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DOCTORAL THESIS

ANTIBACTERIAL AND ANTIFUNGAL MANAGEMENT CORRELATED WITH THE CLINICAL FEATURES OF ENDOCARDITIS IN ELDERLY PATIENTS

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CHAPTER 1. ANTIBACTERIAL AND ANTIFUNGAL MANAGEMENT IN RELATION TO THE CLINICAL CHARACTERISTICS OF ELDERLY PATIENTS WITH INFECTIVE ENDOCARDITIS

CONTEXT

Research indicates that the proportional increase in the prevalence of IE has been highest among the elderly population aged 65 years or older. The risk of endocarditis for the elderly has been shown to be almost five times that of the general population. The high frequency of undetected degenerative valve disease and the increasing use of invasive procedures and implanted medical devices may be examples of such reasons, which may also affect the prognosis of older people with IE. Several procedures require antibiotic prophylaxis for patients with IE at high risk of infective endocarditis, including maxillofacial procedures and non-dental invasive procedures of the upper and lower gastrointestinal tract, genitourinary and gynaecological procedures, and those of the upper and lower respiratory tract, including ENT procedures and bronchoscopy. The first objective of this study is to observe the characteristics of patients over 65 years of age affected by infective endocarditis, focusing in particular on antibiotic and antifungal treatments administered to this population. The second objective of this study is to determine the frequency of treatment resistance and complications in older patients with infective endocarditis compared to their younger counterparts. The third objective of this study is to compare the mortality rates of patients over 65 years of age with infective endocarditis with those of patients younger than 65, with a focus on the impact of antibiotic and antifungal treatments.

RESULTS

A total of 78 cases of infective endocarditis were found in adults younger than 65 years and 131 in the elderly, with a mean age of 59.6 years in the former group and 67.5 years in the latter (p-value < 0.001). The majority of patients were male-55.1% among those younger than 65 years and 51.8% in the elderly group. It was observed that 55.1% of the entire cohort of patients were overweight (BMI > 25 kg/m2). The tobacco and alcohol survey determined that about 30% of all patients were smokers and 4% used to drink alcohol daily. Comorbidities involved the cardiovascular system in more than 40% of the cohort, followed by digestive and metabolic diseases, with no significant difference between groups.

The median time from symptom onset to treatment was approximately three days in younger patients and two days in older patients. On ultrasonographic examination, it was observed that about 80% of all patients had vegetations and almost 20% of them had the presence of a cardiac abscess. In total, 140 patients had endocarditis on native valves and 69 had endocarditis on prosthetic valves, with a statistically significant difference between the study groups (p-value = 0.040). The most common valve involved was the mitral valve - it was involved in about 45% of all patients. Most infections had a vascular cause, followed by dental, maxillofacial and ENT procedures. The third most common cause of infection was a gastrointestinal source.

The etiology, procedures and interventions of patients with infective endocarditis showed that a total of 57.3% of patients over 65 years of age required surgery of the involved valve compared to 42.3% of younger patients (p = 0.036), while younger patients were significantly more likely to be referred for valve repair instead of valve replacement (36.4% vs. 24.0%, p = 0.044). The most common complication of IE was systemic sepsis (48.1% of patients over 65 vs. 30.8% in the younger group, p = 0.014). A significantly higher proportion of elderly patients were observed to show signs of heart failure on admission (51.9% vs. 32.1%, p = 0.005). The severity of valve regurgitation was also significantly higher in the elderly group, where 45.0% had moderate regurgitation compared to 28.2% in younger patients (p-value = 0.010). Oxygen supplementation was required in a significantly higher proportion of elderly patients (65.6%), while 60.3% were admitted to the intensive care unit

during hospitalization. The length of ICU stay was significantly longer in patients over 65 years of age (7.7 days vs. 5.9 days of ICU hospitalization, $p < 0.001$). Finally, the mortality rate was significantly higher in the elderly population (40.5% vs. 26.9%, $p = 0.047$).

The etiological diagnosis of endocarditis was made by conventional culture in about 60% of cases, followed by 25% involving PCR testing, while the remaining 15% of patients were tested by both culture and PCR. It was observed that 85% of cases had a bacterial origin and the remaining 15% were cases of fungal endocarditis. The most common bacterium involved was Staphylococcus aureus, followed by Streptococcus spp. in a total of more than 50% of all patients. Other bacteria involved were CoNs and Enterococcus faecalis. A total of 19 patients had candidal endocarditis, and Aspergillus was identified in 9. There was a significant difference in severe complications of treatment: 17.6% of elderly patients were affected compared to 7.7% of younger patients (p-value = 0.046). The most commonly used antibiotics were cephalosporins (in 33.5% of cases), followed by penicillin (in 31.2%) and glycopeptides (in 28.7%). Fluconazole was the initial treatment option for fungal endocarditis in 24.9% of cases.

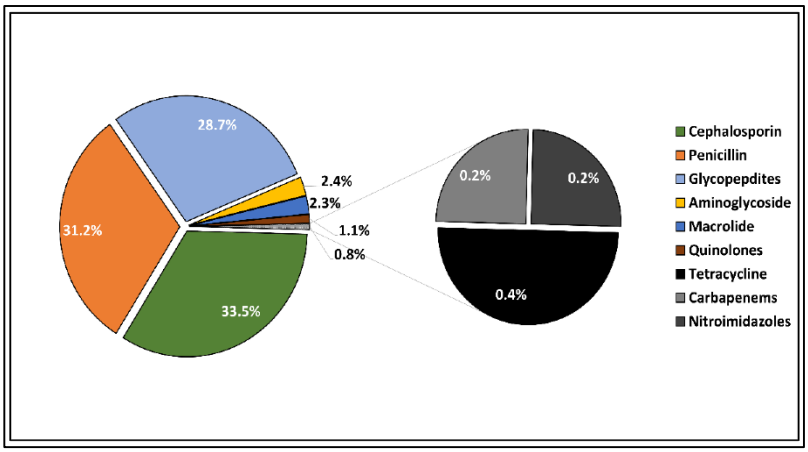

Image 1 - Distribution of antibiotics used for patients with endocarditis.

It was observed that patients older than 65 were more likely to develop side effects of antibiotic drugs, such as nephrotoxicity: 13.7% of the elderly were affected, compared with 5.1% of those younger than 65. As for nephrotoxic effect in the elderly, it was observed that six patients taking cephalosporins had renal damage as a side effect, followed by five patients on glycopeptide treatment. The most common cause of nephrotoxicity among elderly antifungal patients was amphotericin B in four patients, followed by four cases of kidney injury in patients taking azoles and caspofungin-induced renal failure in three patients. Other significant side effects among the elderly were enterocolitis, liver damage, delirium and falls, the former being the most common side effect in both study groups, although in a significantly higher proportion in the elderly group (29.0% vs. 14.1%, p-value = 0.013). The most common causes of enterocolitis in the elderly were penicillin and cephalosporins. Similarly, antifungals caused a significantly higher proportion of falls and delirium among the elderly (20.6% vs. 0.0%, $p = 0.037$). The risk factor analysis shown in Table 3 identified, using multiple logistic regression analysis, that heart failure on admission, occurrence of septic shock, nephrotoxicity of treatment, severe treatment complications and antibiotic resistance were significant independent risk factors for mortality in both younger and older patients, although the odds ratio (OR) was higher in patients over 65 years of age.

Table 3. Identification of significant risk factors for mortality in patients with endocarditis.

Risk factors	<65 years	P	>65 years	P
Heart failure	3.15 (2.87-5.21)	0.001	4.07 (3.44-6.90)	0.001
Septic shock	3.08 (2.66-6.09)	0.001	6.19 (4.15-8.28)	0.001
Nephrotoxicity after antibiotic therapy	1.66 (1.07-2.34)	0.001	3.14 (2.36-4.03)	0.001
Severe complications following treatment	3.39 (2.25-5.11)	0.001	4.65 (3.82-6.21)	0.001
Antibiotic resistance	2.61 (1.71-4.06)	0.001	3.24 (2.09-5.52)	0.001

CONCLUSIONS

The study shows that endocarditis disproportionately affects older patients compared to younger ones. Artificial valve endocarditis and endocarditis associated with medical therapy and vascular interventions are on the rise, regardless of patient age. This highlights the need for greater awareness of risk factors and early detection in both younger and older patients. Furthermore, healthcare professionals should consider these factors when treating patients with endocarditis and when performing invasive procedures, especially in the elderly population, who may be more susceptible to complications.

Maxillofacial surgery and ENT procedures have been identified as significant sources of infection, often associated with Streptococcus spp. and extensive vegetations on ultrasound. These factors have been linked to an increased risk of cardioembolic events. Interestingly, negative blood cultures were also frequently observed despite the presence of infection. This highlights the importance of comprehensive diagnostic approaches, including imaging studies, to accurately identify the causative organism and tailor treatment accordingly.

The study also showed that Staphylococcus aureus infections were associated with large vegetations and intracardiac abscesses, particularly in inflammatory endocarditis with prosthetic valve. Infections caused by Staphylococcus aureus were serious and were linked to poor outcomes such as congestive heart failure and embolic events. In addition, Staphylococcus aureus has been found to be linked to mortality. On the other hand, Streptococcus spp. infections were often exacerbated by dense vegetation and stroke, while enterococcus infections were more common in patients with multiple comorbidities.

The analysis found that a higher incidence of gram-negative bacilli infections was associated with a severe clinical course in the elderly, often exacerbated by septic shock, compared with younger patients. Antifungal treatment showed greater toxicity than antibiotics used in the study population, although infection severity and mortality rates were higher in patients with fungal infections. These findings highlight the importance of considering patient age, comorbidities, and causative organism when selecting treatment strategies for endocarditis, and the need for further research on optimal treatment approaches for different patient populations.

CHAPTER 2. EVALUATION OF ANTIMICROBIAL RESISTANCE IN GRAM-NEGATIVE AND GRAM-POSITIVE INFECTIVE ENDOCARDITIS

CONTEXT

Infections with Gram-positive streptococci, staphylococci and enterococci account for the vast majority of IE cases, with Staphylococcus aureus alone accounting for approximately 30% of infections. Other common oropharyngeal colonizers, such as HACEK organisms (Haemophilus species, Aggregatibacter species, Cardiobacterium hominis, Eikenella corrodens and Kingella species), most of which are of Gram-negative classification, account for approximately 20% of all endocarditis infections. The underlying aetiology of IE can be considered as early community-acquired or nosocomial prosthetic valve endocarditis within the first 60 days after surgery or following recent angiography, haemodialysis or extra-cardiac surgical procedures. S. aureus causes approximately 50% of all nosocomial IEs, while less pathogenic coagulase-negative staphylococci generally originate from intravascular devices or newly implanted prosthetic valves. Enterococci are implicated in approximately 15% of nosocomial IE cases and 20% of non-nosocomial cases.

Community-acquired infections are more likely to occur in the presence of immunosuppression, intravenous drug use, poor dentition, degenerative valve disease and rheumatic heart disease. Intravenous drug use, which accounts for nearly 10% of cases of infective endocarditis, involves frequent inoculation with skin flora such as S. aureus and S. epidermidis, with S. aureus showing a preference for healthy, native tricuspid valves. Approximately 20% of community-acquired infections are caused by streptococci of the Viridans group. Infections with Streptococcus gallolyticus organisms should traditionally raise suspicions of colon cancer. Given the importance of understanding antimicrobial resistance patterns in the context of IE, the primary objective of this study was to observe and analyze these patterns among IE patients, stratified by Gram-positive and Gram-negative bacteria. By knowing antimicrobial resistance patterns, healthcare professionals can make better informed decisions when selecting appropriate treatment strategies for patients with IE.

The secondary objective of the study was to describe the clinical characteristics of patients with IE, taking into account the low incidence of the disease. A comprehensive understanding of the clinical characteristics of patients with IE is crucial for early detection, diagnosis and effective management of the condition. By examining the clinical characteristics of patients with IE, the study aimed to provide healthcare professionals with valuable information that can help identify risk factors and inform patient care, ultimately improving patient outcomes.

RESULTS

The database search conducted during the study period identified a total of 29 patients diagnosed with infective endocarditis monoinfection caused by a Gram-negative bacterium and 142 cases of endocarditis monoinfection with a Gram-positive bacterium. By comparing the two groups, the researchers aimed to identify any significant differences in background characteristics and patient demographics that might impact disease presentation and management. In this way, the study aimed to provide a more comprehensive understanding of infective endocarditis and its relationship to the causative bacteria.

Following analysis of the data, no significant differences were observed between the mean age of the participants and the gender of the patients in both groups. Patients in the Gram-negative group had a mean age of 62.6 years, while those in the Gram-positive group had a mean age of 60.9 years. However, there was a notable difference between the two groups in terms of the body mass index (BMI) of the participants. In the Gram-negative group, 17.2% of patients were underweight, as opposed to only 8.5% in the Gram-positive group.

It is important to note that this difference in BMI may be correlated with other patient characteristics. For example, a higher percentage of patients with Gram-negative infective endocarditis (37.9%) were living under institutional care compared to 11.3% of patients in the Gram-positive group. This statistically significant difference (p-value < 0.001) suggests that the living conditions and general health status of the patients may be contributing factors to the observed differences in BMI between the two groups. Further research is needed to explore the potential impact of these patient characteristics on the presentation, management and outcome of infective endocarditis.

Other characteristics included patients' substance use behaviour, with a significantly higher proportion of patients in the Gram-positive group being smokers (36.6% vs. 17.2%, p-value = 0.043). Patient comorbidities with significant differences between groups were cerebrovascular disease, chronic kidney disease and poor oral hygiene, all of which were more common among those with Gram-negative IE ($p < 0.05$). The study found that there were no significant differences in diagnostic delays, onset of empiric treatment, presence of vegetations and cardiac abscesses between Gram-negative and Gram-positive infection groups. Vegetations were documented in patient records for 65.5% of Gram-negative infections and 73.2% of Gram-positive infections (p-value = 0.399). This similarity between the two groups indicates that certain clinical features of infective endocarditis may not be significantly influenced by the type of causative bacteria.

However, there was a significant difference between the two groups in the proportions of predisposing valvulopathies. In the Gram-negative group, 80.0% of patients with infective endocarditis had aortic valvulopathy, compared with 64.7% of patients in the Gram-positive group with mitral valvulopathy (p-value = 0.034). It is important to note that this difference could be attributed to the small sample size in the Gram-negative group. Further research with a larger sample size could provide more information about the relationship between valvulopathies and the type of infective endocarditis. Another key variable examined in the study was the aetiology of infections. The researchers observed that significantly more Gram-negative infections were associated with peripheral and central venous catheter use (31.0% vs. 12.7%, p-value = 0.013). While the other sources of infection documented in patient records were not significantly different between the two groups, many patients with infective endocarditis caused by a Gram-negative pathogen were diagnosed after undergoing maxillofacial surgery or dental and ENT procedures (17.2% and 15.5%, respectively).

Significantly fewer patients with Gram-negative endocarditis were observed to have fever (79.3% vs. 93.0%, p-value = 0.021) and constitutional symptoms of IE (62.1% vs. 80.3%, p-value = 0.033). However, neurological impairment was significantly more common among those with Gram-negative IE (44.8% vs. 26.1%, p-value = 0.042), although we cannot exclude the confounding factor of a significantly higher prevalence of cerebrovascular comorbidities among the same patients. Cardiac signs of new-onset murmur were not significantly different and there was no difference in EKG abnormalities. However, valvular regurgitation was more severe among those with Gram-negative IE, correlating with the presence of signs of heart failure (48.3% vs. 31.7%, p-value = 0.044). Following the severity of regurgitation, ICU admission, ICU hospitalization and mortality rates were significantly higher among patients with Gram-negative IE.

In this study, most infections were confirmed by conventional bacterial culture methods, with three cultures obtained for each patient. For cases with negative culture results, PCR testing was used, depending on its availability. No differences in bacterial identification methods or false-negative test results were observed between the two study groups. This consistency of diagnostic methods helped to ensure that comparisons between Gram-negative and Gram-positive groups were as accurate and reliable as possible. In addition, no significant differences were found between the two study groups in the proportion of antibiotic side effects and severe treatment complications. Resistance to at least one antibiotic was identified in 82.7% of patients with infective endocarditis in the Gram-negative group and in 71.1% of patients in the Gram-positive group. The distribution of antimicrobial resistance in

Gram-negative and Gram-positive infections also showed no significant difference. Among patients with infective endocarditis, 37.9% in the Gram-negative group and 28.2% in the Gram-positive group showed resistance to three or more antimicrobials.

The Gram-positive pathogen most commonly implicated in cases of infective endocarditis was Staphylococcus aureus, accounting for 39% of all cases. This was followed by Enterococcus spp. in 23% of patients and coagulase-negative staphylococci in 13% of patients. These findings highlight the importance of understanding the distribution of causative pathogens in order to tailor appropriate treatments for patients with infective endocarditis. Among cases of Gram-negative infective endocarditis, Pseudomonas aeruginosa was the most frequently implicated pathogen, accounting for 31% of cases. This was followed by Haemophilus influenzae in 20% of patients and Escherichia coli in 15% of patients.

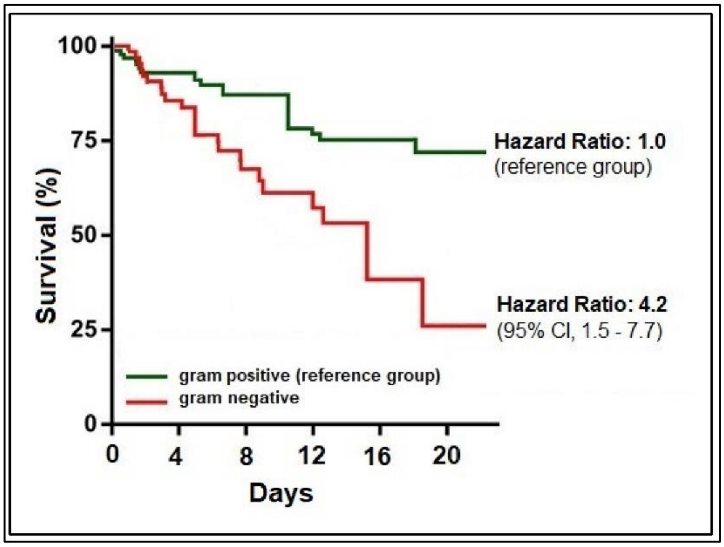

Image 2 - Kaplan-Meier probability curve for mortality by type of infection.

The mortality curve illustrates the differences in survival rates between groups of patients with infective endocarditis caused by Gram-negative and Gram-positive pathogens. The hazard ratio for mortality was found to be 4.2 times higher in patients with infective endocarditis caused by a Gram-negative pathogen compared to the reference group of patients with Gram-positive infections (95% CI = 1.5-7.7). This finding suggests that Gram-negative pathogens may pose a higher risk for patients with infective endocarditis. When survival was analysed according to the antimicrobial resistance pattern, it was observed that patients with infective endocarditis with a pathogen resistant to a specific antibiotic had a 3.3-fold higher probability of death. This highlights the importance of understanding and addressing antimicrobial resistance in the treatment of infective endocarditis, as it can have a significant impact on patient outcomes.

For resistance to two antimicrobials, the hazard ratio increased to 4.0 (95% CI = 1.6-6.2), further highlighting the negative effect that antimicrobial resistance can have on patient survival. As the number of resistant antimicrobials increased, so did the risk of mortality for patients with infective endocarditis. When a pathogen was resistant to three or more antibiotics, the risk of mortality increased further, reaching 5.7 times that of the reference group without specific antibiotic resistance (95% CI = 2.3-9.5). This underscores the critical need for continued research into new antibiotics and alternative treatment strategies to combat the growing challenge of antimicrobial resistance in the context of infective endocarditis and other serious infections.

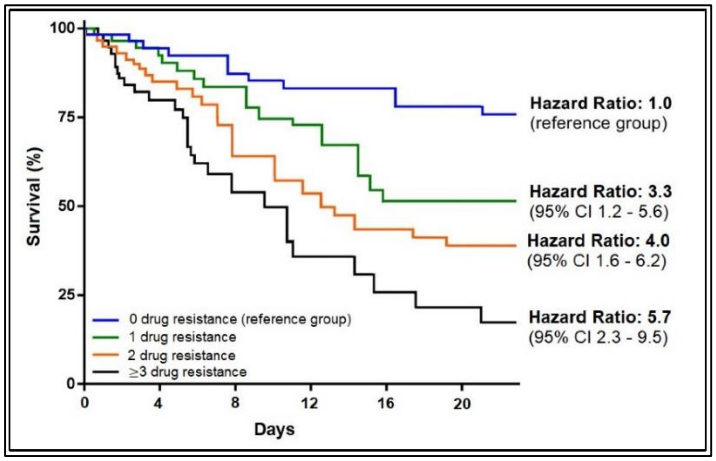

Image 3 - Kaplan-Meier probability curve for mortality as a function of the antimicrobial resistance.

CONCLUSIONS

Infective endocarditis caused by Gram-negative bacteria resulted in a higher mortality rate than Gram-positive IE in the study population. This significant finding highlights the need to pay more attention to the potential risks and complications associated with Gram-negative infections. However, it is essential to consider the limitations of the study, such as the small sample size of Gram-negative IE cases, which could impact the generalizability of the results.

In addition, the findings should be adjusted to account for potential biasing factors, as patients with Gram-negative infections had a higher proportion of comorbidities and predisposing factors such as institutional residence and underweight. These factors may contribute to the observed differences in outcomes between Gram-negative and Gram-positive infections, and understanding their impact is crucial for developing targeted prevention and intervention strategies.

Although the severity of IE was considerably higher where Gram-negative pathogens were involved, with poorer outcomes, more ICU admissions and a higher mortality rate, the pattern of resistance between Gram-negative and Gram-positive bacteria was not significantly different. This finding suggests that differences in outcomes could be driven by factors other than antibiotic resistance, such as bacterial virulence or underlying patient health conditions.

Another important finding is that many bacteria associated with IE appear to be highly resistant, regardless of their category. The high prevalence of antibiotic resistance among these pathogens is a worrying trend as it may lead to increased morbidity and mortality rates if alternative treatments are not developed.

As the structure of the population is changing and increasing numbers of elderly patients are returning to institutional care, it appears that being underweight and having poor dentition and poor oral hygiene predisposes them to Gram-negative IE, associated with a poorer prognosis. Recognition of these risk factors can help healthcare professionals better identify and manage patients who are at higher risk of developing severe infections with Gram-negative pathogens.

In order to analyse the development of pathogens involved in infective endocarditis and to examine the resistance pattern of these bacteria, further epidemiological studies over a longer period of time are needed. This ongoing research will be essential for understanding the evolving landscape of infective endocarditis and the growing threat of antibiotic resistance. Ultimately, it will contribute to the development of new prevention and treatment strategies to reduce mortality and morbidity associated with this serious condition.

CHAPTER 3. CLINICAL PRESENTATION AND RISK FACTORS FOR INFECTIVE ENDOCARDITIS IN THE ELDERLY

CONTEXT

The most prevalent risk factors for IE found in the elderly are increased numbers of comorbidities, increased numbers of predisposing events such as surgery or hemodialysis, use of prosthetic materials and dental procedures, and increased rates of nosocomial infections which generally increase the chances of developing IE. Repercussions of nosocomial infections are another challenge, resulting in a higher incidence of methicillin-resistant organisms among individuals in this specific age group. Although studies state that surgery can minimise mortality, when it comes to the older age group, the risks to which the elderly are exposed during surgery can keep mortality rates high, especially for the population aged over 80 years. Complications that may occur following surgical treatment for the elderly are usually sepsis, renal failure, pneumonia and postoperative delirium. However, early surgery remains associated with lower in-hospital mortality. Surgery is still recommended, despite the risks involved, as it is currently the only method that can successfully replace the involved valves and eliminate infection.

Although IE was first classified as acute, subacute or chronic, there has been a change in its classification, which is now based on several factors, such as the source of acquisition or the individual's background, such as intravenous drug users or the elderly. Another distinction is also made between community-acquired IE and healthcare-associated IE, such as nosocomial IE, which has been more common in recent years for the aging population, along with comorbidities and staphylococcal infections. When it comes to the individual context, IE appears to have increased negative outcomes for the elderly and for the younger population who are intravenous drug users. There have been many reviews that have focused on the prevalence and aetiology of infective endocarditis, but there have only been a few that have focused on the specific age group that is most vulnerable, which includes people over 65 years of age. Infective endocarditis has a poor prognosis for this specific population.

The first objective of this study is to identify the clinical features of infective endocarditis (IE) in older adults. The second objective of this study is to assess risk factors contributing to adverse outcomes in older adults with IE. The third objective of this study is to explore effective treatment methods for older adults with IE, particularly those who cannot undergo surgery due to increased risk of postoperative complications.

RESULTS

All included studies were observational; seven were retrospective studies, while the other three were prospective studies. Most of the research was conducted in Europe, namely in Romania, France and Portugal. These were followed by two studies conducted in the United States and one study conducted in Japan. The articles included had a wide range of publication years, from 1998 to 2022. Two studies reported only grouped age, i.e. over 65 years and over 64 years respectively. For the remaining studies, the average age was around 70 years. With the exception of one study that did not report gender prevalence, all other studies reported a higher prevalence of men. In terms of the nature of infection, half of the studies had a higher incidence of community-acquired IE, two of the studies reported more cases of healthcare-associated IE, and three studies did not describe the source of infection. Within the study population, the causative staphylococcal pathogens and streptococcal species had the highest prevalence. S. aureus and coagulase-negative staphylococci were the staphylococcal types that were found most frequently, as shown in Figure 2, where 33.4% of infections were caused by S. aureus and 32.0% were caused by streptococcal species, respectively. S. bovis and streptococci viridans were the types of streptococci that were found most frequently. Enterococci, Gram-negative bacteria and fungal pathogens were among the other categories of infectious agents that were analysed. Although the articles included were quite heterogeneous in terms of the prevalence of different types of staphylococci and

streptococci, studies that have taken place in recent years have found a higher prevalence of staphylococci. However, some report a similar prevalence between the two species. In terms of comorbidities, each study included a substantial number of participants with various comorbidities. Heart-related conditions and diabetes were the most common, followed by kidney disease, lung disease, cancer and liver disease. In terms of unfavourable outcomes, mortality rates ranged on average from 16% to 42.1% and were consistently high across all studies. Clinical information and outcomes are presented in Table 2. Complications such as acute heart failure, acute kidney injury and sepsis were observed in patients who were diagnosed with IE. In terms of diagnosis, most studies relied on transthoracic echocardiography (TTE) or transesophageal echocardiography (TEE) in addition to blood cultures. During the investigation, patients diagnosed with IE were assessed using a modified version of the Duke criteria. The primary criteria included detection of two positive blood cultures with organisms compatible with IE and confirmation of endocardial damage identified by echocardiography. Other minor criteria, such as comorbidities or other risk factors, were also included in the list. Patients described in these studies presented with a range of symptoms such as fever, heart murmur, anaemia or other systemic symptoms such as weight loss or anorexia.

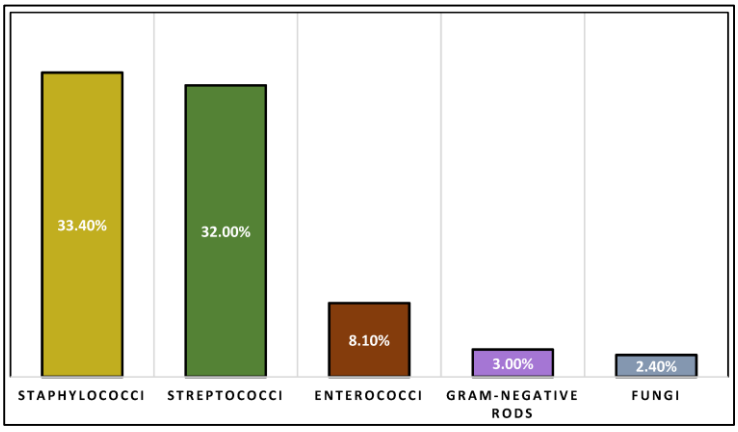

Image 4 - Distribution of identified pathogens.

However, some report a similar prevalence between the two species. Cardiac complications, sepsis, renal problems, neurological problems, increasing age and prosthetic endocarditis were the most frequent risk factors associated with an increased mortality rate. As can be observed, the variables that had the highest odds ratio of occurrence were septic shock, with an OR of 20.26 (4.04-1-2.74) in one study and 12 (6-24) in another, and heart failure, OR = 4.80 (3.59-71.53) and renal failure, OR = 4.8 (1.8-13.1) and HR = 8.68 (2.32-32.4), respectively. In addition to the most common causes, some studies found that metabolic disease, vascular problems, antibiotic resistance and absence of surgery were statistically significant as risk factors for death.

Of the protective factors identified in the included studies, early consultation and surgery were found to adjust the death rate to a low incidence. Each research study found that older people were more likely to experience poor outcomes compared to the younger group. Native IE was found more frequently than prosthetic IE. In investigations involving surgery, the types of surgery that were performed were aortic valve replacement, mitral valve replacement, both valve replacement and mitral valve repair. As for other types of treatment, such as the use of antibiotics, it has been reported that surgery remains the best treatment option. However, in cases where the patient is at high risk of mortality due to surgery, medical treatment will be preferred.

Table 2. Predictors of mortality.

Risk factors	Size of risk	Confidence interval	P
Pre-existing cardiac pathology	4.12	1.53-71.53	0.001
Septic shock	10.61	2.50-102.74	0.001
Chronic kidney disease	4.58	1.23-32.40	0.001
Old age	4.54	1.01-46.17	0.001
Neurological pathology	3.30	1.10-12.30	0.001
The existence of prosthetic valves	3.42	1.47-12.69	0.001

CONCLUSIONS

Elderly patients seem to be the most affected by IE, as old age is a significant risk factor contributing to adverse outcomes, among other complications they face. The ageing population is more susceptible to infections and has a higher prevalence of comorbidities, making the management of IE in this demographic group particularly challenging. As life expectancy continues to increase, it is critical to understand and address the unique needs of elderly patients with IE.

These factors make IE a condition that requires immediate medical attention. Timely diagnosis and intervention are essential to improve prognosis and reduce complications associated with IE in elderly patients. Healthcare professionals must be vigilant in identifying signs and symptoms of IE, especially in patients with known risk factors, to ensure the best possible outcomes.

Even though IE has been researched for a considerable period of time, the incidence of mortality is still very high, especially among the more susceptible population, which includes the elderly. This highlights the need for further research and innovation in the prevention, diagnosis and treatment of IE. A better understanding of the factors contributing to the high mortality rate can help guide the development of targeted interventions to reduce the burden of disease among vulnerable populations.

Considering that most elderly patients with IE suffer from significant complications and cannot undergo surgery due to the increased risk of complications after the procedure, it is imperative to investigate effective treatment methods. Alternative therapeutic approaches, such as less invasive interventions or new drug therapies, may offer promising options for elderly patients who are not suitable candidates for surgery.

In addition, preventive measures targeting modifiable risk factors for IE, such as improved oral hygiene and appropriate use of prophylactic antibiotics, can play a key role in reducing the incidence of the disease in elderly patients. By focusing on prevention, health professionals can help protect vulnerable populations from the potentially devastating consequences of IE.

In conclusion, addressing the unique challenges associated with IE in elderly patients requires a comprehensive approach encompassing prevention, early diagnosis and effective treatment strategies. Continued research in this area is essential to reduce the burden of IE in this growing population and improve the overall quality of life for older adults.