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Systematic Research And Case Report: A 60 Year-Old Caucasian Male With Mycotic Aneurysm In The Right Middle Cerebral Artery Stemming From Infective Endocarditis

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Abstract
Our study combines a systematic review with a detailed case report to provide a comprehensive overview of Mycotic Aneurysms in the context of Infective Endocarditis. Mycotic Aneurysms, though infrequent (2%-4% incidence), are most commonly associated with Streptococcus viridans and Staphylococcus aureus in cases of acute infective endocarditis. Notably, mycotic aneurysms tend to develop at proximal arterial branches, with a predilection for the middle cerebral artery (57.4%) and cerebellar posterior artery (17.6%) or their proximal branches.

Age and gender appear to play no specific role in pathological predisposition. Globally, Staphylococcus aureus remains the predominant pathogen, while neurological complications, including intracranial hemorrhage, are common and often contribute to higher mortality rates.

Diagnostic criteria encompass clinical presentation, radiological imaging techniques (e.g., CT, MRI), blood cultures, and surgical evaluation. Blood culture results indicate a shift from Streptococcus to Staphylococcus aureus as the predominant pathogen. This trend aligns with an evolving demographic, with infective endocarditis increasingly affecting older patients with comorbidities and no known structural heart diseases.

Complications, particularly neurological, are prevalent in left-sided native valve infective endocarditis, leading to challenges in diagnosis and management. Echocardiography plays a pivotal role in monitoring complications and valvular dysfunction. Treatment strategies involve extended courses of intravenous antibiotics (≥6 weeks), endovascular or surgical interventions, and withholding anticoagulation in patients with hemorrhagic neurological complications.

Prognosis varies widely, emphasizing the need for a multidisciplinary approach in managing mycotic aneurysms within the context of infective endocarditis. Our case report exhibits a prolonged and complicated course of treatment. Despite initial interventions, our patient's condition continued to deteriorate, with fluctuating hemodynamics and an increasing need for vasopressors. Notably, on 17 April, 2023, our patient suffered a bradycardia episode, which transitioned to asystole. Although cardiopulmonary resuscitation was initiated promptly, and despite continuous efforts, the patient eventually succumbed to biological death.

These additional case data emphasize the complex and difficult nature of managing mycotic aneurysms in the setting of infective endocarditis, emphasizing the need for more study and better treatment approaches in situations with comparable complications, like the one involving our patient. To manage mycotic aneurysms in the context of infective endocarditis, it is crucial to comprehend age and gender correlations, diagnostic criteria, causative organisms, comorbidities, treatment methods, and prognosis. This combined systematic review and

case report highlights the importance of above mentioned.

Understanding age and gender relationships, risk factors, clinical manifestations, and treatment outcomes should be a priority in future research to improve the prevention, identification, and management of these complex disorders.Long intravenous antibiotic courses (6 weeks) are part of treatment plans, coupled with possible endovascular or surgical procedures. The type of microorganism and patient-specific characteristics are just two examples of the many variables that can affect prognosis.

To manage mycotic aneurysms in the context of infective endocarditis, it is crucial to comprehend age and gender correlations, diagnostic criteria, causative organisms, comorbidities, treatment methods, and prognosis. This combined systematic review and case report highlights the importance of this.

Keywords: *Mycotic aneurysm, Intracranial mycotic aneurysm, Infectious aneurysm, Infective Endocarditis.*

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I. Introduction

Infective endocarditis is an infection of the endothelium of the heart and is a potentially life-threatening condition. It is predisposed to occur in some individuals with multiple cardiac valve conditions, with an annual incidence of 3–10 per 100,000 people. [1] It is characterized by vegetation within the heart that is composed of infectious agents, platelets, and fibrin. These vegetations can give rise to various symptoms, including fever, edema, Janeway lesions, and Osler's nodes. [2] The disease is categorized as either acute or subacute, depending on the speed of progression of the illness, before a diagnosis is established. Acute infective endocarditis (IE) is characterized by rapid development over a span of days to weeks, often accompanied by pronounced toxicity in affected patients. On the other hand, subacute IE follows a more gradual and indolent course, progressing slowly over several weeks or months. [3]. The diagnostic criteria for IE are called the Duke criteria, which provide a structured approach considering various clinical, imaging, and microbiological factors to make an accurate assessment(Table 1).

Table 1:Modified Dukes' Criterion

Major Criterion	Minor Criterion
Positive blood cultures (for the typical organism)	Underlying cardiac predisposition/ IV drug use
Imaging evidence of endocardial Involvement: ECHO (Vegetation, dehiscence, abscess, new valvular regurgitation murmur)	Fever (Temperature >38)
	Vascular (emboli to organ or hemorrhages)
	Immunological manifestations
	Microbiological and echocardiographic indications

Table 2:Conclusion Of Infective Endocarditis

Confirmed Infective Endocarditis	2 major criterion 1 major + 3 minor criterion 5 minor criterion
Possible Infective Endocarditis	1 major criterion + 1 minor criterion 3 minor criterion
Rejected Endocarditis	Resolution within < 4 days No evidence of IE found at surgery or autopsy (after antibiotic therapy for < 4 days) Definite criteria not met

The clinical diagnosis of definite infective endocarditis (Table 2) is confirmed when both major criteria are simultaneously present. Additionally, a diagnosis of definite IE can be established through the following: the presence of one major criterion along with three minor criteria, or the fulfillment of five minor criteria. [4] The

most common and severe extracardiac manifestations of infective endocarditis, as we move from the area of the disease to its complex repercussions, are neurological problems. According to the studies, about 25% of patients with IE experience at least one neurological event. [5]

Infectious intracranial aneurysms, also called mycotic aneurysms, are localized arterial dilatations that arise as a consequence of septic emboli stemming from the complications of infective endocarditis and are reported to constitute a range of 0.5% to 6.5% of all aneurysmal cases. [6] The term "mycotic aneurysm" was first introduced by William Osler back in 1885 when he described where he described a man with multiple aortic mycotic aneurysms in a patient with valve vegetations, which resembled the appearance of a fleshy fungus, It does not refer to fungal etiology, as the majority of infected aneurysms are caused by bacterial pathogens. Therefore the correct term of these aneurysms can be an infected aneurysm. Infectious aortitis refers to vessel infection without aneurysmal dilation. An infected aneurysm develops in the setting of an antecedent systemic infections with bacteremia or through the direct local invasion of the vessel wall (e.g., IV drug users) in the pre-existing aneurysm or atheromatous plaques. [7] It was firstly by Osler described abnormal dilatation of the aortic arch vessel wall in a patient with subacute infective endocarditis. [8] Predominantly, these aneurysms tend to localize themselves along the peripheral branches of the middle cerebral artery. (fig. 1) [5] Inflammatory processes trigger the influx of neutrophils that infiltrate the affected area. Subsequent stages encompass the breakdown of the arterial media and adventitia, along with the fragmentation of the internal elastic lamina. The weakened vessel wall, in combination with the pulsatile pressure in the vasculature, leads to aneurysm formation and consequential growth. [9] The mortality linked to the rupture of intracranial mycotic aneurysms, precipitating either subarachnoid hemorrhage or intracerebral hemorrhage, is documented to reach staggering levels, with reported rates as high as 80%. [10]

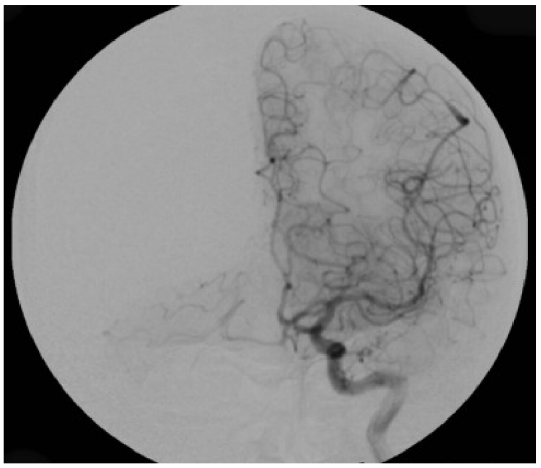

Fig 1. Digital subtraction angiography (DSA) shows a fusiform mycotic aneurysm of the distal (parietal branch) left middle cerebral artery

In this systematic review, we aim to carefully examine all the information about mycotic aneurysms in connection with infective endocarditis that already exists. This research seeks to provide doctors, researchers, and healthcare providers with a clear grasp of this intricate interplay. It aims to simplify the underlying pathogenic processes, analyze the clinical consequences, and assess alternative therapeutic approaches.[11] Moreover, the review aims to focus on areas in need of further research, gaps in current knowledge necessitating deeper investigation, and aid in the development of evidence-based strategies for the prevention, diagnosis, and treatment of mycotic aneurysms in patients with infective endocarditis.

This review aims to carefully examine existing literature, in order to comprehend the intricate relationship between infective endocarditis and mycotic aneurysms. By doing so, it aims to enhance awareness of these critical clinical challenges. Thus, it is believed that this systematic study would eventually aid in enhancing clinical decision-making, improving patient care, and shaping the next research initiatives in this dynamic field.

II. Case Presentation

Mr. David Kordzadze, a 60-year-old caucasian male, presented to the emergency department on February 2, 2023 at 19:50 with the chief complaint of fever. His vital signs at presentation were as follows: respiratory rate (RR) 17/min, blood pressure (T/A) 118/54 mmHg, body temperature (T°C) 38°C, oxygen saturation (O2) 96%, and heart rate (HR) 60/min. His Glasgow Coma Scale (GCS) assessment revealed an eye-opening score of 4 (spontaneous), a verbal response score of 5 (oriented), and a motor response score of 6 (obeying commands), resulting in a total GCS score of 15. Notably, his blood tests revealed negative results for HIV, anti-TP (Treponema pallidum), HBV (hepatitis B virus) surface antigen (HBsAg), and anti-HCV (hepatitis C virus) antibodies. His blood group was identified as B, with a positive rhesus factor (Rh+).

Coagulation studies showed a prothrombin index of 91.20%, a prothrombin time of 13.10 seconds, an INR of 1.05, an aPTT of 57.4 seconds, and a fibrinogen level of 3.70 g/L. Serum creatinine levels were found within the normal range at 96.00 µmol/L, with an estimated glomerular filtration rate (eGFR) of 78.00 mL/min. His complete blood count (CBC) revealed decreased levels of erythrocytes (RBC), hemoglobin (HGB), and hematocrit (HCT) at 3.64 10^12/l, 98.00 g/l, and 29.40%, respectively. Other CBC parameters, including mean corpuscular volume (MCV), red cell distribution width (RDW), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC), were found within or slightly below the normal range.

Platelet count was 98.00 10^9/l, with platelet large cell count (P-LCC) 27.00 10^9/l and platelet large cell ratio (P-LCR) 27.10%, respectively. Additionally, his white blood cell (WBC) count was 5.49 10^9/l, with a neutrophil count of 3.52 10^9/l and a percentage of 64.20%. Lymphocytes, monocytes, eosinophils, and basophils were within the reference ranges. Immature granulocyte levels were also within normal limits. This comprehensive assessment of Mr. Kordzadze's clinical and laboratory findings provides valuable insights into his current health status, aiding in appropriate diagnosis and management.

A CT scan conducted on 3rd of March 2023 revealed several notable findings. In the left frontotemporal lobe area, minimal subarachnoid hemorrhage was detected. Additionally, the images showed a metallic implant (coil) fixed in the right middle cerebral artery, along with areas of hyperdensity and early signs of cerebral edema. Moreover, calcification was observed in the choroid plexuses of the lateral ventricles. The optic nerves were visualized with evidence of optic nerve atrophy due to cerebral damage. Paranasal sinuses were clear, and the cranium (skull's bony part) did not exhibit any damage. Cerebral structures in the left hemisphere appeared normal, while the right hemisphere showed hyperdense subarachnoid spaces and gyral deformation. The cerebellar tonsils were descended.

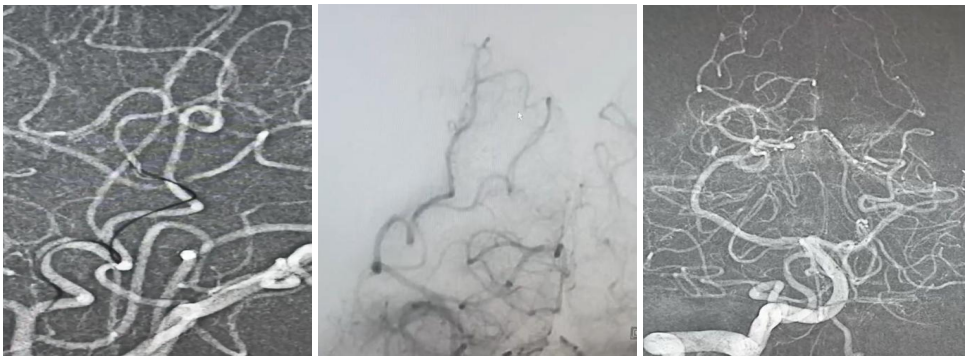

Fig 2. Intracranial mycotic aneurysms on cerebral angiography seen on day 29 of hospitalisation

The patient's treatment plan included intravenous administration of 500 ml NaCl 0.9% for hydration, 1000 mg/100 ml Infulgan for pain, and 1g of ceftriaxone for infection control. Oral medications include 30 mg of Nimodec and occasionally 20 mg of Omez for gastrointestinal concerns. IV infusions of 500 ml Ringer's solution and 1000 mg Vancomycin are administered, with 500 mg/5 ml Tranedex taken orally and subcutaneous lidocaine used as needed. There was occasional use of oral Epixx, IV propofol, fentanyl citrate, and IV midazolam. A one-time IV dose of Rocuronium bromide was planned, and as required, IV Infulgan and Analgin

were given for pain relief. The main treatment approach involved ceftriaxone and Sinogal (Sol Ampicillin Sulbactam).

Subsequent chest X-rays revealed the placement of the intubation tube above the tracheal bifurcation and the presence of a central venous catheter shadow towards the right atrium. Imaging also indicated light lung fields and a normal diaphragm size. The heart, aortic arch, and tracheal location were within normal limits. The CT scan depicted no bony skull damage, a slight subarachnoid hemorrhage, and a metallic implant in the right middle cerebral artery. Areas of cerebral edema and localized hypodensity were observed in the posterior cerebral artery, particularly in the medial parts (ASPECTS: 3).

A further comprehensive analysis revealed notable values in the correlogram. The prothrombin index (80.40%) and the prothrombin time (12.80 seconds) were slightly increased. INR was around 1.12, within the acceptable range. aPTT (25.2 seconds) and thrombin time (16.50 seconds) were both within normal limits, and fibrinogen levels were 3.30 g/L and showed a slight elevation.

The CBC+Diff and ESR results revealed erythrocyte count-RBC (3.30 x 10^12/l), hemoglobin (89.00 g/l), and hematocrit (27.60%) were decreased. Mean corpuscular volume (83.70 fL) and mean corpuscular hemoglobin (27.00 pg) were within normal limits. Red cell distribution width (20.20%) was increased. Platelet count (109.00 x 10^9/l) was decreased, while platelet large cell count (24.00 x 10^9/l) and platelet large cell ratio (21.10%) were within normal limits. Thrombocrit (0.10%), mean platelet volume (9.10 fL), and platelet distribution width (16.10%) were within normal limits. Leukocyte count:WBC (5.57 x 10^9/l), neutrophils (3.96 x 10^9/l), lymphocytes (1.22 x 10^9/l), monocytes (0.24 x 10^9/l), eosinophils (0.07 x 10^9/l), basophils (0.07 x 10^9/l), and immature granulocytes (0.20 x 10^9/l) were within normal limits. Notably, medication adjustments include the administration of various medications such as Infulgan, Analgin, Epixx, Vancomycin, Midazolam, Nimodec, Propofol, Fentanyl Citrate, Manitec, and Ceftriaxone. Liver function tests revealed normal ALT (9 U/L), AST (22 U/L), GGT (29 U/L), and ALP (117 U/L) levels, with total bilirubin (T-BIL) at 6.40 µmol/L and direct bilirubin (D-BIL) at 2.40 µmol/L.

On March 7, 2023, adjustments to the medication regimen included Epixx administration, Vancomycin, Midazolam, Nimodec, Propofol, Fentanyl Citrate, Manitec, and Ceftriaxone. The patient's PCT (procalcitonin) level was 0.060 ng/mL. In terms of normal ranges, the PCT result places the patient within the low-risk category for sepsis and septic shock (< 0.5 ng/mL). The laboratory findings also encompass the CBC+Diff and ESR outcomes, demonstrating decreased erythrocyte count-RBC (3.32 x 10^12/l), hemoglobin (90.00 g/l), and hematocrit (28.20%). Mean corpuscular volume (85.20 fL) and mean corpuscular hemoglobin (27.10 pg) were within normal limits, with an increased red cell distribution width (21.00%). Decreased platelet count (94.00 x 10^9/l). Platelet large cell count (23.00 x 10^9/l), platelet large cell ratio (24.20%), thrombocrit (0.09%), and mean platelet volume (9.40 fL) are within normal limits. Furthermore, the leukocyte count-WBC (7.57 x 10^9/l) and neutrophils count (5.62 x 10^9/l) increased. Lymphocytes (1.42 x 10^9/l), monocytes (0.42 x 10^9/l), eosinophils (0.05 x 10^9/l), basophils (0.06 x 10^9/l), and immature granulocytes (0.20 x 10^9/l) were within normal limits. This comprehensive update enhances the understanding of the patient's evolving condition and ongoing medical interventions.

Table 3: Patient's medical progress report

Date	Event	Patient's Condition
8th March	Medical Evaluation	General condition critical, requiring attentive care. Mechanical ventilation with selected parameters and mode. Bilateral lung aeration was observed with improved aeration in the lower lobes. Neurological status: Not adequately responding to ongoing medical sedation, multiple non-reactive pupils. Recommended slight head tilt to the right for better venous drainage and to prevent aspiration and reflexes. Non-stable hemodynamics, requiring vasopressor support. Increased central venous pressures and rhythmic Cor tones. Mild rubella rash and mild conjunctival bleeding. Fever episodes were observed. Blood and endotracheal aspirate were sent for bacteriological analysis – no significant bacterial growth was noted. The timely intervention led to condition improvement.

9th March	CT Scan of the Head	Minimal subarachnoid hemorrhage on the left posterior temporal lobe
10th March	Medical Evaluation	Unaltered general condition, heart X-ray showed no significant pathologies
12th March	Medical Evaluation	Critical, neurological status not improving despite sedation, stabilized hemodynamics, prolonged cardiopulmonary support
14th March	Medical Evaluation	General condition critical, mechanical ventilation adjusted based on ABG results, neurological status not responsive
19th March	Medical Evaluation	Critical condition, respiratory support ongoing, cardiopulmonary transfusion administered for coagulopathy, stable hemodynamics
23rd March	Medical Evaluation	Prolonged oxygen deprivation due to analgesia, sedation, and mechanical ventilation in the background of myocardial infarction. Dilatation of the tracheostomy was performed, with posterior positioning, under strict monitoring. Critical overall condition, mechanical ventilation, tracheostomy tube in place, selected mode, and parameters controlled by ABG, SpO2 at 98%. Bilateral lung auscultation revealed clear breathing in the lower lobes. Neurological status: Spontaneous eye-opening, no reaction to light, incomplete adherence to instructions, pinpoint pupils with miosis noted. Gag reflex intact. Hemodynamic display: Stable T/A at 131/84 mmHg, HR at 90 bpm, no fever. Normal central venous pressure.

Later in the left lung, a small-size tube was observed in the bronchial act during deep suctioning, while mild resistance was noted. A third-degree decubitus ulcer was identified on the left heel and managed daily and aseptically. Hemodynamics remained stable, with regular sinus rhythm on the EKG, normal heart sounds, and no murmurs. The abdomen was soft and nontender, with a palpable spleen tip. The neurological status remained unchanged. Blood tests showed a hemoglobin level of 9 g/dL. Due to persistent high fever, endotracheal aspirate was sent for bacterial culture, and guided by the results, ceftriaxone was initiated. Despite treatment, the patient's condition deteriorated, with an increasing severity of infection and recurrent episodes of fever

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On March 30, 2023, an esophagogastroduodenoscopy was performed, revealing multiple bleeding ulcers in the antrum. Hemostasis was achieved, and gastroprotection was initiated. Hemostasis remained successful, and hemoglobin levels stabilized. However, on April 16, 2023, the patient's condition deteriorated critically, with fluctuating hemodynamics and an increasing need for vasopressors. Attempts at stabilizing hemodynamics were unsuccessful. On April 17, 2023, the patient suffered a bradycardia episode, which transitioned to asystole. Cardiopulmonary resuscitation was initiated, but the patient could not be revived. Despite continuous efforts, the patient eventually succumbed to biological death.

III. Methodology

In May 2023, the PRISMA 2020 (Figure 1) and Preferred Reporting Items for Overviews of Reviews (PRIOR) criteria were incorporated to be used as the guiding framework for this study's objectives. The strict adherence to these rules upheld the ideals of transparency, scientific rigor, and the possibility of reproducibility inherent to this systematic review. The central focus of this systematic review is to elucidate nuanced insights within an area of paramount complexity, one that has regrettably remained understudied. Specifically, the study endeavors to comprehensively analyze the intricate pathology of mycotic aneurysm in the context of infectious endocarditis, thereby contributing to a more profound comprehension of this multifaceted domain.

Inclusion Criteria

This study project's methodical and thorough approach to the identification of relevant papers provided insight into the complex phenomenon of mycotic aneurysms in infective endocarditis patients. We carefully searched the well-known academic databases on PubMed, NCBI, Google Scholar, and Medline using precise search phrases such as "mycotic aneurysm, intracranial mycotic aneurysm, infectious aneurysm, and infective

endocarditis."

The study's demographic scope spans adults aged 18-69, encompassing both genders for equitable representation. Individuals who exhibited a confirmed clinical diagnosis of mycotic aneurysm concomitant with infective endocarditis were incorporated within the inclusion criteria of this research. Each individual profile encompassed essential clinical particulars, imaging outcomes, laboratory findings, and comprehensive neurological and cardiac assessments.

The scope of admissible study designs encompassed a range of methodologies, which include retrospective investigations, observational inquiries, cohort analyses, and randomized clinical trials (RCTs). This deliberate inclusivity mirrored the multifaceted nature of the research subject and aimed to capture insights from various research paradigms. This study has focused on research contributions that covered the time period from 2018 to 2023, which makes it both current and relevant.

Adequate follow-up data should have also been supplied, with either a minimum follow-up length or a set number of follow-up consultations, in order to examine the long-term neurological and cardiac outcomes and issues related to mycotic aneurysm and infective endocarditis.

This study encompassed a diverse spectrum of individuals who were afflicted by mycotic aneurysms caused by a variety of underlying etiologies, which can be broadly categorized into infectious (bacteria Streptococcus viridans, fungal Aspergillus fumigatus, and potentially viral triggers) and non-infectious causes (familial predisposition, pertinent medical histories, pharmacological influences, environmental factors, and other determinants).

Exclusion Criteria

To maintain study focus and minimize variability, individuals both below the age of 18 and above the age of 65 were deliberately excluded from this systematic review. Depending on the scope of the review, studies published before 2015 are excluded to ensure the inclusion of more recent evidence.

Furthermore, patients presenting with pre-existing neurological or cardiac conditions not directly pertinent to mycotic aneurysms or infective endocarditis were purposefully left out of the analysis. Studies that centered on non-infectious etiologies of endocarditis, such as rheumatic or degenerative origins, were also exclusively eliminated. Also, individuals with conditions such as severe trauma or states of immunosuppression were conscientiously omitted from the study's purview.

Additionally, studies lacking the provision of relevant results on mycotic aneurysms within the context of infective endocarditis had been excluded from the review process. Also, studies that were not published in the review team's primary language(s) or those without available translation resources were deliberately excluded. This stringent approach ensures alignment with the review's primary investigative objectives, mitigates the influence of linguistic bias, and upholds both the review's viability and methodological integrity.

The thoroughness of the data was carefully considered, leading to the exclusion of studies marked by insufficient follow-up information or data pertinent to mycotic aneurysms in the population of patients with infective endocarditis. Consequently, studies that were duplicates or that manifested as multiple iterations of the same scientific endeavor were disregarded.

Information Sources and Search Strategies

A methodical approach was meticulously employed throughout the course of this systematic review. The initial step involved formulating precise key search terms, guided by meticulous inclusion and exclusion criteria. To ensure the utmost relevance of the identified studies, exclusion criteria keywords played a pivotal role in fine-tuning the search process.

In the pursuit of reliable and comprehensive research materials, prominent databases, including but not limited to PubMed (Medline), Cochrane Review, and the National Library of Medicine databases, underwent rigorous and extensive study in the hunt for trustworthy and exhaustive research materials. Extensive screening of several clinical trials was carried out from 2016 to 2023 This thorough search technique carefully selected a current and extensive reservoir of applicable papers, which laid the foundation for the subsequent phases of the

review. The conscientious and comprehensive nature of this methodology facilitated a robust and rigorous evaluation of mycotic aneurysms in the context of infective endocarditis patients.

Selection and Data Collection Process

Review Selection

The process of selection was meticulously executed to ensure relevance and rigor. Initial database searches on platforms such as PubMed, NCBI, Google Scholar, and Medline were guided by specific search terms, including "mycotic aneurysm, intracranial mycotic aneurysm, infectious aneurysm, and infective endocarditis." The demographic scope encompassed adults aged 18-69 with confirmed mycotic aneurysms concomitant with infective endocarditis. A range of study designs were considered, aiming to capture insights from diverse research paradigms.

Data Extraction

Data extraction was conducted systematically from selected studies to ensure robustness and consistency. Essential clinical particulars, imaging outcomes, laboratory findings, and neurological and cardiac assessments were extracted from individual profiles. The focus on research contributions from 2018 to 2023 ensured the study's relevance and current applicability. Long-term outcomes were assessed using adequate follow-up data. This meticulous data extraction process laid the foundation for subsequent analysis and synthesis.

Primary Outcome

The primary outcome of this systematic review was to comprehensively assess the different types and frequencies of mycotic aneurysms in patients with infective endocarditis. This encompassed both desirable and undesirable outcomes, allowing for a comprehensive assessment of all the outcomes of the pathology. The favorable outcomes included successful blood culture results, which indicated that Streptococcus was a more prevalent causative agent as compared to Staphylococcus and improved patient survival. Whereas the unfavorable outcomes included complications such as rupture and hemorrhage of aneurysm, septic embolism, invasive infection spread, persistent endocarditis, delayed diagnosis, long-term morbidity, and mortality.

By understanding the primary outcome and focusing on infective endocarditis complications, this systematic review aims to provide valuable insights into the overall effect of mycotic aneurysms in patients with infective endocarditis, thereby informing clinical decision-making and improving patient care in this specialized population.

Secondary Outcome

This systematic review examined secondary variables, including patient age, gender distribution, total subjects in the studies, optimal mycotic aneurysm treatments in infective endocarditis, causative microorganisms, prognosis with concurrent mycotic aneurysm and infective endocarditis, treatment protocols for complications, and follow-up procedures.

The secondary goal was to assess diagnostic methods for detecting mycotic aneurysms in infective endocarditis. This involved evaluating CT angiography, MRI, and echocardiography to ensure sensitivity, specificity, and accuracy. The review also aimed to link mycotic aneurysm detection with its clinical outcomes, such as complications, treatment successes, and patient prognosis.

Preparation for Synthesis

Data was gathered from various databases such as Medline (Pubmed), NCBI, and the Cochrane Library using specific keywords like "mycotic aneurysm, intracranial mycotic aneurysm, infectious aneurysm, and infective endocarditis" for patients with mycotic aneurysm in the context of infective endocarditis. Clinical trials were sorted and presented in a table based on their year and category to streamline the data analysis process. This summary table, created using Microsoft Excel, played a pivotal role in categorizing and organizing the information from the studies, forming the basis of the systematic review's outcomes.

Tabulation and Graphical Methods

To ensure transparency and compliance with inclusion and exclusion criteria, a PRISMA flow chart was generated in Microsoft Word. Data analysis encompassed descriptive, bivariate statistics, and numeric outcome predictions using SPSS software, enabling a comprehensive exploration of data and potential variable

associations. Notably, diversity among sub-group variables in the studies emphasized the need for meticulous result synthesis and interpretation.

Methods to Explore Heterogeneity

Heterogeneity within the systematic review was assessed by tabulating the collected data. Diverse clinical trial types emerged from the findings, yet uniformity in outcomes regarding mycotic aneurysms in infective endocarditis patients was evident across all trial categories.

Assessment of Bias Risk

To boost the systematic review's reliability and minimize bias, we employed strict inclusion criteria, particularly focusing on clinical trials. Additionally, we utilized specialized tools like the Agency for Healthcare Research and Quality (AHRQ) bias assessment to systematically identify and rectify bias possibilities in the selected papers. This approach significantly enhanced the review's credibility and validity.

Reporting Bias

To mitigate bias, we followed predetermined methodology criteria diligently. Objective evidence was substantiated through strong statistical analysis, while any observed inconsistencies were openly acknowledged and resolved in both the results and discussion sections of the systematic review.

IV. Results

Table 4: Variables identified across the studies collated for the analysis of this systematic review on the mycotic aneurysm in infective endocarditis patient

Publication	Type of Study	Age (years)and Gender	Presenting Symptoms	Microbiology	Imaging and Diagnostic	Treatment Regimens	Complications	Surgical Interventions	Post Surgery Management	Outcome and Follow-up protocol
Elsevier (2021)	Case Study	55yr /male	Fever (37–38°C) for 6 weeks Systolic Murmurs on Auscultation Low Back Pain on Percussion	Streptococcus oralis	**White Blood Cell Count**: 8100 cells/μL **C-reactive Protein Level**: 9.79 mg/dL **Brain Natriuretic Peptide Level**: 224 pg/mL Severe Mitral Regurgitation **Transesophageal Echocardiography**: Vegetation on Mitral Valve (15 mm) **Whole Body Contrast-Enhanced CT**: No Mycotic	Initial: Ceftriaxone (2g every 24 hours) Antibiotic Switch: Benzylpenicillin Potassium (4 × 106 every 4 hours) and Gentamicin (1 mg/kg every 8 hours) Gentamicin Monitoring: Trough Blood Test	Cerebral Hemorrhage on Day 7 Cerebral Ischemia with Visual Field Defect Ruptured Spleen on Day 17 with Splenectomy Splenitis on Pathological Findings	Mitral Valve Replacement Left Atrial Appendage Closure Embolization of Left Angular Artery MA Embolization of Right Middle Cerebral Artery MA, Hepatic Artery MA, and Gastroepiploic Artery MAs	Antibiotic Treatment for 4 Weeks Antibiotic Switch to Ampicillin/Sulbactam	Resolution of Cerebrovascular Artery MAs at 7 Months Post-Cardiac Surgery Development of Pancreatic Fistula, Leading to Distal Pancreatectomy No Additional MAs After Cardiac Surgery

					Aneurysms (MAs), No Abscess **MRI (Day 5 and Day 20**): No Spinal Inflammation	Improvement in Fever and CRP Levels on Day 4	Multiple MAs in Hepatic and Gastroepiploic Arteries			
Surgical Neurology International (2021)	Case Report	69yr /male	Hypertension Dry cough, night sweats, and weight loss for 5 months 2/6 diastolic murmur Elevated blood pressure (151/61) First-time seizure during antibiotic therapy (Day 26/28) No previous history of seizures	Streptococcus anginosus	**Head CT** revealed a 1.5 cm rim-enhancing lesion **MRI** confirmed pyogenic brain abscess and cerebritis **CTA** showed a 1 mm mycotic aneurysm **Cerebral angiogram** with endovascular embolization performed	IV Ceftriaxone	Nil	Minimally invasive endovascular approach Onyx 18 embolization of the aneurysm Subarachnoid hemorrhage post-embolization No external ventricular drain placed Aortic and mitral valve replacement without complication.	NICU stay for 22 days Seizure control with Levetiracetam, Clobazam, and Lacosamide Triple antibiotic treatment for pneumonia and brain abscess Physical therapy, occupational therapy, and speech therapy	6 months without major hospital admissions Improved mood post-steroid therapy cessation Readmitted at 6 months with a seizure and pulmonary embolism IVC filter placement Adherent to antiseizure regimen 1½ years post-initial rupture of the IIA. Alive and confident. Considering eligibility for driving school

Elsevier (2020)	Case Report	24yr /male	2 weeks of low-grade fever (102°F), cough, sore throat, and malaise	methicillin-sensitive Staphylococcus aureus (MSSA) Positive COVID-19 PCR	**Echocardiogram** showed multiple large mobile echogenic masses on the tricuspid valve with valve perforation Follow-up **echocardiogram** revealed a 1.0 cm tricuspid vegetation **Chest CT** showed numerous pulmonary nodules and masses in bilateral lungs (septic emboli) Multifocal aneurysmal dilatations in pulmonary arteries (mycotic aneurysms) Eccentric filling defects in aneurysmal portions (septic or bland pulmonary emboli) Bilateral pleural effusions (atypical for COVID-19)	Intravenous antibiotics for MSSA endocarditis Remdesivir and dexamethasone for COVID-19	Persistent symptoms despite antibiotics	Open surgical bioprosthetic tricuspid valve replacement Valve vegetation culture positive for MSSA Loculated empyema found intraoperatively in the right pleural effusion (positive for MSSA)	Conservative approach for mycotic pulmonary artery aneurysms A 6-week course of intravenous antibiotics	Successful valve replacement Resolution of MSSA infection Resolution of pulmonary artery aneurysms No recurrent pleural effusions or empyema
Cardiac Surgery Wiley (2020)	Case Report	57yr /male	Hemodynamically stable High-grade fever-39°C (3 months) Dyspnea (NYHA class III)	Streptococcus viridans	**Hemoglobin**: 9.8 g/dL **WBC**: 10,900/µL **ESR**: 60 seconds Large mobile mass on the atrial side of the posterior mitral valve leaflet with	Intravenous ceftriaxone (patient became afebrile within 5 days)	Nil	Mitral and aortic valve replacement with tissue valves Coronary artery bypass grafting to the LAD using a saphenous	Antibiotic therapy for 6 weeks postoperatively	Referred to vascular surgery for further management of the superior mesenteric aneurysm Resolution

			Pansystolic murmur at the apex Palpitation Weight loss Widespread vasculitic cutaneous lesions		severe **mitral regurgitation** Moderate-size mobile mass on the ventricular aspect of the left coronary cusp of the aortic valve with severe **aortic regurgitation** **Mild tricuspid regurgitation** Pulmonary artery systolic pressure: 30 mm Hg **Ejection fraction**: 55% **Head MRI:** Minimal subarachnoid hemorrhage **Abdominal CT**: Mycotic aneurysm of the superior mesenteric artery **Cardiac catheterization:** Aneurysm of the LAD coronary artery			vein graft Ligation of the LAD aneurysm with a pericardial pledget		of fever Successful valve replacement and coronary artery bypass grafting Ligation of LAD aneurysm Completion of 6 weeks of postoperative antibiotic therapy
Elsevier (2019)	Case Report	21yr /male (Previous balloon aortic valvuloplasty at age 9)	High-grade fever (39°C) Acute renal failure Proteinuria Anemia night sweats	Bartonella henselae	Elevated **Brain Natriuretic Peptide (BNP)** (1453 pg/ml) **Transthoracic echocardiography** :Thickened and dysplastic aortic valve, Moderate to severe aortic	Completed 6 weeks of intravenous antibiotic treatment	Nil	Aortic root replacement with a 24 mm aortic homograft valved conduit Closure of a patent foramen ovale via median	Discharged home 8 days after surgery	Uneventful recovery Continued doxycycline oral treatment for life

			(1-year) dry cough (2-months) bilateral ankle leg swelling (1-month) Bicuspid aortic valve		insufficiency, Mild aortic valve stenosis, Moderately reduced left ventricular systolic function, and No vegetations were seen **Cerebral MRI** showed a small mycotic aneurysm (2.5x2mm) in the right middle cerebral artery (M3) distribution **Cerebral angiography** followed by MRI-guided stereotactic right frontotemporal craniotomy and clip ligation of the mycotic aneurysm			sternotomy on cardiopulmonary bypass support Operative findings: Degenerated and necrotic aortic valve, aortic root abscess extending into the annulus of the right coronary artery cusp		
Elsevier (2019)	Case Report	20yr /male (Noonan syndrome, von Willebrand disease, and Previous pulmonary valve balloon valvuloplasty at age 1)	New onset chest pain and shortness of breath Renal failure Severe proteinuria Elevated BNP (>5800 pg/ml) Anemia	Bartonella vinsonii	**chest X-ray**: Pulmonary edema **Echocardiography :** Thickened mitral valve, Mild insufficiency, Severe stenosis (mean pressure gradient: 17-18mmHg), Good biventricular function, and No evidence of vegetations **Cerebral MRI** showed a partially thrombosed left frontal middle cerebral artery	Intravenous ceftriaxone	Chylus pericardial effusion requiring drainage	Cerebral catheterization followed by CT-guided stereotactic left frontoparietal craniotomy for resection and ligation of the aneurysm Mitral valve replacement with a mechanical 29mm prosthesis Operative findings:	Extubated on postoperative day	Continued intravenous antibiotic treatment per protocol Continued oral doxycycline

					mycotic aneurysm (1.3 cm x 1 cm)			Thickened left atrial wall, severely diseased mitral valve with infection involving anterior and posterior leaflets		
Elsevier (2018)	Case Report	56yr /female (Familial cardiomyopathy, Ventricular tachycardia (ICD implanted), and LVAD implant as a bridge to transplant)	Fever and chills (3 months post-LVAD implant) Febrile (102.6°F) Unremarkable LVAD drive line site Acute onset severe headache, blurred vision, change in mental status on hospital day 15	oxacillin-resistant S. epidermidis	**Elevated white cell count**: 13,800/mm³ **INR**: 1.2 **Partial thromboplastin activation time:** 35 seconds **CT abdomen**: small rim-enhancing fluid collection surrounding LVAD outflow tract at aortic insertion **CT head**: large left subdural and intraventricular hemorrhage, Intraparenchymal hemorrhage in left parietal lobe, and Midline shift of 14 mm toward the right side **Cerebral Angiogram:** Irregular distal middle cerebral artery and posterior cerebral artery irregularities suggestive of	Empiric intravenous vancomycin (goal trough: 15-20 micrograms /milliliter) **Anticoagulation:** Warfarin held, bridged with heparin in anticipation of ICD extraction Protamine sulfate given to reverse heparin anticoagulation	Multiple mycotic aneurysms detected	Emergent left craniotomy with hematoma evacuation	Empiric intravenous vancomyci later changed to daptomycin on day 14	Neurologic status continued to deteriorate Transitioned to comfort care

					infectious vasculopathy					
Neurological Medicine (2022)	Case Report	64yr /female	Fever (41°C) Sudden onset left upper limb motor deficit Speech disorders Mitral focus murmur Left brachial monoplegiaand Dysarthria	Streptococcus oralis	**CRP**: 123 mg/l Normal Troponin and ProBNP levels **Brain MRI:** Subacute ischemic lesions in both cerebral hemispheres and Significant lesion in the right internal capsule **Cerebral Angiography:** Amputation in the M2 segment of the left sylvian artery **Transthoracic echocardiography :** Vegetations of the mitral valve, Oslerian graft of both mitral leaflets, small prolapse, and vegetation (22 mm by 10 mm)	Penicillin (4 million units every 6 hours) initiated initially	Endocarditis complicated by stroke	Endovascular embolization of the aneurysm Valve replacement performed successfully	Switched to amoxicillin (2 g every 4 hours) Preventive anticoagulation with 4000 IU of enoxaparin	Patient transferred to cardiac surgery with valve replacement Aphasia and hemiplegia persisted post-surgery

Age of the patient

In individuals with underlying reasons, including valve disease or other cardiac issues, mycotic aneurysms frequently coexist with infectious endocarditis. As a result, mycotic aneurysms and infectious endocarditis are more likely to develop in middle age and the elderly (age spanning from 35 to 80 years). The age range might change depending on a number of variables, including location, lifestyle, healthcare practices, and prevalence in particular communities.

Gender of patient

Patients of any gender can develop mycotic aneurysms linked to infective endocarditis. When it comes to infective endocarditis, there is no particular gender propensity for the growth of mycotic aneurysms. Males and females might both be impacted. And it mostly depends on the underlying risk factors.

Causative organism of infective endocarditis

According to blood culture reports, the common pathogen found is streptococcus. But anyhow, Staphylococcus aureus is routinely cultured around the world, which makes S. aureus the most frequently isolated pathogen. There are also other pathogens like brucella, listeria, S. bovis, coagulase-negative staphylococci, and Coxiella burnetii.

Complications observed after infection

The neurological presentation often involves intracranial hemorrhage. The complication involves cardiovascular and pulmonary involvement as well. According to univariate research, several factors contribute to higher fatality rates. These include aneurysm rupture, involvement of the parent vessel, aneurysm progression, and the decision between non-surgical and interventional aneurysm treatment.

Treatment protocol for patients experiencing mycotic aneurysm coexisting with infective endocarditis

Long-term intravenous antibiotic therapy for at least 6 weeks is the medical intervention that is universally advised. Morawetz and Karp discovered in 1984 that unruptured MAs might undergo spontaneous thrombosis, implying that MAs could be entirely resolved with antibiotic therapy alone.

Endovascular therapy has advanced rapidly in terms of efficacy and ability to treat more distant aneurysms. The safety profile of this technique is difficult to assess because it is based mainly on anecdotal and case-report information. Endovascular treatment was significantly more likely than open craniotomy with surgical ligation to result in parent artery sacrifice. This affects the treatment of sick veins that supply eloquent brain parenchymas such as language, sensorimotor cortex, visual cortex, hypothalamus, thalamus, cerebral peduncles, and brain stem.

Open craniotomy and aneurysm clipping are reserved for individuals with intraparenchymal bleeding or who require clot evacuation and urgent reversal of rising intracranial pressure. Another significant benefit of surgical intervention is the potential for vascular bypass to protect distal blood flow, which is critical when the aneurysm involves eloquent territory.

In the Setting of Intracranial Septic Emboli, Valvular Repair. The goal of cardiac surgery is to eliminate the cause of cerebral emboli and enhance hemodynamics. The timing and order of cardiothoracic and neurosurgery are affected by whether the aneurysm has ruptured. If the MA is not ruptured, cardiac surgery is relatively safe.

Prognosis and follow-up protocol for the patient

Patients with infective endocarditis (IE) and mycotic aneurysms have varying prognoses depending on factors such as the type of microorganism causing the infection, the patient's overall health, the extent of cardiac involvement, the presence of complications, and the timeliness of appropriate treatment. Mycotic aneurysms are a dangerous consequence of infective endocarditis that causes infected outpouching in the arterial wall. Therefore, proper antimicrobial treatment is advised. Early administration of antimicrobial treatment emerges as a pivotal strategy to mitigate the potential catastrophic neurological complications arising from IE. As a recommendation, individuals afflicted with both IE and intracranial hemorrhage are advised to undergo vascular imaging, preferably in the form of cerebral angiography. This comprehensive approach aims to enhance understanding and management of IE-related neurological intricacies while minimizing associated risks.

A multidisciplinary team is often involved in the follow-up routine for a patient with infective endocarditis with mycotic aneurysms. It is necessary for the patients to undergo imaging studies to detect any further complications after the treatment. It is also mandatory to assess the cardiac function on a regular basis. Routine blood tests are advisable. The patient's overall clinical status, infection-related symptoms, and any new neurological symptoms that might point to emboli should be frequently monitored. Prior to some medical or dental operations, patients with a history of mycotic aneurysms and infective endocarditis may require antibiotic prophylaxis to prevent recurrence.

V. Discussion

Age and gender of patients in correlation with infective endocarditis and mycotic aneurysm

It is essential for healthcare providers to understand the connection between age and gender in infective endocarditis and mycotic aneurysm. [12] This understanding helps with evaluating risks, diagnosing them and customizing treatment approaches based on the requirements of various patient groups. [13] Future research should prioritize investigating the factors that contribute to age and gender differences in infectious endocarditis and mycotic aneurysm. By doing so, we may discover approaches for prevention and treatment. Following patients' progress over a period of time through studies can offer further valuable insights. By examining the frequency factors that contribute to risk, how patients present clinically, and the results obtained, we can acquire

knowledge that can improve the treatment of patients and direct future research in the field of medicine. Recognizing these differences among populations is a step towards enhancing the prevention, detection, and handling of these extremely serious conditions.

Diagnostic criteria for mycotic aneurysm and infective endocarditis

Clinical Presentation: Patients may experience symptoms such as fever, chills, localized pain, and indications of an infection. These symptoms can be non-specific. It may overlap with other medical conditions. Imaging Studies: Radiological imaging techniques like computed tomography (CT) echocardiograms or magnetic resonance imaging (MRI) play a role in making a diagnosis. The findings may show a widening of an artery accompanied by signs of infection (such as the formation of an abscess, the presence of gas within the artery, or infiltration into surrounding soft tissues). Blood Cultures: Obtaining blood cultures is necessary to identify the microorganism responsible for the infection. This step is vital in determining antibiotic therapy. Surgical Evaluation: It is often necessary to consult with a surgeon to evaluate the extent of the infection and determine the course of action. This may involve repair, debridement (removal of tissue), and antibiotic treatment. [14]

Causative organism of infective endocarditis

Blood culture results indicate that Streptococcus is a more prevalent pathogen compared to Staphylococcus, with Streptococcus being the most prevalent. But globally, Staphylococcus aureus (S. aureus) takes the lead as the most commonly isolated bacteria, followed by coagulase-negative staphylococci, Streptococcus viridans, and enterococci. [15] (S. aureus) is more common in older patients and those with healthcare-associated IE. Infective endocarditis (IE), even though uncommon, causes significant morbidity and mortality in both children and adults. The trend of IE has evolved to affect older patients with co-morbidities and no known structural heart disease.

Complications of Infective Endocarditis in Association with Mycotic Aneurysm

A neurological complication is a common manifestation of left-sided native valve infective endocarditis. Septic embolization may cause ischaemic stroke, mycotic aneurysm, intracranial hemorrhage, and brain abscess. This is due to the changing epidemiology of the disease, the wide spectrum of presentation extending from the neonate to the elderly, diagnostic difficulties, delayed surgical interventions, and embolic complications. Echocardiography plays a crucial role in the diagnosis of IE, monitoring for complications and progression of valvular dysfunction and assessing the outcome. > Heart failure is Commonly associated with valve dysfunction. Surgery is indicated for those with acute decompensated heart failure due to valvular dysfunction. Persistent infection and perivalvular extensions: Monitor for conduction abnormalities, e.g., atrioventricular (AV) block. TEE should be performed to look for perivalvular extensions. Systemic embolism usually occurs in left-sided IE and within the first 2 weeks of therapy. Common sites are the brain and the spleen. [16]

Risk factors for embolism are associated with vegetation size (> 10 mm), mobility, location (anterior mitral valve leaflet), and the causative microorganism (S. aureus). Neurological complications: it occurs early in the course of IE (the first 2 weeks). Common complications are ischaemic or hemorrhagic strokes and mycotic aneurysms. Management should be individualized, and care plans should be decided by a multidisciplinary team that also includes neurologists and neurosurgeons. It is advisable to withhold anticoagulation in mechanical prosthetic valve endocarditis (MPVE) patients who have hemorrhagic neurological complications for at least 2 weeks with close monitoring of the valves and the patient's clinical condition. The duration of withholding anticoagulation is dependent on the severity of the neurological complication and the patient's clinical condition. [17]

Treatment protocol for a patient with mycotic aneurysm coexisting with infective endocarditis

The management of IE is aimed at eradicating the infection and preventing and treating both intracardiac and extracardiac complications. Patients with complicated IE should preferably be referred to a specialist center. Specialist centers are those with cardiothoracic, cardiac imaging, and specialized cardiology services. The management of infective endocarditis is challenging, as the 1-year mortality rate is approximately 30%. Neurological complications, most commonly cerebral embolism, are seen in 20–40% of the patients and are associated with high morbidity and mortality. [18] The reported incidence of mycotic cerebral aneurysms is 2–3% of all the patients with infective endocarditis. This is possibly underestimated because the majority of the patients remain asymptomatic and the aneurysm may resolve after antibiotic therapy. Mycotic aneurysm is an

ominous finding, with high mortality rates ranging from 30% in untreated unruptured cases to 80% in cases of rupture. MAs are most common in the anterior circulation. The mainstay of treatment is appropriate and adequate antimicrobial therapy. The minimum inhibitory concentration (MIC) should be achieved to ensure optimal antimicrobial therapy.

For penicillin-susceptible (MIC ≤ 0.125 μg/ml) Viridans streptococci, monotherapy with benzyl penicillin, ampicillin, or ceftriaxone is adequate. [IIa/B] » The duration of therapy is 4 weeks for native valve endocarditis (NVE) and 6 weeks for prosthetic valve endocarditis (PVE). Antimicrobial prophylaxis is not routinely recommended for cardiac patients undergoing invasive dental or other medical procedures and should be limited only to cardiac patients associated with the highest risk of adverse outcomes from IE.

[19] Those with a high predisposing risk for developing IE should be advised to maintain good oral and skin hygiene.

Prognosis and follow-up protocol for a patient with mycotic aneurysm coexisting with infective endocarditis

Follow-up management: Monitor for relapse and reinfections, review indications for elective cardiac surgery, education on preventive measures, prognosis and patient counseling. Mycotic aneurysms are rare but life-threatening. Infected aortic aneurysms have a high rate of rupture if not treated promptly. Histopathological examination (HPE) of cardiac tissue or vegetation obtained during surgery is of diagnostic value and is recommended. A transthoracic echocardiogram (TTE) should be obtained without delay if the diagnosis of IE is suspected. [20] Echocardiogram findings should be interpreted in the context of the clinical scenario and repeated if the clinical suspicion of IE persists despite a negative initial echocardiogram. A transoesophageal echocardiogram (TOE/TEE) should be done if the initial TTE examination is negative, in patients with strong clinical suspicion of IE, in those with prosthetic valves or cardiac material, and in those with high-risk features. Echocardiography plays a crucial role in the diagnosis of IE, monitoring for complications and progression of valvular dysfunction, assessing the outcome of surgical repair, and in the follow-up after completion of antimicrobials (refer to Table: Role of Echocardiography in the Diagnosis and Management of IE, below). [21] In patients with S. aureus bacteremia from an unknown etiology or persistent bacteraemia despite antimicrobials, echocardiography should be considered. Some newer imaging modalities (multislice computed tomography; MSCT; magnetic resonance imaging; MRI; and nuclear imaging) can assist in diagnosing IE and its complications. The modified Duke criteria is used to diagnose IE but has limited diagnostic accuracy in the early phase of the disease and in those patients with prosthetic valve or cardiac implantable electronic device (CIED) endocarditis.

According to the virulence of the infecting organism, some patients seek medical attention with a prolonged history of systemic symptoms such as low-grade fever, weight loss, anorexia, or weakness, while others present with typical local symptoms such as aneurysm rupture or sepsis. [21] Aorto-enteric or aorta-bronchial fistulas are one of the most disastrous clinical features in patients with infected aortic aneurysm. As a remote symptom of infected aortic aneurysms. we encountered one patient complaining of eye pain and swelling, which rapidly progressed into septic endophthalmitis requiring enucleation. [16]

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