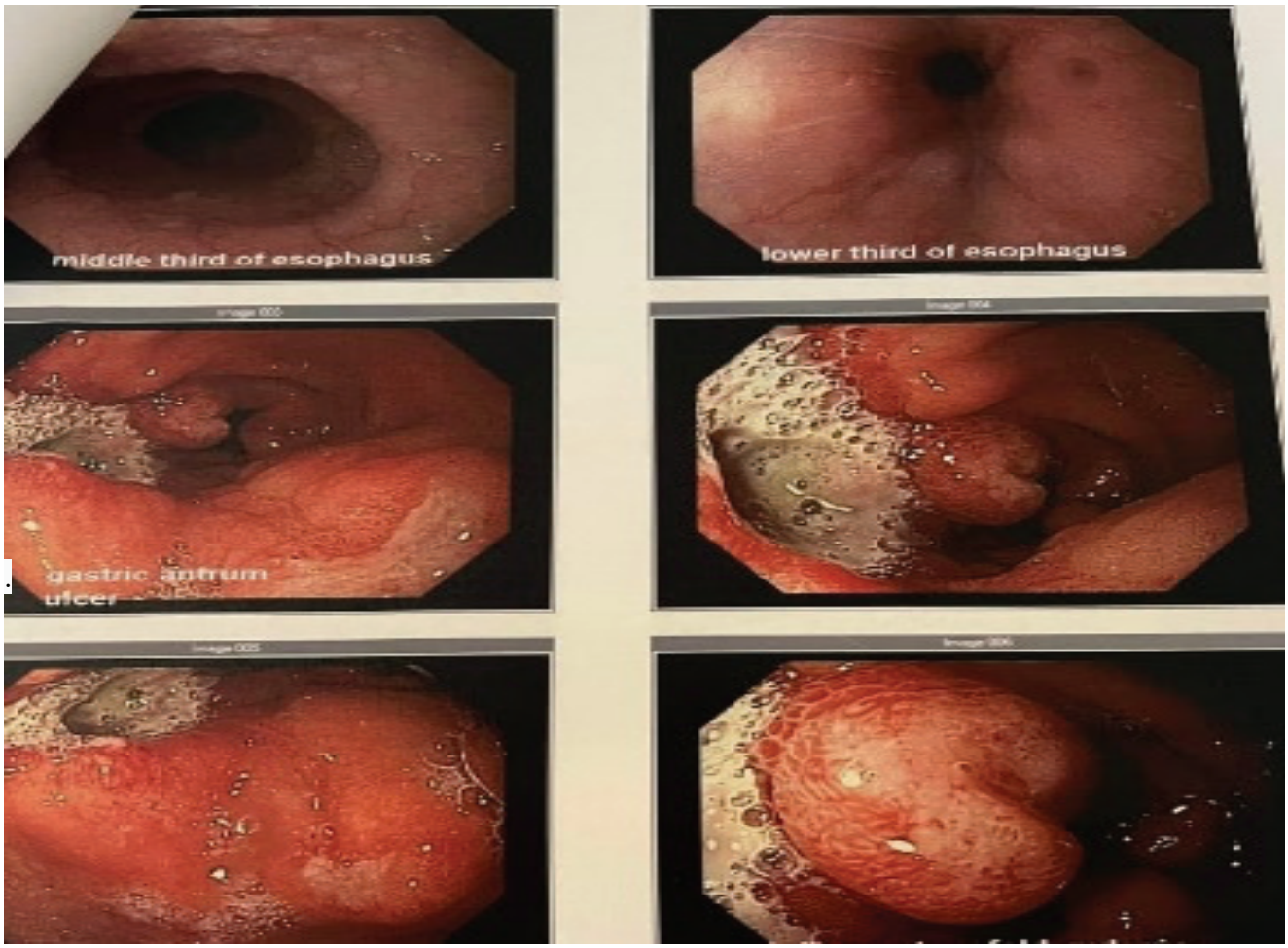

Figure 6 - EGD (Esophagogastroduodenoscopy) images after treating H. Pylori. The ulcer is presenting now, like Forrest III (from II-c before)

Lymphoma type	Endoscopic presentation
Normal/hyperemic mucosa	Normal mucosa/ hyperemicmodification
Petechial hemorrhages	Presence of mucosal petechialhemorrhages
Hypertrophic	Nodular pattern; large or giant folds
Exophytic	Irregular mucosa – tumor-likeappearance or polypoid mass
Ulcerative	Multiple erosions/single or multipleulcerations
Mixed	A combination of more than onepattern

Table 1 - Endoscopic classification of gastric MALT-lymphoma after Zullo A. et al. (5).

Often, patients attempting to hide important anamnestic data can contribute to misdiagnosis or late diagnosis of this pathology. However, the backbone of GML diagnosis remains histology, and it is important to highlight that a sufficient number of biopsies (at least 10) from the lesions and outside des lesions is necessary for a reliable diagnosis (histology, IHC, and detection of *H. pylori*) [12,13]

Conclusions

Primary gastric lymphoma remains a rare pathology. Histologically, the majority of PGL are MALT and DLBCL lymphomas. MALT lymphoma is related to Helicobacter pylori infection. Eradication therapy can reduce gastric MALT lymphoma in the early stages of the disease.

The early diagnosis of gastric MALT lymphoma is difficult because its symptoms and endoscopic findings are nonspecific. Therefore, if an abnormal mucosa is observed during EGD, gastric MALT lymphoma should be considered, and multiple biopsies and EUS should be performed.

A large number of biopsy samples are necessary from the first endoscopy. In addition, the possibility of false-negative results from endoscopic biopsy should be considered, and more invasive tissue biopsy, such as EUS-FNA, EMR, and ESD, may be necessary.

Authors declaration

The authors whose names are listed certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria, educational grants, participation in speakers' bureaus, membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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OPEN ACCESS JOURNALS

CASE REPORTS

Noninvasive Polypoid Malignant Mixed Mullerian Tumor of the Uterus: A Case Report and Literature Review

Leon Kaza[1], Leart Berdica[2,3*], Teona Bushati[2,3], Albina Ndoja[3]

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Abstract

Introduction: Malignant mixed Müllerian tumors (MMMT), also known as carcinosarcomas, are rare and highly aggressive neoplasms of the uterus, accounting for less than 5% of all uterine malignancies. These tumors are biphasic, comprising both carcinomatous (epithelial) and sarcomatous (mesenchymal) components, and are typically associated with poor prognoses due to their rapid progression and high metastatic potential.

In this report, we present a unique case of noninvasive polypoid MMMT of the uterus, highlighting its clinical presentation, diagnostic challenges, and management. We also provide a comprehensive literature review, which enriches our understanding of this case within the broader context of uterine carcinosarcomas.

Results: This is the first documented case in English literature of a polypoid uterine carcinosarcoma without endometrial infiltration. It is significant because it adds to the limited literature on noninvasive polypoid MMMTs, typically aggressive and diagnosed at advanced stages. Uterine carcinosarcomas are generally aggressive, with most cases diagnosed at advanced stages.

Conclusion: Uterine carcinosarcomas are indeed rare, aggressive, and rapidly progressing neoplasms with poor prognoses. It is crucial to include carcinosarcomas in the differential diagnosis of high-grade uterine neoplasms, especially for polypoid tumors. This inclusion is not just essential, but it is the key to ensuring accurate and timely diagnosis, underscoring the significant role of medical professionals in this process.

Keywords: Noninvasive polypoid MMMT, uterine carcinosarcoma, endometrial neoplasms, polypoid uterine tumors,

Introduction

Malignant mixed Mullerian tumors (MMMT), or Carcinosarcomas, are rare biphasic, aggressive malignant tumors with high-grade epithelial and sarcomatous components. Due to metaplasia/transdifferentiation (epithelial to mesenchymal transition), the sarcomatous component can derive from the carcinomatous component. [1] Endometrial Malignant Tumors (EMTs) are most commonly seen in postmenopausal females, with a higher incidence among African lineage.[2]

Regarding the origin of the neoplasm, four theories have been proposed:

1. *Collision theory:* the sarcoma and carcinoma are independent neoplasms;
2. *Combination theory:* both components are derived from a single stem cell that undergoes divergent differentiation early in the evolution of the tumor,
3. *Conversion theory:* the sarcomatous element derives from the carcinomatous component during the evolution of the cancer,
4. *Composition theory:* The spindle cell component is a pseudo sarcomatous stromal reaction to the carcinoma [4].

The Cancer Genome Atlas (TCGA) data supports the conversion and combination theories [5]. The most common epithelial component is adenocarcinoma, but clear cell, mucinous, and papillary serous components can also

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occur, and the most common mesenchymal component is undifferentiated sarcoma in homologous tumors and rhabdomyosarcoma in heterologous tumors [6].

In our case, the patient is a 56-year-old who complained of postmenopausal bleeding and abdominal pain. She had a history of four successful vaginal deliveries and no prior gynecological problems were referred. The patient's symptoms included abnormal vaginal bleeding and lower abdominal pain over the last 3 months.

This patient was diagnosed with a Malignant Mix Mullerian Polypoid Tumor that does not infiltrate the mucosa or the other histologic layers.

To the best of our knowledge in English literature, this is the first case of a polypoid uterine carcinosarcoma without endometrial infiltration. Most uterine carcinosarcomas have an aggressive course and are presented in advanced stages at the time of diagnosis.

Case presentation

A 56-year-old postmenopausal woman presented with a history of abnormal vaginal bleeding and lower abdominal pain in the last 3 months. The patient has successfully undergone four vaginal deliveries (G4P4). No prior gynecological problems were referred, and there was no history of other diseases. In the pelvic exam, normal external genitalia were observed. The cervix was in standard shape and appearance, and the uterus was motile, with mild tenderness in typical dimensions. The fornices were free. The transvaginal ultrasound exam revealed the presence of a 40 mm intracavitary, non-homogenous mass with increased vascularity. The uterus was homogenous, with no signs of myometrial involvement. The ovaries were atrophic, with no evident lesions. No free fluid was noted.

Based on these findings, a hysteroscopic and pathologic examination was recommended. The diagnostic hysteroscopy showed an enlarged, irregular uterine cavity and the presence of a white-gray mass, with increased vascularity, that occupies the uterine cavity (Figure 1 - A).

Several samples were taken for histopathological evaluation, which revealed that the intracavitary mass had highly atypical epithelial and mesenchymal components, raising suspicion for MMMT. Subsequently, the patient underwent an abdominal MRI, which showed a mass in the uterine cavity with no signs of myometrial involvement and without the presence of any other suspicious lesion in other abdominal organs (Figure 1 - B).

Given the diagnostic evidence, it was decided to proceed with surgery for FIGO Stage I – C uterine Carcinosarcoma. The patient underwent a type A - extra fascial total abdominal hysterectomy with bilateral salpingo-oophorectomy and bilateral systematic pelvic lymphadenectomy. The pathologic findings in the final biopsy are as follows.

Macroscopically, we observe the uterus together with the cervix and both adnexa 8 x 9 x 5 cm. A polypoid mass measuring 4 cm in diameter protrudes from the endometrial cavity (Fig.2). The tumor was sectioned carefully in parallel sections on the long axis. Near the center of the cancer, we noticed difficulty in cutting because of the bony, delicate trabecula appearance. The right and left lymph nodes were included after properly dissecting the surrounding fatty tissue.

Microscopically, the tumor reveals a third-grade endometrioid carcinoma and a heterologous sarcomatous component, which consists of osteoid malignant tissue. Cancer presents pronounced necrosis in the areas of attachment to the endometrium through a fragile short, almost 1 mm thick, and 3x4 mm wide peduncle. Neither the endometrium nor the myometrium is invaded in all the circumscribed contact areas of the tumor with the endometrium. Neither lymphatic vascular nor perineural invasion is observed. Twenty-one pelvic lymph nodules were examined, which were reactive without tumor metastasis.

The patient was informed about the diagnosis and the recommended treatment plan. She expressed understanding and consented to the surgery. Post-surgery, the patient was

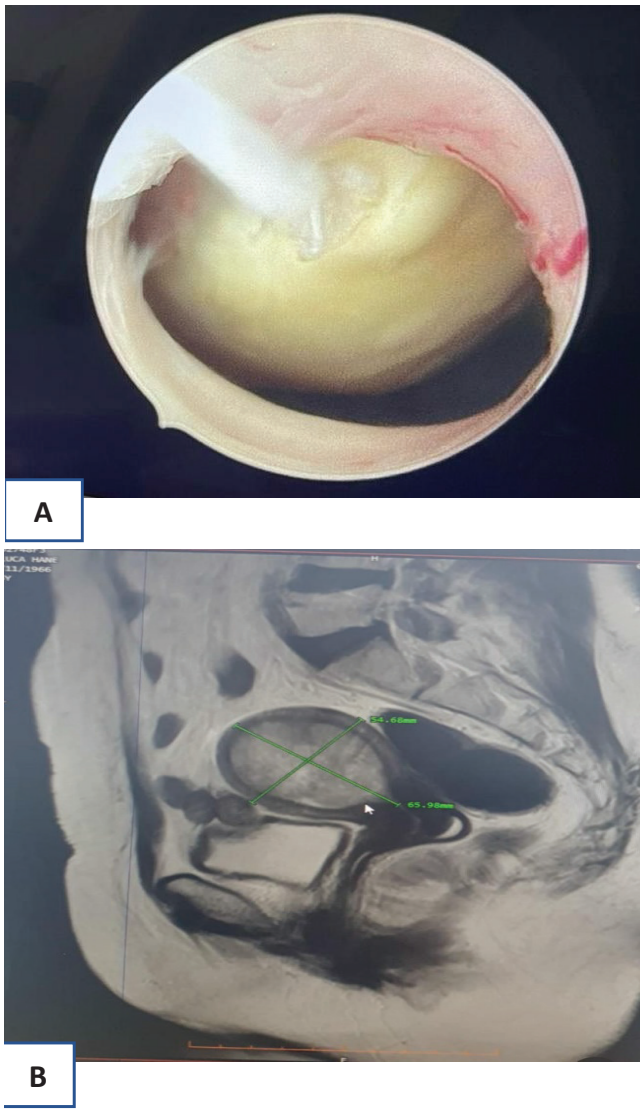

Fig.1 A) Hysteroscopy image B) The MRI imaging

monitored closely and showed a positive response to the treatment, with no signs of recurrence at the last follow-up.

Immunohistochemical exams were performed. Epithelial markers (AE1/AE3) are positive in the epithelial component, while the mesenchymal component exhibited focal positivity for vimentin and smooth muscle actin. Also, ER has a positivity of around 30% in epithelial component, PDL1 scores 0 % in tumoral cells and 80 % in intratumorally inflammatory cells. S100 and Her2 were negative, while p53 was positive in 5% of cells with aberrant expression. Some of the antibodies are shown in the figure 3. Based on the appearance of Hematoxylin Eosin and the Immunohistochemical profile of the tumor, the diagnosis of a Polypoid noninvasive MT of the uterus was established. After multidisciplinary oncologic consultations, it was concluded that the patient should not undergo radiotherapy or chemotherapy because there was no endometrial infiltration, and the stage was T0.

In the follow-up performed every three months for a year, which included an ultrasound examination and a PET scan, the patient had no metastatic lesions, and further routine follow-up was programmed.

Discussion

Uterine carcinosarcoma is a rare, highly aggressive, rapidly progressing neoplasm associated with a poor prognosis that has not significantly improved in the past thirty years despite advances in imaging and adjuvant therapies.[7] Carcinosarcomas, though rare, representing less than 5% of all uterine tumors, account for 16.4% of all deaths caused by a uterine malignancy [8]. Gerhardt reported the first case in 1989, which Meyer confirmed by examining the slides [9]. Women are usually over the age of 50, with most cases

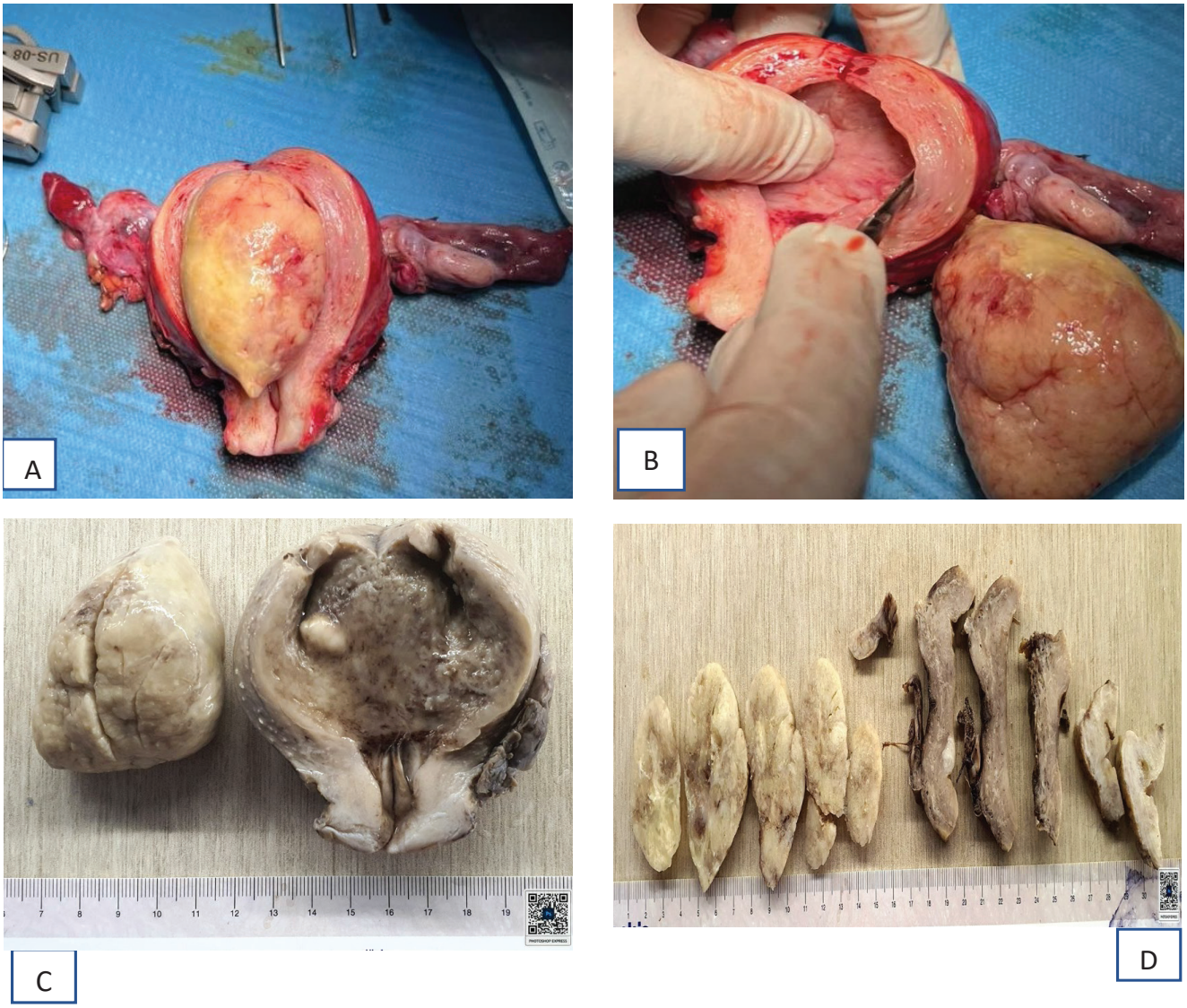

Figure 2. Macroscopically, a polypoid mass measuring 4 cm in diameter. A) The mass immediately after the uterine excision. B) The surgeon removed the mass, and no invasion was observed macroscopically. C) The lesion after the formalin fixation. D) The uterus was cut longitudinally together with the tumor to better evidence the place of insertion of the polypoid mass.

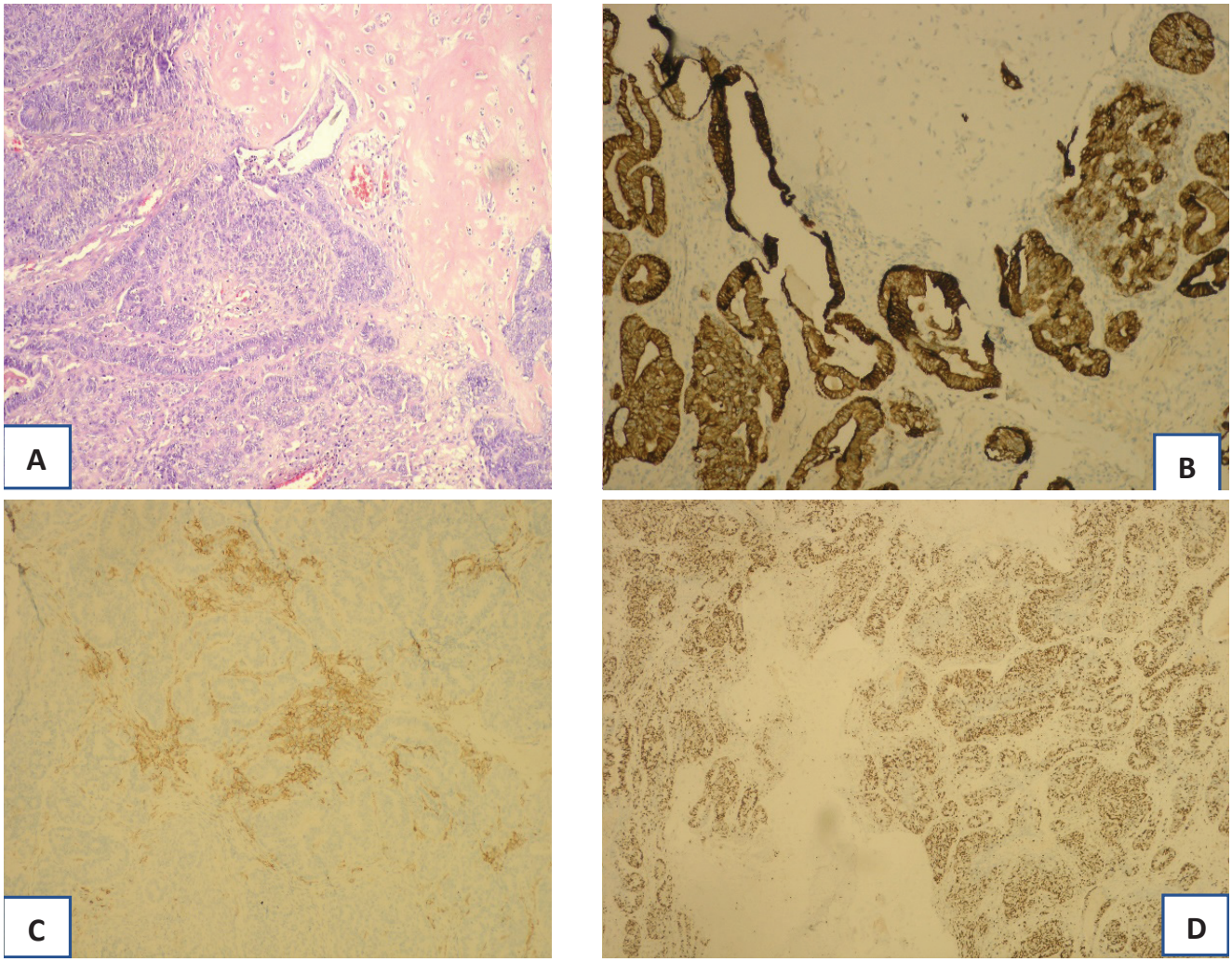

Figure 3. A) Hematoxylin Eosin x20. B) CK7 stain. C) PDL1 stain. D) ER stain.

occurring between the sixth and seventh decade [10], with a median age of 62 years [11]

Cases younger than 40 years old are sporadic. MMMT commonly affects the uterus; however, other parts include the cervix, ovaries, fallopian tubes, vagina, peritoneum, and extra-genital sites [12]. In our case, the patient is 56 years old, which corresponds to the average age of previous studies, and the tumor is located in the back of the corpus uteri.

MMMT has a poor prognosis, and most patients have extrauterine spread at the time of diagnosis [13]. Extension to the pelvis, lymphatic and vascular permeation, distant lymph nodes, and blood-borne metastasis are common [14]. It is crucial to mention that the epithelial component is frequently found at distant metastatic sites. In contrast, the sarcomatous component is linked to the extension of the tumor in the local area [14].

The case we present is unique in the English literature as a T0 case, exclusively polypoid without endometrial infiltration. Other cases in the literature range from at least T1 to stage IV. In a study by Rajshekar SK et al. [15], six patients were in the first stage, four in the second stage, and eight in the third stage. In a clinical case published by Emmanuel D. Morgan et al. [5], the patient was in stage II. Even in other studies or case reports, we did not find a case where the endometrium was not infiltrated by uterine carcinosarcoma.

Analyzing the macroscopic and microscopic findings, we have a previous adenomatous dysplastic endometrial polyp, which was grown sustained by a peduncle to expand the endometrial cavity. Then, malignant transformation occurred, with the subsequent transdifferentiation into the osteosarcoma component.

The symptoms and diagnosis of endometrial carcinosarcomas are vague and generally resemble those of many other types of endometrial cancers. It is challenging to differentiate endometrial carcinosarcoma from different types of uterine tumors based solely on clinical presentation. Clinical signs of uterine carcinosarcoma include vaginal bleeding, abdominal pain, and discharge. [18] Even in our case, the patient presents with postmenopausal bleeding and lower abdominal pain.

For the etiology of MT, nulliparity, diabetes mellitus, obesity, chronic stimulation with estrogen, history of pelvic radiation, and long-term use of tamoxifen are considered predisposing factors. In our case, apart from the fact that she is overweight with a BMI of ~ 25, the patient does not refer to this other predisposing factor. Regarding the treatment, there is no consensus on the gold standard treatment for uterine MT. The optimal treatment remains uncertain, partially because the histogenesis remains controversial. The primary treatment remains surgery with total hysterectomy and pelvic lymph node resection, although the benefits of lymph node resection have not been fully confirmed. A multimodality treatment plan has been suggested, with results indicating that surgery followed by a combination of both chemotherapy and radiation therapy leads to a significantly longer median disease-specific survival (DSS) of 31 months versus surgery alone (DSS = 3 months), radiation therapy alone (DSS = 15 months), or chemotherapy alone (DSS = 14 months). Recently, based on the results of several trials, immunotherapy (with or without tyrosine kinase inhibitor) has emerged as the standard treatment modality after the failure of platinum-based chemotherapy. Around 10% of endometrial carcinosarcomas are MSI-H, 5% are POLE mutated, and 60% show PD-1/PD-L1 immunohistochemical expression; immunotherapy (alone or in combination with tyrosine kinase inhibitor) may be particularly promising in these molecular subgroups. In our case, the patient underwent a total hysterectomy with resection of the pelvic lymph nodes, all of which were found to be reactive. After multidisciplinary oncologic consultations, it was decided that the patient should not undergo radiotherapy or chemotherapy because there was no endometrial infiltration, and the stage was T0. The patient has no metastatic lesions in the follow-up performed every three months for a year with an ultrasound examination and a PET scan.

Regarding the histopathological features, MMMTs express epithelial features through the positivity of epithelial markers such as pan-cytokeratin and epithelial membrane antigen and stromal features through the positivity of stromal markers such as Desmin and S-100. [18] In our case, in the examination with immunohistochemistry, the tumor results in positive CKAE1/AE3, positive Vimentin, and positive smooth muscle actin, supporting the diagnosis and adhering to the histopathological features of uterine carcinosarcomas.

MMMT has a poor prognosis, with extrauterine spread at the time of diagnosis in most of the patients [19]. Extension to the pelvis, lymphatic and vascular permeation, distant lymph nodes, and blood-borne metastasis are common [14]. The patient has no metastases in stages T0 and 12 months after the initial treatment. However, taking into account the aggressiveness of the tumor, it remains to be seen whether it will continue to be without metastases in the future or not. The metastatic spread of MT is similar to high-grade endometrioid carcinoma, and most patients die of local pelvic recurrence or abdominal recurrence. The risk for the advanced stage of the disease and recurrence is closely related to the depth of myometrial invasion. [20]. Moreover, the 3-year disease-free survival rate was 87% for cases with high-grade adenocarcinoma compared to 42% for cases with MMMT [19]. The average 5-year overall survival for patients with MTC was previously to be 21%, and 70%–90% of tumor-related deaths occurred within 18 months of diagnosis [21].

The strength of this case lies in the successful treatment outcome. The fact that the patient, after undergoing surgery without accompanying chemotherapy or radiotherapy, has shown no signs of disease recurrence after 12 months is a testament to the potential for successful treatment of uterine carcinosarcoma.

Conclusion:

Since uterine carcinosarcoma is a rare, highly aggressive, rapidly progressing neoplasm associated with a poor prognosis, it is necessary to include them in the differential diagnosis of uterine high-grade neoplasm. It is essential to make an accurate diagnosis in the cases of polypoid tumors of the uterus. Multiple punch biopsies and deep levels through a hysteroscopic procedure are the only procedures to approach a correct preoperative diagnosis. Considering carcinosarcomas in the differential diagnosis will make treatment more accurate and improve survival. From the clinical and imaging point of view, not all polypoid tumors are benign.

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Authors Contribution: L.K: Conceptualization of the case, revision, the surgeon who made the surgery of this case; L.B: The supervision, investigation, and collection of data; and the pathologist who diagnosed the case.; T.B: Helped in the revision, the collaborator pathologist of the diagnosis.; A.N: The data collection and the article's writing helped structure the article.

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OPEN ACCESS JOURNALS

CASE REPORTS

Diagnosing and Treating ANCA-Associated Vasculitis within the COVID-19 Era: A Challenging Case Report

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Abstract

Introduction: Anti-neutrophil cytoplasmic antibody (ANCA)- associated vasculitis (AAV) is a rare group of systemic autoimmune diseases that primarily target small blood vessels. Renal manifestations often present as pauci-immune focal and segmental necrotizing crescentic glomerulonephritis (PI-NCGN), which can progress to acute or chronic kidney failure and multiorgan involvement. It is frequently associated with poor outcomes.

We report a case of PR3-positive ANCA-associated vasculitis complicated by rapidly progressive glomerulonephritis, acute kidney injury, and diffuse alveolar hemorrhage during the COVID-19 pandemic. This case highlights the diagnostic challenges of differentiating AAV from conditions associated with SARS-CoV-2 infection, as the clinical and radiological presentations of pulmonary-renal syndromes may overlap.

The findings underscore the importance of maintaining a comprehensive differential diagnosis in patients with pulmonary and renal involvement, particularly in the post-COVID-19 era, to ensure timely and accurate management of rare autoimmune conditions such as AAV.

Conclusion: ANCA-associated vasculitis (AAV) remains a diagnostic and therapeutic challenge, particularly in the post-COVID-19 era, where overlapping clinical and radiological features with SARS-CoV-2 complications can obscure timely identification. This case highlights the critical importance of maintaining a broad differential diagnosis in patients presenting with pulmonary-renal syndromes to differentiate AAV from more common conditions associated with COVID-19.

Keywords: ANCA-associated vasculitis, crescentic glomerulonephritis, acute kidney injury, plasma exchange, hemodialysis, pulmonary-renal syndrome.

Introduction

Anti-neutrophil cytoplasmic antibody (ANCA) - associated vasculitis (AAV) is a rare group of autoimmune, systemic vasculitis affecting small vessels, mainly capillaries, arterioles, and venules. [1-4]

Based on their histopathological and clinical spectrum, AAVs constitute three distinct entities: MPA, GPA, and EGPA. [1-4] Based on the serology findings, they are classified as PR3-positive, MPO-positive, or ANCA-negative vasculitis. [1-4]

It has an estimated prevalence of 200-400 cases per million people and an equal distribution among males and females. [1-3] Clinical presentation is heterogeneous, and multiple organ involvement is often present primarily renal and pulmonary involvement. Manifestations include

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constitutional symptoms like arthralgia, myalgia, fatigue, and malaise, as well as shortness of breath, wheezing, and hemoptysis. [1-4]

Kidney involvement with hematuria, proteinuria, hypertension, and occasionally interstitial nephritis are frequent, as well. [1-4] Purpuric and petechial lesions are the most common cutaneous manifestations. [1-4]

ENT involvement, including chronic rhinitis, otitis, sinusitis, and laryngitis, is frequently observed in GPA. [1-4] Neurological manifestations are less common and they typically include mononeuritis multiplex and symmetrical polyneuropathy. [5] Treatment consists of immunosuppressive therapy to induce remission and prevent relapses.

Case presentation

A 34-year-old woman presented to the Emergency Department with a two-week history of flank pain, abdominal discomfort and diarrhea, gross hematuria, bilateral lower extremities paresthesia, and a progressive decline in urine output.

On physical examination, high blood pressure (140/80 mmHg) and peripheral pitting edema were noted. The rest of her examination was unremarkable. She reported an eight-month history of recurrent and prolonged sinusitis with episodes of epistaxis, for which she had received antibiotics with some improvement, as well as polyarthralgia and anemia, for which she had seen a rheumatologist. Family medical history was insignificant.

A complete blood count (CBC) and a comprehensive metabolic panel revealed the presence of severe anemia (RBC = 2.46 x 106/uL, Hgb = 5.9 g/dl), elevated levels of serum urea = 161.6 mg/dl, creatinine = 4.92 mg/dl and uric acid = 7.9 mg/dl. Urinalysis was positive for protein (75 mg/dL) and red blood cells (>50 RBC/HPF). A 24-hour urine collection revealed an albuminuria of 1788 mg/24-h. G6PD levels were within normal range. Viral serology for Hepatitis B and C, HIV, and SARSCoV-2 was negative. The indirect Coombs test was positive. Immunological assays revealed elevated serum levels of PR3 = 76.84 U/ml and rheumatoid factor, RF = 35.2 UI/ml. The rest of the examinations were negative, including complement C3 and C4 levels, ENA panel, anti-ds-DNA, MPO, and ASLO.

A high-resolution chest CT (HRCT) showed decreased ventilation, more pronounced in the left inferior lobe and superior lobes bilaterally, with ground-glass opacities varying 1.5-2 cm in size, with a peripheral distribution. No evidence of pleural effusion was present.

Kidney biopsy revealed crescentic glomerulonephritis. Ten glomeruli were examined. Global sclerosis was observed in seven of them, and crescents were present in three of them. In the interstitial area, there were pronounced inflammatory lymphocytic infiltrates and tubular necrosis. Arteriolar hyalinosis was also observed.

IHC staining for IgG, IgM, IgG4, and C3d were negative, suggesting pauci-immune crescentic glomerulonephritis,

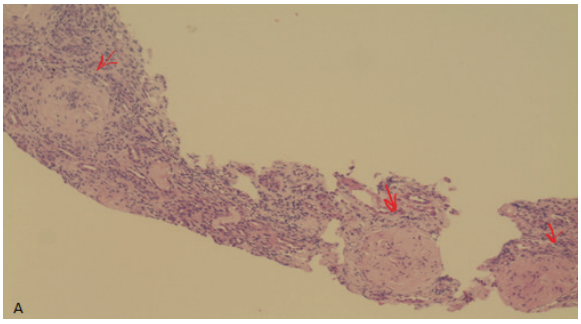

Fig. A. *Light microscopy of rapidly progressive glomerulonephritis (H&E staining). 3 glomeruli showing global sclerosis with all architectural landmarks and capillaries obliterated. There is marked interstitial inflammation.*

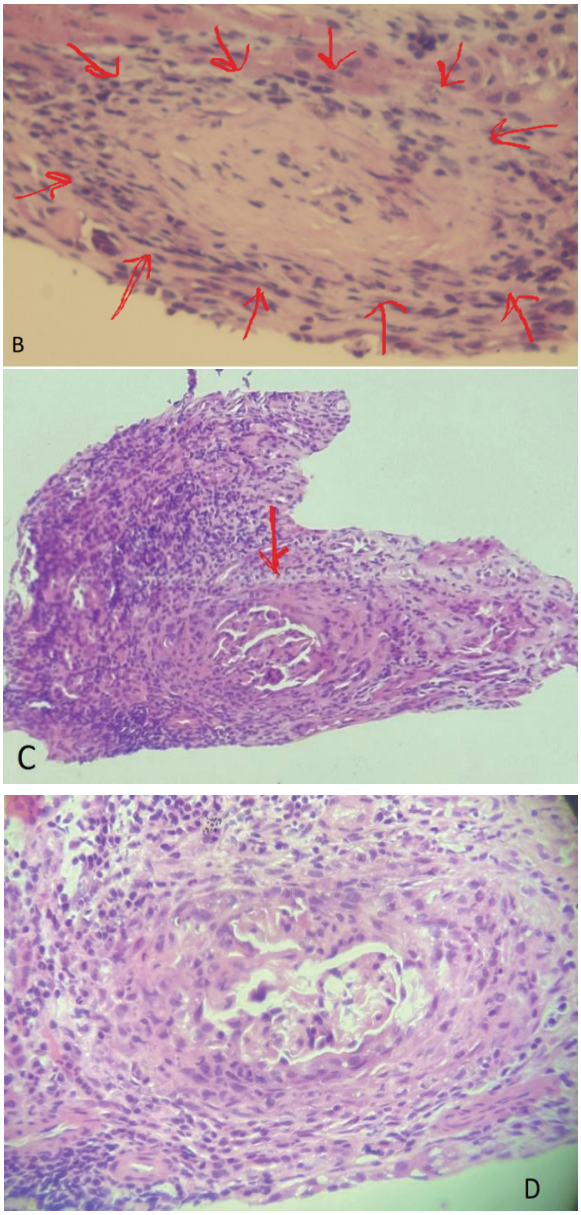

***Figure** B **- D.** (H&E staining). Light microscopy shows the vast destruction of Bowman's capsule.*
The glomerular tuft is collapsed by extra capillary cellular proliferation (crescents)

the sclerotic variant, with sclerosis in more than 50% of glomeruli.

In light of the clinical, radiological, and pathology findings, PR3-positive ANCA-associated vasculitis was diagnosed. During her hospital stay, her kidney function continued to deteriorate at a rapid pace, and she developed episodes of hemoptysis. Considering the urgent and rapidly progressive nature of her presentation and the multiple organ involvement, hemodialysis was initiated, as well as five sessions of plasmapheresis every 3 to 5 days. She was started on induction therapy with Cyclophosphamide and corticosteroids. She initially received a three-day course of high-dose pulse methylprednisolone (500 mg IV/daily) and was switched to 0.5 mg/kg/day of prednisone. She received Cyclophosphamide 500 mg IV for six rounds, three doses every two weeks, and the remaining three doses every three weeks until she was in complete remission. She was started on Azathioprine 2 mg/kg/daily as maintenance therapy, but after a few months, she developed HSV1-induced pancytopenia, and she was switched to mycophenolate mofetil 2g/daily.

The patient underwent hemodialysis sessions for a couple of weeks, but eventually, her kidney function improved, and she was weaned off dialysis. She is currently in complete remission.

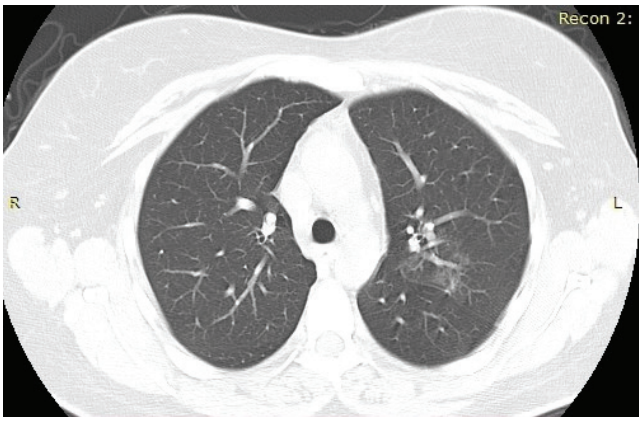

Figure. E. Chest CT scan after plasma exchange.

Discussion

The pathogenesis of AAV is complex and not fully elucidated. Genetic, environmental, and infectious factors have all been implicated in initiating an abnormal immune response, leading to the formation of autoantibodies (ANCA) directed against one of two neutrophil proteins, PR3 and MPO. [1-4]

PR3 and MPO are mainly found within neutrophil primary granules and lysosomes of monocytes. [1-4] Despite their presence in other autoimmune diseases or healthy individuals, ample evidence points to ANCA's pathogenicity. [1-4]

Neutrophils are key players in AAV pathogenesis, as they are both targets of autoimmunity and one of the primary effector cells. [1-4] Neutrophil priming implies an amplified neutrophil response to activating stimuli and represents a crucial step in the pathogenesis of AAV. [1,4]

It has been postulated that loss of B and T cell's immunologic tolerance to PR3 or MPO leads to the development of autoantibodies (ANCA) that, in turn, promote activation of neutrophils, adherence to the microvascular endothelium of the renal and respiratory system and other organs, ultimately inducing inflammation and tissue injury. [1-4] Monocytes and macrophages are important effector cells, contributing to the ongoing inflammation and granuloma formation. [1,2,4] Their pro-inflammatory and pro-fibrotic cytokines are instrumental in both acute and chronic injury. [1,2,4]

Radiological findings in HRCT include solid pulmonary nodules of varying size, usually of bilateral distribution, mainly in subpleural regions. [7-12] Focal "halo sings" surrounding solid nodules can also be appreciated in HRCT. [7-12] Central cavitation, without calcifications, may be present, and it is more prominent in larger nodules. [7-12] Air-space consolidations, ground-glass opacities (GGO), and mosaic attenuation patterns corresponding to areas of diffuse alveolar hemorrhage and vascular inflammation can be noted, as well. [7-12] They commonly present as diffuse, patchy opacities. [7-12] Occasionally, centrilobular nodules and a tree-in-bud pattern can be visualized. [7-12] Bronchial wall thickening and peri-bronchovascular interstitial thickening may be evident. [7-12] Pleural effusions and wedge-shaped consolidations may be present in some cases, representing possible pulmonary infarcts. [13]

Bronchial involvement with decreased ventilation, more pronounced in the left inferior lobe and superior lobes bilaterally, was observed in our patient. Ground-glass opacities measuring 1.5-2 cm with a peripheral distribution were noted. No evidence of pleural effusion was present. Considering that ground-glass opacities were a ubiquitous finding in HRCT of patients with COVID-19 and our patient presented in the midst of the COVID-19 pandemic, the differential diagnosis was challenging, as the radiological findings initially suggested a potential COVID-19 infection.

Kidney involvement is very prevalent in AAV and is considered an important predictor of mortality, associated with a 50% risk of death or ESKD at five years in patients presenting with an eGFR < 50 ml/min. [14] It is characterized by rapidly progressive glomerulonephritis (RPGN) with proteinuria, microscopic hematuria, and rapid decline of kidney function in a few days to months. [14] Kidney biopsy typically shows the presence of pauci-immune focal necrotizing crescentic glomerulonephritis. [14]

Nevertheless, the biopsy findings were typical of pauci-immune crescentic glomerulonephritis, the sclerotic variant with more than 50% of glomeruli showing global sclerosis. Crescents were found in 3 out of 10 glomeruli. Overall, the clinical, laboratory, and histopathological findings all pointed to a diagnosis of PR3-positive ANCA vasculitis.

Treatment of AAV consists of a two-step approach: an induction therapy to achieve clinical remission and a maintenance therapy to maintain remission. [3,4,13,15]

Combined therapy with glucocorticoids and an immunosuppressive agent has been traditionally used to induce remission. [3,4,13,15] A three consecutive day IV pulse of methylprednisolone, then switched to oral prednisone of 1 mg/kg/daily, has been generally used. [3,4,13,15] Nevertheless, new studies advocate the adoption of reduced-dose and rapid tapering glucocorticoid protocols. [3,4,13,15] They have been shown to be non-inferior to more traditional, slower-tapering regimens and associated with fewer side effects. [3,4,13,15]

Cyclophosphamide is an alkylating agent that, for decades, has been the cornerstone of induction therapy in AAV. It is associated with 75% to 90% remission rates at three to six months, respectively. [3,4,13,15] Both oral and intravenous administration have been used. However, the intravenous route at weeks 0, 2, 4, and every three weeks is preferred as it leads to less exposure and smaller cumulative doses of Cyclophosphamide. [3,4,13,15]

Rituximab is a chimeric monoclonal anti-CD20 antibody used to induce remission in combination with glucocorticoid therapy. [3,4,13,15] Cyclophosphamide remains the preferred agent in organ and life-threatening diseases, including severe kidney disease and diffuse alveolar hemorrhage (DAH). [3,4,13,15] In these patients, the use of plasmapheresis to aid in removing immune complexes from serum has also been advocated. [3,4,13,15]

Currently, rituximab is considered first-line therapy following induction with rituximab or Cyclophosphamide, as studies show it is associated with lower relapse rates. [3,4,13,15] Azathioprine, mycophenolate mofetil (MMF), and methotrexate can be used as alternatives, coupled with low-dose steroids. [15] Patients remain on maintenance immunosuppression for two to four years. [15]

In our patient, considering the severe kidney involvement, as well as the development of diffuse alveolar hemorrhage, we opted for the use of plasmapheresis, five sessions in total every 3 to 5 days, and induction therapy with pulse glucocorticoids for three consecutive days, then switched to a reduced-dose steroid regimen and intravenous Cyclophosphamide, for a total of six doses until achieving complete remission. As rituximab is not reimbursed in Albania, she was started on Azathioprine as maintenance therapy and subsequently switched to mycophenolate mofetil (MMF) due to adverse effects associated with Azathioprine. She remains in complete remission.

Conclusion

This is one of the first documented cases in our country where the complete recommended therapeutic regimen has been successfully implemented to achieve remission in ANCA vasculitis. Initially, the radiological findings were suggestive of a COVID-19 infection, a common diagnostic challenge during the pandemic era. The overlap of imaging findings between COVID-19 and other systemic diseases with pulmonary involvement posed a significant obstacle in the differential diagnosis.

Prompt diagnosis followed by a targeted and aggressive treatment approach, including the rare use of plasmapheresis in our institution, was pivotal in achieving complete remission. This case emphasizes the importance of considering a broad differential diagnosis and the potential utility of plasmapheresis in severe ANCA vasculitis with DAH, even in resource-limited settings.

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Abbreviations

ANCA - Anti-Neutrophil Cytoplasmic Antibody; AAV - ANCA - Associated Vasculitis; PI-NCGN - Pauci-Immune Focal and Segmental Necrotizing Crescentic Glomerulonephritis; GPA - Granulomatosis with Polyangiitis; MPA - Microscopic Polyangiitis; EGPA - Eosinophilic GPA; ENT - Ear, Nose and Throat; RBC - Red Blood Cell; HPF - High Power Field; G6PD - Glucose-6-Phosphate Dehydrogenase; HIV - Human Immunodeficiency Virus; SARSCoV2 - Severe Acute Respiratory Syndrome Coronavirus 2; PR3 - Antimicrobial Proteins Proteinase 3; RF - Rheumatoid Factor; ENA - Extractable Nuclear Antigen; DNA - Deoxyribonucleic Acid; ds - double stranded; MPO - Myeloperoxidase; ASLO - Antistreptolysin O; HRCT - High-Resolution Chest CT; IHC- Immunohistochemistry; IgM – Immunoglobulin M: IgG - Immunoglobulin G; IgE - immunoglobulin E; H&E - Haematoxylin & Eosin: PR3 - Proteinase 3; RPGN - Rapidly Progressive Glomerulonephritis; DAH - Diffuse Alveolar Hemorrhage; CD20 - Cluster of Differentiation 20; MMF - Mycophenolate Mofetil;

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CASE REPORTS

Successful Management of Refractory Heart Failure and Multi-Organ Dysfunction in a Patient with CRT-D and Acute Pulmonary Edema: A Case Report

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Abstract

Introduction: Heart failure with reduced ejection fraction (HFrEF) is a progressive condition often complicated by acute decompensations that require advanced medical interventions. Cardiac resynchronization therapy with a defibrillator (CRT-D) has significantly improved outcomes in patients with severe heart failure. However, challenges persist when faced with acute events such as pulmonary edema, pneumonia, and multi-organ dysfunction syndrome. Multidisciplinary, intensive care unit (ICU)-based management is critical for these complex cases.

This case report presents the successful management of a 61-year-old female patient with a history of severe HFrEF and implanted CRT-D. Despite severe hypoxemia, hypotension, and metabolic acidosis, a multidisciplinary approach—including mechanical ventilation, intra-aortic balloon pump (IABP), continuous renal replacement therapy (CRRT), and transfusion—enabled recovery. The patient was admitted to the ICU with acute pulmonary edema, pneumonia, and multi-organ dysfunction syndrome, characterized by severe hypoxemia, hypotension, and metabolic acidosis. Over three weeks, the patient regained hemodynamic stability, renal function, and respiratory independence.

This case demonstrates the potential for recovery in patients with severe heart failure complicated by acute pulmonary edema and multi-organ dysfunction when treated with an integrated, multidisciplinary approach.

Conclusion: Advanced critical care strategies, including mechanical ventilation, intra-aortic balloon pump support, and continuous renal replacement therapy, were essential in stabilizing the patient. The outcome underscores the value of personalized, team-based critical care in managing life-threatening complications in heart failure patients with CRT-D.

Keywords: Heart failure, HFrEF, CRT-D, APE, MOD, IABP, CRRT, multidisciplinary management.

Introduction

Heart failure with reduced ejection fraction (HFrEF) is a progressive condition affecting millions worldwide and is a leading cause of hospitalization and mortality [1]. Advanced therapies, including CRT-D, have been shown to improve cardiac function and reduce hospitalizations in selected patients [1, 2].

However, these individuals remain vulnerable to acute decompensation due to infections, arrhythmias, or other triggers [2]. Such episodes often lead to multi-organ failure and require a complex, multidisciplinary approach.

Here, we present a unique case of a patient with advanced HFrEF who overcame severe pulmonary edema, refractory hypotension, and multi-organ dysfunction.

Despite prolonged ICU care and the occurrence of complications, including a femoral artery hematoma, the patient's full recovery is a testament to the resilience of critical care protocols and the human body under expert management, instilling a sense of hope in the audience.

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***Case Presentation**: Patient History and Initial Presentation*

A 61-year-old woman with a history of severe HFrEF and an ejection fraction (EF) of 15–20% underwent CRT-D implantation two years prior. Her past medical history included a prolonged ICU stay one year earlier for multi-organ failure, secondary to severe heart failure decompensation, during which she developed sacral decubitus ulcers. She had since recovered to baseline functional status and was maintained on optimal guideline-directed medical therapy for heart failure.

She presented to the emergency department with acute shortness of breath, productive cough, and altered mental status. Her family could not distinguish between a psychotic attack or cardiac problems because she was under treatment for psychiatric disorders.

On examination, her respiratory rate was 35 breaths per minute, oxygen saturation (SpO_2) was 40–60% on room air, and she exhibited diffuse bilateral crackles on auscultation.

Their blood pressure was 78/50 mmHg, and she had cold extremities with a delayed capillary refill, indicative of cardiogenic shock.

Laboratory and Imaging Findings

Arterial blood gas analysis showed severe metabolic acidosis with a pH of 6.98, partial pressure of carbon dioxide ($PaCO_2$) of 62 mmHg, bicarbonate (HCO_2^-) of 16 mmol/L, and lactate of 6.5 mmol/L. Chest X-ray revealed diffuse bilateral pulmonary infiltrates consistent with pulmonary edema. Echocardiography demonstrated an EF of 15% with severe global hypokinesis and elevated left ventricular end-diastolic pressure. (Fig. 1)

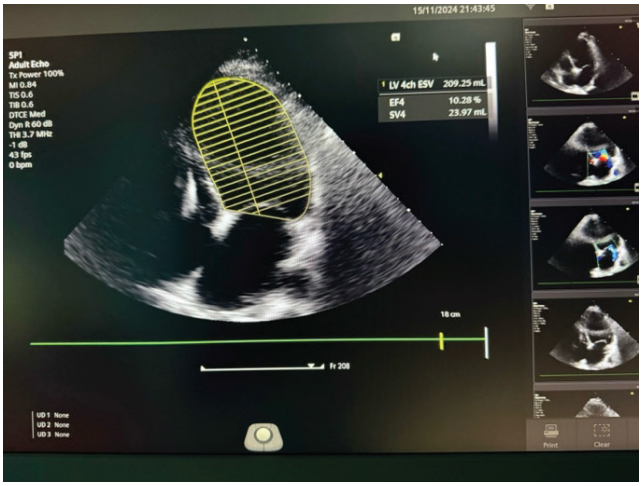

Figure 1. Echocardiography in admission shows low EF with severe global hypokinesis.

Initial laboratory tests revealed:

- White blood cell count: 18,000/μL
- Hemoglobin: 9.8 g/dL
- Creatinine: 2.8 mg/dL (baseline: 1.2 mg/dL)
- Blood urea nitrogen: 68 mg/dL
- Potassium: 5.6 mmol/L

Management

The patient was started on high-flow oxygen therapy and intravenous (IV) diuretics, but her oxygen saturation and urine output continued to decline. CPAP was initiated, and IV inotropic support with dobutamine (5 μg/kg/min) was administered, but these measures failed to improve hemodynamics. She was intubated and placed on mechanical ventilation.

Intra-Aortic Balloon Pump Support

To stabilize refractory hypotension, an IABP was inserted via the right femoral artery. Within 12 hours, mean arterial pressure improved to 65 mmHg, urine output increased to 50 mL/hour, and lactate levels decreased to 3.2 mmol/L [3]. However, after 48 hours of IABP support, when vital parameters were under typical values and IABP support was not needed, vascular complications developed.

Complication and Management

Upon removal of the IABP, the patient developed a large hematoma at the femoral artery insertion site, leading to recurrent hypotension (blood pressure 70/45 mmHg), atrial fibrillation (AF), severe anemia (hemoglobin 6.7 g/dL), and oligoanuria. Duplex ultrasonography confirmed a pseudo-aneurysm at the femoral artery. She was transfused with three units of packed red blood cells and underwent vascular compression therapy [4].

Renal Support and Recovery

Due to worsening metabolic acidosis and persistent oligoanuria, CRRT with Prismaflex was initiated. Over five days, serum creatinine decreased to 1.6 mg/dL, urine output improved to 1,000 mL/day, and metabolic parameters normalized [5]. Inotropic agents were gradually weaned, and she was extubated on day 10.

Outcome

After extubation, the patient, with normal vital parameters, was neurologically not responding well, developing muscular weakness and severe fatigue. However, with close monitoring in the ICU, enteral hypercaloric nutrition through

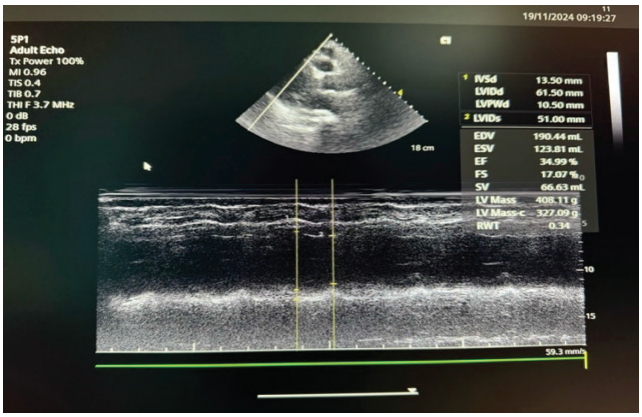

Figure 2. Echocardiography of the patient 1 day before discharge.

NG tube feeding, and a daily intensive physiotherapy program, she showed steady improvement. By day 15, she had regained hemodynamic stability, full renal function, mobility, and muscle strength, leaving the audience feeling optimistic about the patient's recovery. After three weeks, she was discharged from the ICU to a general ward. At discharge, echocardiography showed an EF of 30-35 %, and she was tolerating oral heart failure medications. (Fig.2)

Discussion

This case exemplifies the challenges and strategies in managing advanced heart failure with multi-organ dysfunction. Key insights include:

IABP for Hemodynamic Support:
IABP is a valuable bridge therapy for refractory cardiogenic shock, improving coronary perfusion and systemic hemodynamics [3]. While complications such as vascular injury are standard, vigilant monitoring and prompt intervention minimize adverse outcomes.

CRRT for Acute Kidney Injury:
CRRT effectively managed volume overload, uremia, and acid-base derangements in this critically ill patient. Early initiation in the setting of oliguria and metabolic acidosis may have prevented irreversible renal injury [5].

Transfusion and Vascular Complication Management:
The femoral artery hematoma posed a significant challenge, exacerbating hypotension and anemia. Timely transfusion and vascular intervention were critical to restoring hemodynamic stability and preventing further complications [4].

Multidisciplinary Approach:
The coordination of cardiology, nephrology, vascular surgery, and intensive care teams facilitated the complex decision-making required in this case [6, 7].

Conclusion

This case highlights the potential for recovery in patients with advanced HFrEF and severe complications through aggressive and well-coordinated critical care. The successful outcome underscores the importance of hemodynamic support, renal replacement therapy, and multidisciplinary management in improving outcomes for this high-risk population.

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Disclosure: The authors declared no conflict of interest. No funding was received for this study.

Abbreviations
HFrEF- Heart Failure with Reduced Ejection Fraction; CRT-D - Cardiac Resynchronization Therapy with a Defibrillator; ICU - Intensive Care Unit; IABP - Intra-Aortic Balloon Pump; CRRT - Continuous Renal Replacement Therapy; APE - Acute Pulmonary Edema; MOD - Multi-Organ Dysfunction; EF - Ejection Fraction; HCO_2^- *- Bicarbonate;* $PaCO_2$ *- Partial Pressure of Carbon Dioxide;* SpO_2 *- Oxygen Saturation; TTE - Transthoracic Echocardiography; CPAP - Continuous Positive Airway Pressure;*

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CASE REPORTS

Candiduria in Pediatric Patients: Two Case Reports and a Review of Management Strategies

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Abstract

Introduction: Urinary infections, while common in intensive care and surgical units, present a unique challenge when fungal pathogens are involved. These fungal urinary infections, known as fungiuria, require a more intricate and prolonged treatment plan involving antifungal medications. This complexity underscores the need for specialized knowledge and skills in managing such cases.

This study aims to present two cases of operated pediatric patients who developed urinary fungal infections following Catheterization and simultaneous treatment with two antibiotics.

Results: Two pediatric patients, aged 12 and 16, underwent surgical procedures in our clinic. The first patient was treated for gangrenous appendicitis complicated by generalized peritonitis. The second patient was treated for a perforation of the small intestine caused by gangrene in a segment of the bowel, resulting from twisting around intestinal adhesions, also complicated by generalized peritonitis.

Both patients, aged 12 and 16, developed urinary symptoms four days after surgery. Microbiological analysis confirmed the presence of fungal infections caused by Candida albicans. However, with the administration of antifungal medications, we were able to successfully eradicate Candida albicans from their urinary tracts, as confirmed by follow-up microbiological cultures after several weeks of therapy. This successful outcome should instill a sense of accomplishment in the audience.

Conclusion: Candidiasis, a significant complication in patients undergoing prolonged Catheterization and simultaneous antibiotic therapy, requires vigilant monitoring. The challenging treatment often necessitates long-term administration of antifungal medications for successful eradication. This underscores the importance of vigilance in monitoring fungal infections in catheterized patients and adopting preventive strategies to minimize their occurrence.

Keywords: Candida, antibiotics, urinary catheter, candiduria

Introduction

Candiduria is typically caused by the overgrowth of *Candida* species in the urinary tract. These pathogens are commonly found in the mouth, skin, and intestines. Children's most frequently associated species include *Candida albicans*, *Candida glabrata*, and *Candida tropicalis* [1]. In healthy individuals, the incidence of candiduria is less than 1%; however, this incidence increases significantly in immunocompromised individuals or those with diabetes and systemic diseases [2, 3].

In pediatric patients, several factors contribute to an increased risk of candiduria. Among the most common causes are:

- Urinary Tract Abnormalities, particularly vesicoureteral reflux.
- Prolonged Use of Broad-Spectrum Antibiotics, which disrupt the natural microbial balance.
- Long-term Catheterization of the urinary tract.
- Poorly Controlled Diabetes, where elevated glucose levels in the urine provide an environment conducive to fungal growth.

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- Immunocompromised Conditions, such as leukemia, solid organ transplantation, or other forms of immunosuppression [1, 2, 4, 8].

These factors highlight the importance of vigilance in managing pediatric patients at risk for fungal urinary infections to minimize their incidence and associated complications.

Case Report 1

An 8-year-old girl was admitted to the Department of Surgery due to a perforated appendix accompanied by generalized peritonitis. Following an appendectomy and peritoneal lavage, the patient was hospitalized. On the fifth day of hospitalization, she developed febrile episodes and suprapubic pain. The discharge from the abdominal drain was minimal and consisted of clear serous fluid, while the urine appeared cloudy and foul-smelling. Despite being catheterized, the patient reported a sensation of urgency to urinate.

After the surgical intervention, the patient's vital signs stabilized, and no significant deterioration was observed at the onset of urinary symptoms. According to the parents, the patient had experienced a urinary tract infection (UTI) two years prior.

Laboratory investigations revealed a white blood cell (WBC) count of 12.8/μL, with 48% neutrophils, a C-reactive protein (CRP) level of 4, a serum creatinine level of 0.16 mg/dL (normal range: 0.03–0.50 mg/dL), and a urea level of 32 mg/dL (normal range: 2.1–8.5 mmol/L). Urinalysis showed 3+ proteinuria, glucose, nitrites, and microhematuria. Abdominal ultrasonography identified minimal fluid in the Douglas cavity without any other abnormalities.

After replacing the urinary catheter and disinfecting it with an alcohol solution, approximately 15 mL of urine was collected for culture. Microbiological examination identified *Candida albicans* in the fungal culture, which was sensitive to fluconazole. Urine samples were inoculated onto blood and chromogenic media. After 16–24 hours of incubation, the colonies were sent for identification, and the genus and species were determined using the Vitek MS system.

The patient was started on fluconazole at a dose of 3 mg/kg/day. Postoperatively, she was also treated with ceftriaxone at a dose of 1 g twice daily, which was continued alongside fluconazole until her discharge from the hospital.

Urine cultures were repeated on the fifth and tenth days after initiating antifungal treatment, and both results remained positive for *C. albicans*. Consequently, fluconazole therapy was continued. The urine culture tested negative for *C. albicans* three weeks after starting treatment, but the patient continued fluconazole therapy for an additional two weeks.

Following the completion of therapy, urine cultures were repeated at intervals of two, five, and eight weeks, and all three results were negative for candiduria.

Case Report 2

A 16-year-old boy was hospitalized with abdominal pain localized across all quadrants. Anamnesis revealed that the patient had undergone surgery six years earlier for a perforated appendix. Physical examination showed a distended and tense abdomen with pronounced tenderness in all quadrants, accompanied by positive peritoneal signs. The patient reported multiple episodes of vomiting and an absence of defecation for the previous three days. Additionally, mucous membranes were dry, and skin turgor was slightly decreased.

Abdominal ultrasonography revealed distended, fluid-filled small bowel loops, while plain abdominal radiography showed multiple air-fluid levels. Laboratory analyses were within normal ranges, except for slightly elevated urea and creatinine levels. The white blood cell (WBC) count was 18.8/μL, and the C-reactive protein (CRP) level was elevated at 84 mg/dL. Electrolyte values were normal: sodium 139 mmol/L, potassium 4.4 mmol/L, calcium 9.4–10.7 mg/dL, chloride 102 mmol/L, and bicarbonate 22 mmol/L.

A nasogastric tube was inserted, draining approximately 300 mL of gastric juice with bile content. A urinary catheter was also placed, yielding only 150 mL of concentrated urine. The patient's treatment included Ringer's solution and gastric antisecretory medication (famotidine).

Despite intensive treatment, the patient's condition worsened, with persistent abdominal distension. A computed tomography (CT) scan of the abdomen revealed an abrupt transition from dilated to collapsed bowel segments, distorting the loops. Additionally, a significant amount of free fluid was observed in the abdominal cavity.

Given the lack of improvement, surgical intervention was performed. Intraoperative findings included an ischemic segment of the small intestine with multiple perforations and extensive adhesions between the small bowel loops and the abdominal wall. A 15 cm ischemic segment of the small intestine was resected, and adhesiolysis was performed. The abdominal cavity was irrigated with a large volume of physiological saline, and a Douglas drain was placed after the procedure.

Postoperatively, the patient was treated with two antibiotics: ceftriaxone and metronidazole. On the fourth day of hospitalization, the patient began to experience suprapubic discomfort and urethral burning, with cloudy urine observed in the urinary collection bag. The patient developed a fever and moderate leukocytosis (WBC count of 12.5/μL), and urinalysis showed proteinuria, glucose, nitrites, and microhematuria.

The urinary catheter was replaced, and a urine sample was collected for culture. Microbiological analysis identified *Candida albicans*. Antifungal treatment was initiated, and a follow-up urine culture conducted 10 days later was negative. The patient continued antifungal therapy for an additional two weeks. Subsequent urine cultures at intervals of three, eight, and twelve weeks were also negative, confirming the resolution of candiduria.

Discussion

Urinary infections remain one of the most common issues among children in surgical wards, with an estimated incidence of approximately 8% [5]. The high incidence is primarily attributed to the need for prolonged Catheterization following surgical interventions. The main clinical concerns associated with these infections include suprapubic discomfort and elevated body temperature. Studies indicate that the incidence of urinary infections varies depending on factors such as gender, age, and race, with the most frequent causative agent being *Escherichia coli* [1, 2, 5, 6].

The *Escherichia coli* group, which typically colonizes the large intestine, is the predominant cause of urinary infections. However, other bacterial species may occasionally be responsible, and in rare cases, fungal pathogens, particularly *Candida* species, can lead to urinary infections [3, 4, 7].

Children with severe illnesses, those admitted to intensive care units, or those with underlying conditions such as diabetes mellitus, indwelling catheters, or recent antibiotic use are at increased risk for fungal infections, including candidemia [6, 7, 8]. Other contributing factors include abnormalities of the urogenital tract (e.g., vesicoureteral reflux), prematurity, prolonged hospitalization, malignant diseases (especially hematological malignancies), and neutropenia [1, 2, 5, 11, 12].

In hospitalized patients and postoperative cases, antibiotic use, mainly when two or more antibiotics are administered simultaneously, is a significant factor in promoting the development of candida infections [10, 15].

Among fungal pathogens, *Candida* species are the most prevalent, accounting for approximately 90% of cases. Though less common, other causative agents include *Aspergillus*, *Blastomyces*, and *Cryptococcus* [4, 7, 9].

Numerous studies have reported an increasing incidence of candidiasis, with some references indicating rates as high as 40% in hospitalized patients [5, 7, 13, 14]. Patients with fungal infections, especially those presenting with systemic symptoms such as fever and dysuria, should be treated with antifungal medications, with fluconazole being the preferred choice [16].

Fluconazole treatment should be prolonged, continuing for at least 21 days after the last negative culture for candiduria or 40–45 days from the initiation of therapy. The recommended dosage is 3 to 6 mg/kg, administered intravenously once daily, followed by oral administration at the exact dosage after discharge.

Amphotericin B is an alternative treatment for systemic and severe fungal infections, including candiduria in specific cases. This antifungal agent is particularly effective in severe or refractory cases and remains an important option in clinical practice.

Conclusion

Urinary infections are among the most common infections in patients admitted to intensive care units and surgical wards. While most of these infections are caused by bacteria, particularly *Escherichia coli*, fungal infections, most commonly due to *Candida albicans*, are also significant contributors.

Several factors influence the development of candiduria, including the concurrent use of multiple antibiotics, prolonged Catheterization, serious chronic illnesses, and abnormalities of the urogenital tract.

The treatment of candiduria requires antifungal medications, with fluconazole demonstrating high efficacy. However, antifungal therapy must be extended for several weeks following the first negative urine culture for *Candida* to ensure complete eradication and prevent recurrence.

COI Statement: This paper has yet to be submitted in parallel, presented fully or partially at a meeting, podium, or congress, published, or submitted for consideration beforehand.

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CASE REPORTS

Thymus Hyperplasia and Thymoma Type B in Patients with Myasthenia Gravis: Two Case Reports and Literature Review

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Abstract

Introduction: The thymus gland plays a pivotal role in immune system regulation. However, conditions such as thymic hyperplasia (TH) and thymoma pose distinct clinical challenges due to their rarity and complex presentation in surgical practice. Both conditions can mimic similar symptoms, particularly in patients with Myasthenia Gravis (MG), where surgery serves as both a diagnostic and therapeutic intervention. This report presents the surgical management and outcomes of two MG patients with distinct thymic pathologies, TH, and Type B thymoma, alongside a review of the relevant literature.

Two MG patients were referred to our clinic for surgical intervention. The first patient underwent a standard sternotomy for the resection of TH, while the second patient underwent a mini-sternotomy for thymectomy targeting a Type B thymoma. Both procedures were completed successfully with uneventful postoperative courses. Surgical resection remains the gold standard for the treatment and definitive diagnosis of thymic gland abnormalities. Advances in surgical techniques, including minimally invasive approaches, offer excellent outcomes with reduced morbidity, providing a viable alternative to traditional methods.

Conclusion: The cases underscore the critical role of surgical intervention in managing thymic pathologies in MG patients. Traditional and minimally invasive techniques yield excellent clinical outcomes, reinforcing their importance in the thymic hyperplasia and thymoma treatment paradigm. Further studies are needed to refine surgical approaches and optimize patient outcomes.

Keywords: Thymoma, Thymic Hyperplasia, Myasthenia Gravis, Surgical Resection, Minimally Invasive Surgery

Introduction

The thymus is located in the anterior of the chest cavity and is essential for developing T-lymphocytes. After puberty, the thymus naturally shrinks in size, but certain pathological conditions can lead to thymic enlargement or tumor formation. Among these conditions, hypertrophic thymus (HT) and thymoma are distinct entities with varying causes, clinical presentations, and treatment approaches [1]. The hypertrophic thymus is typically a benign condition characterized by an enlargement of the thymus gland without any signs of cancerous changes. It is often associated with stress, infections, or autoimmune diseases. Myasthenia Graves' disease in 50-70% of cases have thymic hyperplasia [2]. This condition may have no symptoms or may present with non-specific signs such as chest pain or cough, often leading to incidental findings on imaging tests [3].

Meanwhile, a thymoma is a tumor originating from the thymus gland's epithelial cells. It is the most common tumor in the anterior part of the chest cavity in adults and can range from benign to highly aggressive. Based on cancer registry data, the overall incidence of thymoma is estimated to be 0.13 per 100,000 person-years. Thymomas are often associated with paraneoplastic syndromes, particularly myasthenia gravis, which occur in 30-50% of patients with thymoma and can cause symptoms that suggest local invasion [4].

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The surgical management of HT and thymoma is vital in treatment and/or appropriate diagnosis to manage these clinical conditions. This article reports two cases, HT and thymoma, surgical treatment, emphasizing the importance of accurate diagnosis, staging, and personalized treatment plans.

Case 1

A 20-year-old female patient is admitted to the Neurology Department, University Hospital Center "Mother Theresa," with complaints of difficulty swallowing, difficulty speaking, and ptosis of the eyelids. The patient was diagnosed with Myasthenia Gravis a year ago, with worsening symptoms recently. She started treatment with Mestinon three months ago and later with prednisolone.

The neurological examination is normal except for the partial eyelid ptosis. A computed tomography scan showed thymus hypertrophy. In the conditions when she was refractory to the medication, she was scheduled to be transferred to the cardiac surgery service for intervention. All laboratory examinations were standard. Acetylcholine receptor antibodies were positive, with a value of 106 nmol/l from a standard range of 0.1 nmol/l. The intervention was performed through median sternotomy under general anesthesia, taking special care of the specifics of the pathology. The thymus is exposed and then resected up to the border of the phrenic nerve bilaterally. The resected lobes are sent for histopathological examination. The patient was dismissed on the fifth day after surgery, with no complications, to continue the therapy with Mestinon, Azathioprine, and Prednisone. She was referred back to the neurology department. Post-operative showed an exceptional clinical amelioration within one month after intervention.

The following is a picture of the CT scan of the patient where thymus hyperplasia is evident.

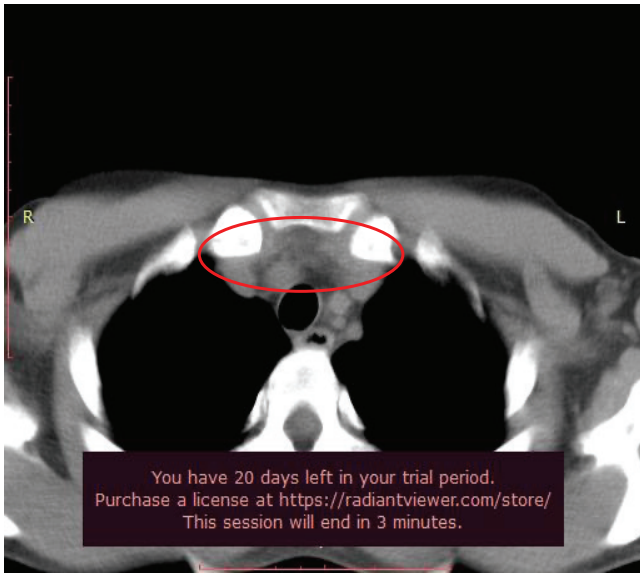

Figure 1. CT scan image of thymus hyperplasia

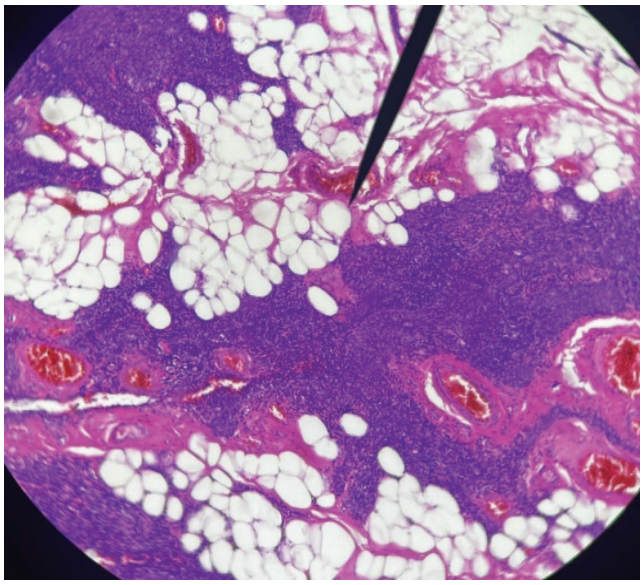

Figure 2. Thymus Hyperplasia

The histopathological analysis reveals normal components of the thymic gland, normal cortex, medulla, and Hassall corpuscles with maintained lobular configuration and preserved corticomedullary junction (Figure 2).

Case 2

A 62-year-old male patient presents to the Neurology Service with complaints of difficulty in swallowing, nasal voice, and tongue numbness. He reports that these complaints started a month ago. All the laboratory examinations were normal except for Acetylcholine receptor antibodies, which were positive 8.5 U/ml from less than 0.4, defined as a negative value. He was diagnosed with Myasthenia Gravis and started on treatment with Mestinon® and Prednisolone. A mediastinal mass, 4 X 4 cm, is noted on a CT scan in the thymus area with an indication for surgery. For this reason, the patient is transferred to the cardiac surgery service.

The surgery is performed under general anesthesia through the right "J" upper hemi sternotomy. Upon exposure, a mass in the anterior mediastinum is observed, which is suspected to be a thymoma. The mass is macroscopically firm on palpation and gelatinous in appearance internally. It is densely adhered to the bilateral phrenic neurovascular bundle and has adhesions to the brachiocephalic vein. The mass is carefully dissected and successfully resected for histopathological analysis.

The patient was discharged on the fifth day after surgery with no further complications and was referred to the neurologist and oncologist for additional follow-up. The microscopic description of the mass shows evidence of solid cellular proliferation divided by fibrotic septa.

The histopathological picture suggests a Thymoma B3. Histopathology showed a lobulated architecture comprised of cellular lobules intersected by sharply demarcated fibrous bands (A). perivascular space, small vessels surrounded by palisading neoplastic cells and scattered thymocytes (B). (Figure 3)

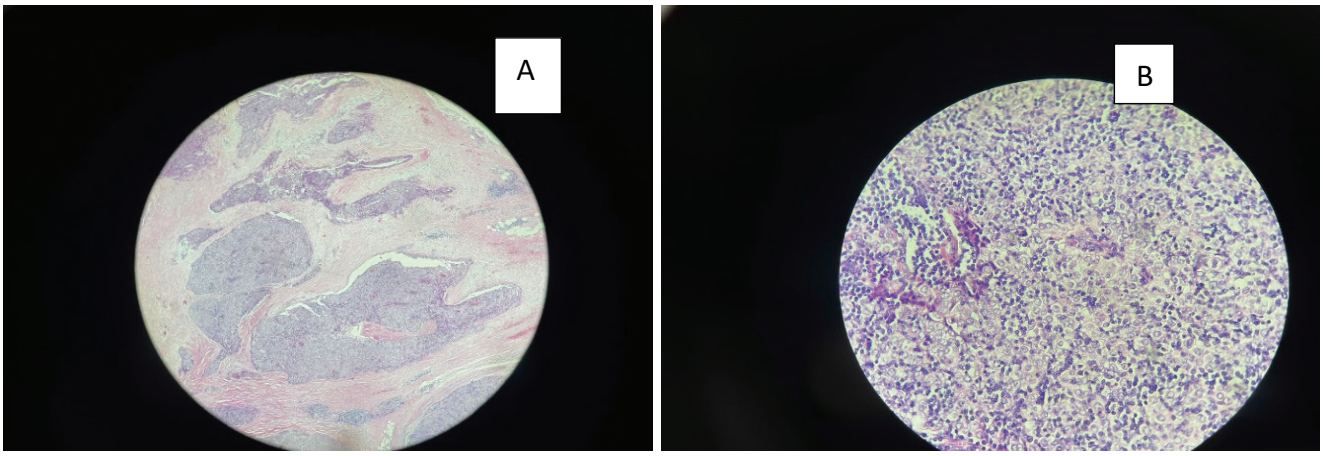

Figure 3. Thymoma Type B.

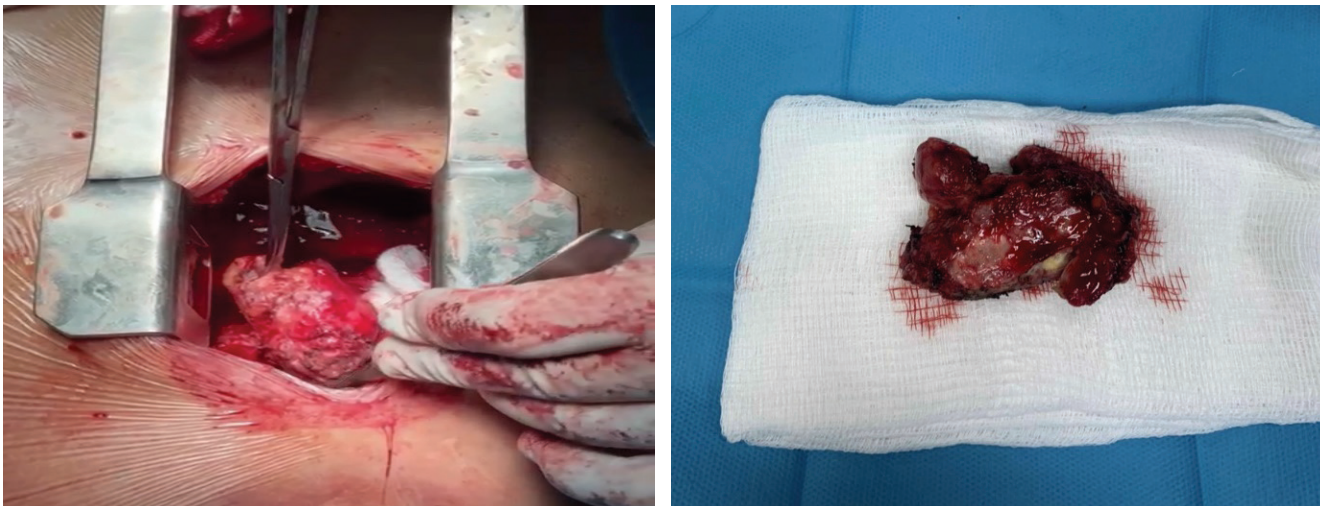

Figure 4. Thymoma operation room pictures

Discussion

Thymic hyperplasia and thymoma are different pathologies in the same organ that can appear with similar clinical signs.

Thymic hyperplasia is an enlarged thymus gland that typically retains its usual structure and can be caused by factors like chronic stress, infections, or autoimmune conditions, leading to thymic hyperplasia [5]. Sometimes, hypertrophic thymus can occur as rebound hyperplasia after chemotherapy or corticosteroid treatment, where it regains its size after shrinking [6].

Hypertrophic thymus usually has no symptoms and is accidentally discovered during imaging for other issues. When symptoms do occur, they typically involve compression of nearby structures, like the trachea or esophagus, causing breathing or swallowing difficulties [7].

Meanwhile, myasthenia Graves' disease appears in 50-70% of MG patients who have thymic hyperplasia [2]. It is a neurological autoimmune disease caused by autoimmunity against the acetylcholine receptor component of the neuromuscular junction. The lymph-follicular form of thymic hyperplasia is involved in the pathogenesis of myasthenia gravis with anti-acetylcholine receptor antibodies.

T-cell-dependent autoantibodies attack the acetylcholine receptors on the postsynaptic membrane, leading to muscular weakness. Laboratory studies may show positive Acetylcholine receptor antibodies. All the imagery examinations are helpful diagnostic tools, but chest CT scans and chest MRIs are the most used [8].

The approach to managing thymic hypertrophy is generally conservative. Surgical intervention is reserved for cases with severe symptoms or uncertain diagnosis. The indications for surgery are short as follows:

- Symptomatic Compression on adjacent mediastinal structures, causing significant symptoms such as dyspnea, chest pain, or dysphagia.
- In diagnostic uncertainty, where imaging cannot distinguish hypertrophic thymus from a neoplastic process, a biopsy or partial resection may be necessary for a definitive diagnosis.
- Association with cases where thymic hypertrophy is associated with autoimmune diseases that are poorly controlled or refractory to medical therapy [9].

Yoshimatsu et al. reported the results of thymectomy in a study including 427 patients with autoimmune disorders such as Myasthenia Gravis and ulcerative colitis nonresponsive to conservative therapy where thymectomy was performed. Follow-up observation from 2 to 17 years after surgery revealed complete recovery and significant improvement in 100 (75%) out of 133 patients with nontumorous thymic abnormalities. In total, follow-up observations showed that 84% of patients were inactive after thymectomy compared with 50% before the operation [10]

Nazarbaghi et al. report that extended transsternal thymectomy, along with a postoperative regimen of prednisolone and pyridostigmine, regardless of the preoperative duration of MG, is a safe and effective treatment modality for MG patients with either thymoma or thymic hyperplasia.[11]

Is thymectomy beneficial in non-thymomatous myasthenia gravis? A definitive study on the effectiveness of thymectomy in non-thymoma MG patients has not been done. The role of this procedure remains uncertain, but the evidence we have currently is from Class II studies, and the existing data seem to support an extended resection that removes as much thymic tissue as possible [12].

Surgical Approach used in cases of hypertrophic thymus: thymectomy is generally a minimally invasive approach, such as video-assisted thoracoscopic surgery (VATS) or robotic-assisted thoracic surgery (RATS), but also total surgical excision via open sternotomy is advised when thymic hypertrophy is not a specific diagnosis. In any case, the gold standard approach for thymectomy is a median sternotomy or transsternal approach. [13]

Our case underwent medical therapy for several months but was refractory to the treatment. The surgical method was a natural part of the treatment in these conditions. The standard sternotomy was the approach of entry. We have performed a full sternotomy to be sure of the total resection of the hyperplasic thymic tissues. The postoperative course was excellent. The patient had a distinguishable amelioration of the myasthenia signs one month after intervention.

Thymomas

Thymomas are tumors in the thymus gland made up of epithelial cells. They are classified based on their characteristics and invasiveness. The World Health Organization categorizes thymomas as Type A (benign), Type B (mixed), and Type C (thymic carcinoma), indicating increasing malignancy and poor prognosis [14]. Thymomas are linked to genetic mutations and changes in the thymic environment, though the exact cause is not fully understood [15].

Symptoms and Diagnosis

Thymomas can cause various symptoms depending on size, location, and invasiveness, including chest pain, coughing, breathing difficulties, or systemic issues like myasthenia gravis or anemia. Imaging tests such as chest X-rays, CT scans, and MRIs are crucial for diagnosing and managing both hypertrophic thymus and thymomas. PET scans can help differentiate thymomas from benign thymic hyperplasia based on metabolic activity, but a histopathological analysis is needed for a definitive diagnosis.

If imaging results are inconclusive, a biopsy may be required to confirm the diagnosis. Under imaging guidance, FNA or core needle biopsies can be performed to collect tissue samples for examination, though thymoma biopsies require caution to avoid tumor spread [3]. Sometimes, surgical removal is necessary to obtain a proper tissue sample and completely remove the tumor.

Indications for Surgery

Surgical resection is the cornerstone of thymoma treatment with the following primary objectives:

- *Complete Tumor Resection:* The goal of surgery in thymoma cases is to achieve a complete (R0) resection, where no microscopic tumor remains. Complete resection is associated with the best long-term outcomes and is particularly crucial in early-stage thymomas.
- *Symptomatic Relief:* Surgery may also be indicated to alleviate symptoms related to mass effect, such as superior vena cava syndrome, which can result from the tumor compressing the superior vena cava.
- *Reduction of Paraneoplastic Syndromes:* Thymectomy is often performed in patients with thymoma-associated myasthenia gravis, as removal of the tumor can lead to significant improvement or remission of the autoimmune symptoms [16].

One of the most recent significant reviews on this topic was by *Zhang Y.et al.* [17], which reviewed articles published from January 1995 to January 2023. The authors reported that surgery remains the primary treatment modality for palliating cancer-related symptoms and prolonging life. The surgeon's experience and skill with this type of patient are critical [17].

VATS and RATS have become standard approaches for early-stage cases. For advanced-stage thymoma, radical resection is considered the primary therapy, though since surgery alone does not necessarily control the disease, a multimodality treatment strategy is often needed [18].

Detterbeck et al., correlating outcomes with surgical approaches and adjuvant therapies, report the critical role of surgery in the management of thymoma [19].

Also, a study published by *Kanzak R.* in 2018 in the Journal of Interactive Cardiovascular and Thoracic Surgery debated the role of multimodal therapy, preoperative chemotherapy, or chemoradiotherapy followed by surgery. It concluded that preoperative chemotherapy or chemoradiotherapy followed by surgery for locally advanced thymoma can be performed with an acceptable degree of surgical risk. Such a strategy should be proactively considered, as it can lead to favorable long-term results [20]

Surgical Approach

The choice of surgical technique depends on the stage of

the thymoma, the patient's overall health, and the surgeon's expertise. The stage is based on the Masaoka-Koga staging system, which classifies thymomas based on tumor invasion and metastasis [21]. Staging is crucial for determining surgical resection, additional therapies, and prognosis [22].

- Stage I indicates complete encapsulation of the tumor without invasion.
- Stage II involves microscopic or noticeable invasion into adjacent tissues.
- Stage III shows macroscopic invasion into nearby organs.
- Stage IV includes spread to pleura or distant metastases.

Surgical approaches include median sternotomy and less invasive VATS or RATS. Sternotomy remains the most common approach for thymectomy in thymomas, particularly in extensive or invasive thymomas (Masaoka-Koga stages III and IV), where extensive dissection may be required. Video-assisted thoracic surgery (VATS) and Robotic-Assisted Thoracic Surgery (RATS) are increasingly used in the resection of early-stage thymomas (Masaoka-Koga stages I and II).

Outcomes depended on the stage of thymomas. Stage I & II: The outlook is very good with just surgical removal, which is linked to low recurrence rates. Adjuvant radiation might be suggested for Stage IIb with positive margins [1]. Stage III: Expectations can vary greatly; surgery is usually combined with additional therapies to improve results. The extent of resection and completeness of tumor removal are critical factors for long-term survival [21, 22]. Stage IV: The prognosis is typically unfavorable, especially in Stage IV-b instances. A combination of treatments involving surgery, chemotherapy, and radiation is generally needed, with an emphasis on supportive care for advanced cases [22].

In our case, we used mini-sternotomy as an entering approach. The patient had an uneventful post-operative course.

Postoperative Care and Monitoring: Postoperative care for individuals with enlarged thymus and thymoma varies significantly. Patients who undergo thymectomy for an enlarged thymus generally have a good outlook and may not need long-term follow-up, except in cases with autoimmune disorders. Follow-up imaging may be done to confirm symptom resolution [23].

Conversely, patients with thymoma require more thorough postoperative care, especially in advanced stages. Regular imaging exams are typically needed to monitor for recurrence. Those with Stage II or higher thymomas may receive additional radiation therapy. Chemotherapy or targeted therapies may be necessary for cases where the tumor hasn't been fully removed or if there are signs of spread [3].

The long-term outcome of thymoma patients is affected by the stage at diagnosis, the extent of surgery, and the effectiveness of follow-up treatments. Continuous monitoring is essential to detect recurrences early and manage potential complications from radiation [24].

Conclusions

Resection of hyperplasic thymus or thymomas remains the gold standard for treatment and/or definitive diagnosis. Standard surgical or minimally invasive approaches can be performed with excellent results.

COI Statement: This paper has yet to be submitted in parallel, presented fully or partially at a meeting, podium, or congress, published, or submitted for consideration beforehand.

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Abbreviations

TH - Thymic Hyperplasia; MG - Myasthenia Gravis; HT - Hypertrophic Thymus; VATS - Video-Assisted Thoracoscopic Surgery; RATS - Robotic-Assisted Thoracic Surgery;

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