International Journal of Infectious Diseases 117 (2022) 312–321

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Clinical, Microbiological, and Imaging Characteristics of Infective Endocarditis in Latin America: A Systematic Review ☆

Manuel Urina-Jassir[a], Maria Alejandra Jaimes-Reyes[a], Samuel Martinez-Vernaza[b], Camilo Quiroga-Vergara[b], Miguel Urina-Triana[a,c,*]

[a] *Fundación del Caribe para la Investigación Biomédica, Barranquilla, Atlántico, Colombia. Full postal address: Carrera 50 # 80 – 216 Office 201, Barranquilla, Atlántico, Colombia*

[b] *Unidad de Infectología, Hospital Universitario San Ignacio, Bogotá D.C., Colombia. Full postal address: Calle 41 #13-06 Piso 2, Bogotá D.C., Colombia*

[c] *Facultad de Ciencias de la Salud, Universidad Simón Bolívar, Barranquilla, Atlántico, Colombia. Full postal address: Carrera 59 # 59 – 65, Barranquilla, Atlántico, Colombia*

ARTICLE INFO

Article history:
Received 6 October 2021
Revised 21 January 2022
Accepted 10 February 2022

Keywords:
Endocarditis
Latin America
Microbiology
Blood Culture
Echocardiography

ABSTRACT

Objectives: We aimed to describe the clinical, microbiological, and imaging characteristics of patients with infective endocarditis (IE) in studies from Latin America (LATAM).

Methods: A systematic search through PubMed, EMBASE, LILACS, and SciELO from inception until February 2021 was conducted. We included observational studies that assessed adults with IE from LATAM and reported data on clinical, microbiological, or imaging characteristics. Data were independently extracted by 2 authors and the risk of bias was evaluated by study design with its respective tool. Findings were summarized using descriptive statistics.

Results: Forty-four studies were included. Most cases were male (68.5%), had a predisposing condition including valve disease (24.3%), or had a prosthetic valve (23.4%). Clinical manifestations included fever (83.9%), malaise (63.2%), or heart murmur (57.7%). A total of 36.4% and 27.1% developed heart failure or embolism, respectively. Blood cultures were negative in 23.9% and *S. aureus* (18.6%) and the viridans group streptococci (17.8%) were the most common isolates. Most cases were native valve IE (67.3%) affecting mainly left-sided valves. Echocardiographic findings included vegetations (84.3%) and regurgitation (75.9%). In-hospital mortality was 25.1%.

Conclusions: This is the first systematic review that evaluated the characteristics of IE in LATAM patients. A lack of multicenter studies reflects the need for these studies in LATAM.

1. INTRODUCTION

Infective endocarditis (IE) is a life-threatening disease resulting from an infection of the endocardial lining of the heart, prosthetic valve, or indwelling cardiac device (Holland et al., 2016 Hubers et al., 2020). The incidence of IE has been increasing worldwide in the last decades. The Global Burden of Disease Study estimated 1.09 million incident IE cases in 2019 with an age-standardized rate of 13.8 per 100,000 persons compared with a 9.9 rate in 1990 (Roth et al., 2020 Yang et al., 2021;). In 2019, the highest incidence rates were seen in tropical and southern Latin America (Yang et al., 2021). Furthermore, mortality rates have also risen throughout the mentioned period, ranging from 0.7 to 0.9 per 100,000 (Roth et al., 2020). Notably, southern Latin America, Oceania, and high-income North America were the regions with higher mortality rates in 2019 (Yang et al., 2021).

☆ PROSPERO registration number: CRD42021239602

* Correspondence: Miguel Urina-Triana, Facultad de Ciencias de la Salud, Universidad Simón Bolívar, Barranquilla, Colombia, Full postal address: Carrera 59 # 59 – 65, Barranquilla, Atlántico, Colombia, Postal code: 080002, Phone: +57 315 721 9287.

E-mail addresses: murinajassir@fundacionbios.org (M. Urina-Jassir), marialejaimes26@gmail.com (M.A. Jaimes-Reyes), samumartinez43@gmail.com (S. Martinez-Vernaza), camiloquiroga@hotmail.com, cquiroga@husi.org.co (C. Quiroga-Vergara), murina1@unisimonbolivar.edu.co (M. Urina-Triana).

https://doi.org/10.1016/j.ijid.2022.02.022

IE diagnosis is challenging due to its various clinical presentations. It requires early clinical suspicion in combination with the use of echocardiography and microbiological testing such as blood cultures (Habib et al., 2015 Hoen and Duval, 2013;). As for incidence and mortality rates, other epidemiological characteristics such as predisposing factors and causative microorganisms differ among world regions (Roth et al., 2020 Vogkou et al., 2016; Yew and Murdoch, 2012;). Predisposing factors vary across countries. For instance, rheumatic heart disease (RHD) is still present in developing nations, whereas other risk factors such as degenerative heart disease or intravenous drug use (IVDU) are less common compared with developed countries (Yew and Murdoch, 2012). Slipczuk et al. reported different trends in etiological agents among continents in a systematic review including studies from five decades (1960s to 2000s). For example, cases of *Staphylococcus aureus* increased and the viridans group streptococci (VGS) decreased significantly in North America, whereas no differences were found in Latin America (LATAM) throughout the decades (Slipczuk et al., 2013). In addition, Vogkou et al. described a predominant presence of *S. aureus* in most continents, whereas the subsequent microbes varied among them in studies published from 2003 to 2013 (Vogkou et al., 2016).

Recently, systematic reviews on IE trends during the last century in North America and Europe were published, identifying a stable incidence in North America and a preoccupying increasing trend in Europe (Talha et al., 2021a, 2021b). In LATAM, synthesized data regarding the characteristics and trends of IE are scarce. Considering the possible differences among regions, the relevance of accurate characterization of the population with IE and the high incidence and mortality estimates in LATAM, we aimed to describe the clinical, microbiological, and echocardiographic characteristics of adult patients diagnosed with IE from this region.

2. METHODS

This systematic review is reported following the preferred reporting items for systematic reviews and meta-analysis (PRISMA) guidelines (Page et al., 2021). The protocol was registered on PROSPERO (CRD42021239602) (Urina-Jassir et al., 2021).

2.1. Information sources and search strategy

We conducted a comprehensive search in PubMed, EMBASE, LILACS, and SciELO from inception through February 26, 2021, without language restriction. We included a combination of keywords related to endocarditis and LATAM for PubMed and EMBASE. For LILACS and SciELO (LATAM databases), only endocarditis-related terms were applied (full search string available in Supplementary Table S1-S4). We supplemented our search by examining the reference lists from articles accessed in full text.

2.2. Inclusion and exclusion criteria

We considered eligible observational studies (cross-sectional, cohort, case-control, and case series [≥5 participants]) that evaluated adult patients (≥18 years) with IE from LATAM countries. Studies reporting data on clinical (symptoms/signs, manifestations, risk factors), microbiological (blood cultures, microorganisms), or imaging characteristics were included. We excluded case reports (≤ 4 participants), review articles, systematic reviews/meta-analyses, trials, and abstracts. Studies reporting data exclusively on one subset of IE (i.e., data exclusive to one microorganism or a unique condition) were also excluded to avoid bias. International studies including participants from other world regions besides LATAM were excluded if variables were not divided by countries or regions. In case of repeated or overlapping data, we included the most comprehensive report. Articles including both participants <18 and ≥18 years were excluded unless the study divided them by individuals or groups whose age was ≥18 years (only data from the latter were extracted). Finally, studies not specifying the adult population and without age range, mean age (SD), or median age (IQR) were excluded.

2.3. Selection process

Two reviewers (MUJ and MAJR) independently screened the records by title, abstract, and subsequently full text for eligibility using the web application Rayyan (Ouzzani et al., 2016). Disagreements were resolved by consensus or by a third author (SMV).

2.4. Data collection process and items

Two authors (MUJ and MAJR) independently extracted the data of included reports into an extraction form (Google spreadsheet) with pre-specified criteria. Disagreements were resolved as stated previously. When available, the following was extracted from each study: (1) general information (author, reference year, study period, country, study design, and objectives); (2) characteristics of the population (total number, gender, and age); (3) clinical characteristics (risk factors, comorbidities, symptoms/signs, manifestations, and nosocomial IE); (4) use of Duke criteria (Durack et al., 1994 Li et al., 2000;) for diagnosis; (5) microbiological characteristics (blood cultures, microbes, resistance patterns, and other microbiological tests); (6) echocardiographic characteristics (modality, type of IE, location, and diagnostic findings); and (7) outcomes (surgery and mortality). We extracted the frequency and percentage for items (2) through (7).

2.5. Study risk of bias assessment

The risk of bias was independently assessed by two reviewers and disagreements were resolved by a third one. The tools varied depending on the study design: cohort studies (Newcastle-Ottawa Scale [NOS] (Wells et al., 2021), cross-sectional studies (AXIS Critical Appraisal Tool for Cross-Sectional Studies (Downes et al., 2016)), and case series (Institute of Health Economics [IHE] Quality Appraisal Checklist for Case Series Studies (Institute of Health Economics (IHE), 2014)). For the NOS, a score from 0 to 9 stars was awarded. For the AXIS tool and IHE checklist, a score from 0 to 20 was given (a point for every positive aspect and in the IHE, a half-point for "partial" aspects). For all of them, the higher the score obtained, the lower the risk of bias. We did not exclude manuscripts based on quality.

2.6. Synthesis methods

Descriptive statistics were used to summarize the findings. For categorical variables, frequencies and percentages were reported. Clinical and echocardiographic variables were calculated as the sum of participants with each variable out of the total number of cases from the studies reporting the variable. Microbiological variables were calculated as the sum of participants with each variable out of the total number of blood cultures reported. Tables are presented as n/N with the number of studies reporting each variable. Studies were divided by decades (those with overlapping years were assigned to the decade with most years assessed) according to their study period. No additional statistical tests were performed, as the number of cases/studies were dissimilar (1970s-1980s: 6 studies, 163 cases; 1990s: 7 studies, 461

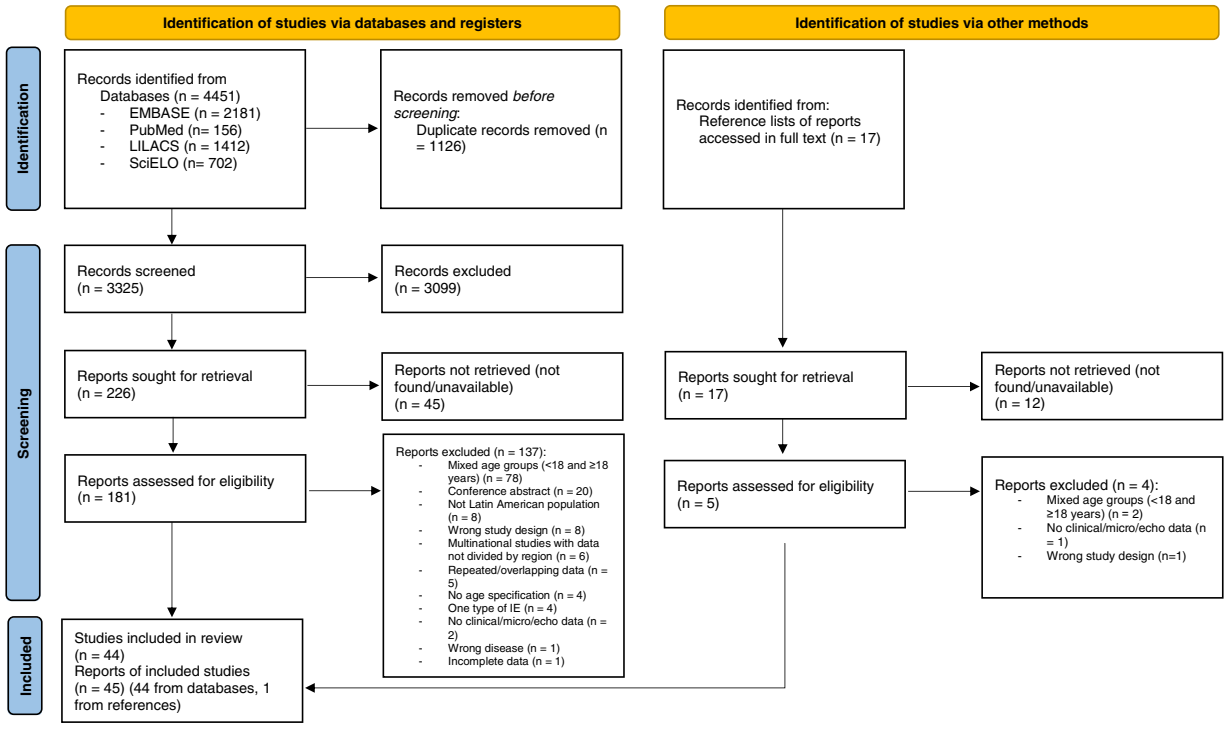

Figure 1. PRISMA (Page et al., 2021) flow diagram for study selection

cases; 2000s: 13 studies, 1834 cases; and 2010s: 18 studies, 1807 cases).

3. RESULTS

3.1. Study selection

Our search yielded a total of 4451 records. After duplicates removal, 3325 records were screened by title and abstracts resulting in 226 reports sought for retrieval. Forty-four reports fulfilled the inclusion criteria in addition to one further report from the reference list review for a total of 45 reports. One study comprised 2 reports, but both were included as one reported data on clinical and imaging characteristics (Casabe et al., 1996b) and the other reported data on microorganisms and further clinical manifestations (Casabe et al., 1996a). We treated this study as one throughout the review, leading to 44 studies (Allende González et al., 2020 Avellana et al., 2018; Bahamondes et al., 2008; Bezerra et al., 2020; Burgos et al., 2019; Casabe et al., 1996b; Corral et al., 1993; Cremona et al., 2007; Damasco et al., 2014; Ediap et al., 2017; Ferreiros et al., 2006; Flores et al., 2017; Fragomeni et al., 2003; Fránquiz Cuéllar and Alvarez Ozambela, 1986; Holanda et al., 2015; Jacob Filho et al., 1988; Jáuregui Camargo et al., 1997; Kaiser et al., 1984; Leyva Quert et al., 2009; Marino et al., 2014; Merello et al., 2019; Monteiro et al., 2017; Murdoch et al., 2009; Negrín Expósito et al., 2003; Nieto et al., 1985; Olaya-Sanchez et al., 2019; de Oliveira et al., 2018; Ortiz et al., 1983; Oyonarte G et al., 2003; Pérez Zerpa et al., 2020; Pinheiro et al., 2018; Pivatto Júnior et al., 2020; Popilovsky et al., 2014; Ris et al., 2019; Romero Flecha and Aveiro Figueredo, 2020; Saito et al., 2014; Siciliano et al., 2014a;, 2014b Stockins et al., 2012; Tagliari et al., 2020; Vega-Sánchez et al., 2016; Velásquez et al., 2018; Wouters et al., 1991; Zalaquett S et al., 2004;) Figure 1. presents a flow diagram for the study selection. Citations that seemed to fulfill inclusion criteria but were excluded can be accessed in Supplementary Table S5 with the reason for exclusion.

3.2. Geographical distribution of included studies

Figure 2 represents the total number of included studies and cases by country. A summary of the studies' characteristics and a table with individual study's data can be accessed in Supplementary Material Table S6.

3.3. Risk of bias in studies

The quality/risk of bias for each study can be reviewed in Supplementary Table S7-9. For the cross-sectional studies, the scores ranged from 13 to 20. The most common missing factors were related to the sample size justification and non-responders. The NOS score for cohort studies ranged from five to nine stars; those with lower scores were due to issues in the "Comparability" section of the scale. Finally, the score for the case series ranged from 8 to 17; the lack of a prospective design and single-center case series were the two most frequent negative factors.

3.4. Clinical characteristics

3.4.1. Demographic characteristics, predisposing factors, and comorbidities of cases with IE

Overall and through all the decades, IE affected predominantly males (43 studies, n: 2851/4160; 68.5%). The most common cardiovascular risk factors were having a history of heart valve disease (24.3%) followed by the presence of a prosthetic cardiac valve (23.4%). By decades, valve disease was the most frequent predisposing factor in the 1970-80s, 1990s, and 2010s, whereas a prosthetic valve was the most common in the 2000s. Prior IE was found in 8.8% of cases among 15 studies, with most of them being from the 2000s (7 studies, 8.7%) and 2010s (6 studies, 8.9%). RHD

Figure 2. Geographical distribution (by country) of included studies (Figure created with MapChart© [https://mapchart.net/])
The number of included studies and cases per country is presented. One study (Murdoch et al., 2009) is not represented, as it includes "South America" as a region, including cases from Argentina, Brazil, and Chile. Abbreviations: AR: Argentina, BR: Brazil, CL: Chile, CO: Colombia, CU: Cuba, MX: Mexico, PA: Panama, PE: Peru, PY: Paraguay, UY: Uruguay.

frequency through the decades ranged from 7.5% to 16.5% (1970s-80s to 2010s). Hypertension (38.1%) and diabetes mellitus (15.8%) were the most frequent comorbidities. Only few studies reported healthcare-related situations associated with IE, such as previous surgical or endoscopic procedures (21.9%), indwelling catheter or devices (20.9%), and previous dental procedures (5.6%) were reported. IVDU overall frequency was 4.0% (15 studies), whereas 13.6% (3 studies) was seen in 1990s, 2.1% (6 studies) in 2000s, and 1.9% (5 studies) in 2010s (Table 1 and Supplementary Table S10 for decades).

3.4.2. Clinical manifestations of cases with IE

The most common clinical manifestation of IE was fever (83.9%), followed by malaise (63.2%) and the presence of a heart murmur (57.7%). Roughly more than one-third (36.4%) and one-fourth (27.1%) of the cases developed heart failure or suffered an embolic event, respectively. Furthermore, septic shock was reported in 12.1% of the cases from 6 of the included studies and immunological phenomena in 11.1% of the cases from 11 studies. Further clinical manifestations are presented in Table 2.

Table 1
Predisposing factors and comorbidities of cases with infective endocarditis in Latin America

Variable	Studies[a]	n/N[b] (%)
Predisposing factors		
Previous valve disease[c]	21	451/1853 (24.3)
Prosthetic valve	26	603/2573 (23.4)
Previous RHD	20	269/2005 (13.4)
Congenital heart disease[d]	24	289/2964 (9.8)
Previous IE	15	233/2647 (8.8)
Previous heart failure	8	272/1178 (23.1)
IV drug use	15	79/1981 (4.0)
Indwelling catheter or device[e]	14	264/1261 (20.9)
Previous surgical or endoscopic procedure	12	326/1491 (21.9)
Previous dental procedure	9	48/856 (5.6)
Comorbidities		
Diabetes mellitus	22	489/3090 (15.8)
Hypertension	12	462/1212 (38.1)
CKD	17	355/2295 (15.5)
Dialysis	13	112/1149 (9.8)
HIV	4	10/374 (2.7)
Immunosuppression or autoimmune disorder[f]	5	26/270 (9.6)
Neoplasia/Cancer	7	95/913 (10.4)

[a] Number of studies reporting each variable.
[b] n is the total number of cases with that variable, N is the total number of cases of the studies reporting that variable.
[c] Includes: degenerative valve disease, mitral valve prolapses, aortic sclerosis, any valve stenosis or regurgitation, non-rheumatic valve disease, previous valve disease (when reported as a distinct group from congenital or rheumatic heart disease), and previous valve dysfunction.
[d] Includes: bicuspid aortic valve, congenital pulmonary stenosis, ventricular septal defect, atrial septal defect, tetralogy of Fallot, Valsalva sinus aneurysm, myxomatosis, congenital aortic stenosis, congenital mitral regurgitation, and "congenital" as a group.
[e] Includes: central venous catheters, pacemakers, "catheters", and unspecified intracardiac devices.
[f] Includes: solid organ transplant, autoimmune disease, connective tissue disease, rheumatoid arthritis, steroids, and immunosuppression.**Abbreviations:** CKD: Chronic Kidney Disease; HIV: Human Immunodeficiency Virus; IE: Infective Endocarditis; RHD: Rheumatic Heart Disease

Table 2
Clinical manifestations of cases with infective endocarditis in Latin America

Variable	Studies[a]	n/N (%)[b]
Fever	22	2109/2513 (83.9)
Dyspnea	5	303/820 (37.0)
Heart failure	28	1108/3047 (36.4)
Malaise	7	312/494 (63.2)
Heart murmur	14	1119/1940 (57.7)
Immunological phenomena	11	206/1851 (11.1)
Osler's nodes	8	59/1536 (3.8)
Roth's spots	5	46/1296 (3.6)
Positive RF	4	23/583 (4.0)
GMN	2	60/297 (20.2)
Vascular phenomena	34	1076/3559 (30.2)
Embolism	33	944/3483 (27.1)
Mycotic aneurysm	7	46/1433 (3.2)
Janeway's lesions	7	44/1170 (3.8)
Conjunctival hemorrhages	4	22/315 (7.0)
Hemorrhagic stroke	2	6/119 (5.0)
Other manifestations		
Ungueal or splinter hemorrhages	6	84/987 (8.5)
Sepsis	7	315/793 (39.7)
Severe sepsis	3	182/1017 (17.9)
Septic shock	6	122/1005 (12.1)
Splenomegaly	8	279/1137 (24.5)
Petechiae	7	291/1400 (20.8)
Hepatomegaly	4	223/783 (28.5)

[a] Number of studies reporting each variable.
[b] n is the total number of cases with that variable, N is the total number of cases of the studies reporting that variable.**Abbreviations:** GMN: Glomerulonephritis; RF: Rheumatoid factor.

3.4.3. Nosocomial or healthcare-associated IE

Frequencies on nosocomial or healthcare-associated IE could be extracted from six studies. The terms and definitions varied among reports. Nieto et al. and Corral et al. reported nosocomial IE in three cases each (16.7% and 13.6%, respectively) in the 1970s-80s and the 1990s, respectively (Corral et al., 1993 Nieto et al., 1985;). In the 2000s, Marino et al. described that 70% were nosocomial IE, whereas Monteiro et al. reported rates for hospital-acquired IE (29.4%) and healthcare-associated IE (5.1%) (Marino et al., 2014 Monteiro et al., 2017;). Two studies were in the 2010s and showed healthcare-acquired IE in 56.3% (Damasco et al., 2014) and nosocomial IE in 9% (Tagliari et al., 2020), respectively.

3.4.4. Duke diagnostic criteria among included studies

From the studies conducted after 1994 (Duke criteria inception (Durack et al., 1994)), 83.8% (n: 31/37) described the use of Duke (Durack et al., 1994) or modified Duke criteria (Li et al., 2000). From the studies conducted before 1994, two out of seven studies used the Von Reyn criteria (von Reyn et al., 1981), whereas the remaining studies defined IE diagnosis based on anatomical diagnosis or a mixture of clinical, blood cultures, and echocardiographic findings.

3.5. Microbiological characteristics

3.5.1. Blood cultures and isolates among cases with IE

A total of 4032 blood cultures were performed among 41 studies. Blood cultures were positive in 76.1%. The proportion of blood culture-negative IE (BCNIE) was 14.2% (6 studies), 26.1% (7 studies), 25.1% (12 studies), and 23.1% (16 studies) in the 1970s-80s, 1990s, 2000s, and 2010s, respectively. When considering genera, *Staphylococcus* and *Streptococcus* were the most common isolates (27.3% and 26.7%, respectively). The two predominant species were *Staphylococcus aureus* and VGS with 18.6% and 17.8% of the isolates, respectively. VGS was the most prevailing microorganism in the 1970s-80s, 1990s, and 2000s, whereas *S. aureus* in the 2010s. Overall, and in each decade, *Enterococcus spp.* was the third most common etiology. Other isolates included coagulase-negative *Staphylococcus* (CoNS) (7.9%) and *Streptococcus gallolyticus* (2.9%). The remaining isolates are presented in Table 3 and Supplementary Table 10.

3.5.2. Resistance patterns for S. aureus

Eight studies described the resistance patterns of *S. aureus*. Overall, methicillin-resistant *S. aureus* (MRSA) was found in 19.6% (n: 18/92) of the *S. aureus* isolates. Five of the studies reporting MRSA were from the 2010s (Corral et al., 1993 Damasco et al., 2014; Ediap et al., 2017; Flores et al., 2017; Marino et al., 2014; Merello et al., 2019; Olaya-Sanchez et al., 2019; Velasquez et al., 2018;).

3.5.3. Other microbiological testing

Only two studies reported data on additional microbiological testing (Murdoch et al., 2009 Siciliano et al., 2014b;). Murdoch et al. reported serologic testing for *Coxiella burnetii* and *Bartonella* (positive in 1 patient each) (Murdoch et al., 2009). Siciliano et al. described the use of indirect immunofluorescence assays for *Coxiella burnetii* and *Bartonella* (positive in 4 and 10 cases, respectively) (Siciliano et al., 2014b).

3.6. Echocardiographic characteristics

Few studies reported the frequency for echocardiographic modality. From those that reported, a transthoracic echocardiogram

Table 3
Microbiological findings of cases with infective endocarditis in Latin America

Variable	n (%)
Total blood cultures	4032
Number of studies[a]	41
Positive	3067 (76.1)
Negative	965 (23.9)
Microorganisms	
Staphylococcus spp.	1102 (27.3)
Staphylococcus aureus	750 (18.6)
CoNS	319 (7.9)
Streptococcus spp.	1075 (26.7)
VGS	718 (17.8)
Streptococcus gallolyticus (bovis)	116 (2.9)
Enterococcus spp.	374 (9.3)
HACEK	57(1.4)
Gram negative[b]	112(2.8)
Fungal[c]	51(1.3)
Candida spp.	28(0.7)
Polymicrobial	26(0.6)
Others/unspecified[d]	74(1.8)

[a] From the 42 studies reporting at least one microbiological variable, one study (Popilovsky et al., 2014) was excluded from the pooled analysis as no data for total blood cultures or positive-negative blood cultures could be extracted.
[b] Includes: Pseudomonas spp, Klebsiella spp, E. coli, Proteus mirabilis, Serratia marcescens, Stenotrophomonas maltophila, Enterobacter spp, Pasteurella spp, Acinetobacter spp, Citrobacter spp, Flavobacterium spp, Brevundimoas spp, Salmonella spp, Bacteroides spp, and "Gram Negatives."
[c] Includes: Candida spp, Aspergillus spp, Histoplasma spp.
[d] Reported as others or unspecified in original studies.**Abbreviations:** CoNS: *Coagulase negative staphylococci;* HACEK: *Haemophilus spp., Aggregatibacter spp., Cardiobacterium hominis, Ekinella corrodens, and Kingella spp.*; VGS: viridans group streptococci.

Table 4
Echocardiographic characteristics of cases with infective endocarditis in Latin America

Variable	Studies[a]	n/N[b] (%)
Echocardiogram modality		
TTE	12	1478/1552 (95.2)
TEE	10	925/1553 (59.6)
Type of IE		
Native valve IE	27	2274/3378 (67.3)
Prosthetic valve IE	24	857/3219 (26.6)
Device related IE [c]	11	132/1344 (9.8)
Native + prosthetic IE	1	2/136 (1.5)
Location of IE		
Native		
Aortic	19	575/2050 (28.1)
Mitral	19	564/2092 (27.0)
Tricuspid	15	123/1928 (6.4)
Pulmonary	6	13/1555 (0.8)
Mitral + aortic	10	117/1489 (7.9)
Other combined	3	6/113 (5.3)
Prosthetic		
Aortic	9	171/1272 (13.4)
Mitral	9	110/1230 (8.9)
Tricuspid	3	2/900 (0.2)
Pulmonary	3	4/927 (0.4)
Mitral + aortic	5	19/1095 (1.7)
Non-specified [d]		
Aortic	11	519/1223 (42.4)
Mitral	11	475/1223 (38.8)
Tricuspid	8	100/1080 (9.3)
Pulmonary	3	8/582 (1.4)
Mitral + aortic	6	62/568 (10.9)
Other combined valves	1	6/71 (8.5)
Unidentified/other location	9	63/777 (8.1)
Echocardiographic findings		
Vegetation	25	2333/2767 (84.3)
Valvular regurgitation	11	1050/1383 (75.9)
Abscess	18	332/2614 (12.7)
Valvular apparatus rupture or perforation	9	168/1426 (11.8)
Dehiscence of prosthetic valve	5	44/1112 (4.0)

[a] Number of studies reporting each variable.
[b] n is the total number of cases with that variable, N is the total number of cases of the studies reporting that variable.
[c] Pacemaker or intracardiac device.
[d] Either prosthetic or native infective endocarditis (location not divided by type of IE in original study).**Abbreviations:** IE: Infective endocarditis; TTE: Transthoracic Echocardiogram; TEE: Transesophageal Echocardiogram.

(TTE) was performed in 95.2%, whereas transesophageal echocardiogram (TEE) in 59.6%. Among patients with available data, native and prosthetic IE occurred in 67.3% and 26.6% of cases, respectively. Native valve IE was the most common type in each decade. On the other hand, prosthetic IE was described in 10.1% (4 studies) in the 1990s and in 31.3% (11 studies) in the 2010s. Irrespective of the type of IE, the most frequent locations were aortic and mitral valves. An infected pacemaker or intracardiac device was reported in 11 studies with a frequency of 9.8%. The main echocardiographic findings were vegetations (84.3%) and valve regurgitation (75.9%). Some IE complications observed in echocardiography were abscesses (12.7%), valvular apparatus rupture or perforation (11.8%), and dehiscence of the prosthetic valve Table 4. summarizes the echocardiographic characteristics. None of the studies reported data on other imaging techniques for IE diagnosis such as cardiac computed tomography (CCT), magnetic resonance imaging (MRI), or ^{18}F-fluorodeoxyglucose (FDG) PET/CT.

3.7. Surgery and mortality among cases with IE

Ten reports were based on solely surgical cases which were excluded from the pooled analysis. From the non-surgical-exclusive reports, the frequency of surgery was 41.8% (26 studies, n: 1224/2931). The proportion of cases needing surgery was 25.9% (3 studies, n: 28/108), 26.4% (3 studies, n: 23/87), 43.9% (10 studies, n: 621/1415), and 41.8% (10 studies, n: 552/1321) for the 1970s-80s, 1990s, 2000s, and 2010s, respectively.

Most of the studies reported in-hospital mortality and only seven studies reported late mortality. In-hospital mortality was 25.1% (n: 1027/4095; 37 studies), whereas overall mortality (including late mortality and those where timeframe was not specified) was 26.6%. In-hospital mortality frequencies through decades were 29.3% (1970s-80s; 3 studies, n: 31/106), 24.2% (1990s; 6 studies, n: 104/429), 23.6% (2000s; 12 studies, n: 421/1781), and 26.5% (2010s; 16 studies, n: 471/1779).

4. DISCUSSION

To the best of our knowledge, this is the first systematic review integrating the clinical, microbiological, and echocardiographic characteristics of patients with IE from LATAM countries. Forty-four observational studies, mostly from Argentina, Brazil, and Chile, were identified, retrieving crucial data on this life-threatening disease.

4.1. Clinical characteristics

Among Latin American patients, IE had a male predominance, which is consistent with national and multinational studies from other regions (Cecchi et al., 2015 Habib et al., 2019; Muñoz et al., 2015; Selton-Suty et al., 2012;). Regarding predisposing factors, not all studies reported data on each of them; for instance, 21 studies provided data on valve disease. Overall, we identified a high proportion of cases with predisposing heart conditions, mainly na-

tive valvular heart disease (24.3%), prosthetic valve (23.4%), RHD (13.4%), and congenital heart disease (CHD) (9.8%). This relates to the findings from a systematic review of 1872 IE cases in Portugal from 1990 to 2020, where 44.5% of them had 'structural heart disease' (de Sousa et al., 2021). **In** addition, Muñoz et al. conducted a prospective, nationwide study of 1804 subjects with IE in Spain describing that 27% had degenerative valve disease (Muñoz et al., 2015).

Data on CHD were assessed from 24 studies (2964 cases), and the frequency found in our review was lower than that reported in the European Endocarditis (EURO-ENDO) registry—a large prospective multinational registry of 3116 patients with IE, where CHD was seen in 11.7% of participants (Habib et al., 2019). On the other hand, RHD information was provided in less than half of the studies (2005 cases). Comparing the presence of RHD in our study to that with other regions, a similar rate of RHD among subjects with IE has been described in Turkey (11%) (Vahabi et al., 2019), but a lower frequency has been reported in higher-income countries such as Spain (8%) (Muñoz et al., 2015). This reflects how RHD continues to be a cause of morbidity in developing nations compared with wealthier regions. The frequency of IVDU was low (4.0%), less than in high-income regions as Europe and the United States (Habib et al., 2019 Rudasill et al., 2019;). However, just over a third of the studies provided data on IVDU, leading to 1981 cases assessed. In the United States, Rudasill et al. found that 22.2% of IE cases between 2010 and 2015 from a large national database were IVDU-related (Rudasill et al., 2019). Moreover, a prior episode of IE was described in 8.8% in one-third of studies, more than in a French nationwide study (5.4%) (Selton-Suty et al., 2012) but similar to the EURO-ENDO registry (8.8%) (Habib et al., 2019). A positive aspect of the reviewed articles was that most of them based their IE definition on the Duke or modified Duke criteria; the latter provides excellent diagnostic value for IE cases according to the PRO-ENDOCARDITIS study (Mahabadi et al., 2021).

4.2. Microbiological characteristics

Data on blood cultures were retrieved from 41 studies, including 4032 cultures. Among these, 23.9% of cases had negative blood cultures. This rate ranged from 14.2% (1970-80s) to 26.1% (1990s), with 23.1% BCNIE cases identified in the last decade. BCNIE is a common finding as reported in studies from different regions, ranging from 14.7% up to 31.1% (Cecchi et al., 2015 Giannitsioti et al., 2021; Habib et al., 2019; Muñoz et al., 2015; Vahabi et al., 2019;). Previous antibiotic exposure is a common reason for BCNIE (Lamas and Eykyn, 2003). In our review, only two studies (Ferreiros et al., 2006 Siciliano et al., 2014b;) reported previous antibiotic use in 57% and 47.1% of BCNIE cases, respectively, suggesting the need for this data to be included in upcoming research in LATAM. Moreover, atypical microorganisms that require additional testing have been reported as etiologies of BCNIE (Lamas and Eykyn, 2003). Fournier et al. described the use of serologic testing as an aid for blood cultures in a series of 759 cases with BCNIE, where a diagnosis was provided by serological analysis in 47.7% of cases. In addition, polymerase chain reaction (PCR) of blood or valve specimen was useful in this study (Fournier et al., 2010). Clinical guidelines recommend the use of serology and PCR assays when presented with BCNIE (Habib et al., 2015). Despite this, only two of the included studies reported the use of serology tests for *Coxiella burnetii* and *Bartonella* (Murdoch et al., 2009 Siciliano et al., 2014b;). This reflects an area for improvement in the diagnosis of fastidious microorganisms in LATAM, as other authors have reported cases of *Bartonella spp. and Coxiella burnetii* in valves of BCNIE cases in Brazil (Lamas et al., 2013).

The most common isolates in this study were *Staphylococcus aureus* and VGS, as reported in a systematic review of observational studies without geographic restriction (Vogkou et al., 2016). In the 2010s, *S. aureus* was the main causative microorganism, followed by VGS and *Enterococcus spp.* Although the EURO-ENDO study described a higher number of *Enterococcus* and CoNS isolates than VGS, *Staphylococcus aureus* was still the most common etiology (Habib et al., 2019). On the other hand, Nakatani et al. reported VGS as the most common microbe among IE cases in a nationwide study in Japan (Nakatani et al., 2013). Just a few studies, mostly from the 2010s, reported *S. aureus* antimicrobial susceptibility; subsequent studies should include this data to clarify MRSA rates among cases of IE in LATAM.

4.3. Imaging characteristics

Echocardiographic data on the type of IE was assessed from at least 27 studies. Despite the higher percentage of patients with native valve IE (67.3%), the number of prosthetic valve (26.6%) and device-related IEs (9.8%) were noteworthy. Notably, in the last decade, 31.3% of 1312 cases and 15.9% of 591 cases had prosthetic valve and device-related IE, respectively. Similar findings were described in the EURO-ENDO study (Habib et al., 2019) and multicenter prospective registers from Spain (Muñoz et al., 2015) and Italy (Cecchi et al., 2015). In this review, IE mainly affected left-sided valves, which is in line with the findings from other authors worldwide (Habib et al., 2019 Muñoz et al., 2015; Selton-Suty et al., 2012;). As expected and consistent with the description of other studies (Habib et al., 2019 Nakatani et al., 2013; Vahabi et al., 2019;), vegetations were the most commonly reported and found echocardiographic findings. Other common findings in our review were valvular regurgitation and abscesses. Imaging techniques such as CCT, MRI, and ^{18}F-FDG PET/CT have been described as complementary tools for IE diagnosis, especially in patients with prosthetic or device-related IE (Gomes et al., 2017). None of the included studies described the use of these additional imaging modalities. The use of these techniques is still low; according to the EURO-ENDO registry, ^{18}F-FDG PET/CT, leucocyte scintigraphy, and CCT were performed in 16.6%, 1.2%, and 9.6%, respectively (Habib et al., 2019).

4.4. Burden of IE

IE has a high burden on LATAM patients. We found a high proportion of cases developing heart failure (36.4%) or embolic events (27.1%) during the course of the disease, consistent with a meta-analysis evaluating 22,382 cases that described a similar rate for embolism (25%) and cardiac complications (39%) (Abegaz et al., 2017). Furthermore, a meta-analysis of 11,215 IE cases reported a median incidence of 29% for embolic events (Yang et al., 2019). The use of surgical treatment has been increasing in the management of IE over time (Tleyjeh et al., 2007). In our review, surgery was more frequently reported in studies from the 2000s decade onward. From 2931 cases in 26 nonsurgical-exclusive reports, surgery was done in 42% of cases. This proportion was lower than that reported in the EURO-ENDO registry (51.2%) and in a Japanese nationwide study (61%) (Habib et al., 2019 Nakatani et al., 2013;).

Data on in-hospital mortality were available in most studies, leading to data on over 4000 cases. In-hospital mortality among these cases was 25.1%, ranging between 23.6% to 29.3% through the decades. Similar in-hospital mortality rates have been described by Muñoz et al. in Spain (28.9%) and by Sousa et al. in Portugal (short-term mortality: 20.8%) (Muñoz et al., 2015 de Sousa et al., 2021;). However, these findings are higher than in other developed countries (Bor et al., 2013 Habib et al., 2019; Nakatani et al., 2013;). Bor et al. described in-hospital mortality of 14.5% in a nationwide study evaluating the hospital admissions of patients with IE across the United States (Bor et al., 2013). In addition,

Habib et al. and Nakatani et al. reported in-hospital mortality of 17.1% and 11% in Europe and Japan, respectively (Habib et al., 2019 Nakatani et al., 2013;). Other authors have described predictors of mortality such as a greater age, *S. aureus* etiology, heart failure (Selton-Suty et al., 2012), and the failure to undertake surgery when indicated (Habib et al., 2019), which may be possible factors to the differences in mortality between regions.

4.5. Limitations of the study

This systematic review has some limitations. First, 45 of 226 potential eligible articles could not be retrieved (especially from 2000 or before) despite exhaustive effort (extensive web search, contact to journals, libraries, or authors), thus leading to possible missing data. Second, 37 of 44 studies were conducted in a single center and all studies were hospital-based, which could be a source for potential biases such as selection or referral bias. Third, there are missing data from some of the countries of the region due to them not fulfilling the initial eligibility criteria. Fourth, heterogeneity in the number of studies/cases used in each variable can be seen, as we depend on the data reported in the published manuscripts. This may lead to possible overestimation or underestimation of some variables. Fifth, data on uncommon microorganisms may have been missed due to our eligibility criteria, as these are commonly described in microorganism-exclusive case series/reports. Sixth, when assessing variables per decade, the differences in the number of cases/studies were considerable, leading us to the use of solely descriptive statistics. Future studies evaluating increasing or decreasing trends in predisposing factors, microbiology, and burden are welcome to further clarify differences through time. Finally, we identified a lack of population-based and multicenter national or international studies in most of the countries. Only four studies from two countries, Chile (Oyonarte G et al., 2003) and Argentina (Avellana et al., 2018 Casabe et al., 1996b;, 1996a Ferreiros et al., 2006;), and one international (Murdoch et al., 2009) were prospective multicenter registries, identifying the need for this type of study in LATAM.

5. CONCLUSIONS

In this systematic review, we identified the most common characteristics of patients with IE in LATAM. Most were male, had a predisposing heart condition (valve disease, prosthetic valve, RHD, or CHD), and presented with fever and a heart murmur. There was a high rate of negative blood cultures, and the two most common isolates were *Staphylococcus aureus* and VGS. IE was mainly native and located in left-sided valves. The disease continues to highly burden patients, with a significant proportion of heart failure, embolism, need for surgery, and in-hospital mortality. There is an area of improvement in the use of serologic testing and new imaging techniques in LATAM. Further prospective and periodical national or international studies, as well as population-based investigations, including Latin American adults are needed for an accurate description of this deadly disease.

Conflicts of interest

The authors have no conflicts of interest to declare.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgments

None

Ethics approval

No ethical approval is required for this study, as it is a systematic review based on published manuscripts and no direct research on subjects was performed by any of the authors.

Availability of data

All information is available on the main text and supplementary material.

Author contributions

MUJ, MAJR, SMV, CQV, and MUT were involved in the conception and design of the study. MUJ, MAJR, and SMV contributed to the literature search, screening of title/abstracts and full texts, and data extraction. SMV conducted statistical analyses. MUJ, MAJR, SMV, CQV, and MUT contributed to the interpretation of data. MUJ wrote the initial draft of the review. MUJ, MAJR, SMV, CQV, and MUT critically revised the draft. CQV and MUT supervised the work. All authors read and approved the final version of the review.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2022.02.022.

REFERENCES

Abegaz TM, Bhagavathula AS, Gebreyohannes EA, Mekonnen AB, Abebe TB. Short- and long-term outcomes in infective endocarditis patients: a systematic review and meta-analysis. BMC Cardiovasc Disord 2017;17:291. doi:10.1186/s12872-017-0729-5.

Allende González A, Bermúdez Yera G de J, Mirabal Rodríguez R, Quintero Fleites YF, de la Cruz Y, Chaljub Bravo E. Caracterización clínico-epidemiológica con enfoque quirúrgico de la endocarditis infecciosa en la región central de Cuba. CorSalud 2020;12:138–45.

Avellana PM, García Aurelio M, Swieszkowski S, Nacinovich F, Kazelian L, Spenato M, et al. Infective Endocarditis in Argentina. Results of the EIRA 3 Study. Rev Argent Cardiol 2018;86:21–9. doi:10.7775/rac.v86.i1.10935.

Bahamondes JC, Merino S G, Silva V A, Salman A J, Redel S I, Droguett G JP. Cirugía de la endocarditis infecciosa en un centro regional en Chile: Análisis de casos y resultados en el largo plazo. Rev Med Chil 2008;136:31–7. doi:10.4067/S0034-98872008000100004.

Bezerra RL, Carvalho TF de, Batista R dos S, Silva YM da, Campos BF, Castro JHM de, et al. Association between Insulin use and Infective Endocarditis: An Observational Study. Int J Cardiovasc Sci 2020;33:14–21. doi:10.5935/2359-4802.20190049.

Bor DH, Woolhandler S, Nardin R, Brusch J, Himmelstein DU. Infective Endocarditis in the U.S., 1998-2009: A Nationwide Study. PLoS ONE 2013;8:1–8. doi:10.1371/journal.pone.0060033.

Burgos LM, Cracco MA, Fernández Oses P, Iribarren AC, Ronderos R, Nacinovich F. Endocarditis infecciosa en Argentina: ¿qué aprendimos en los últimos 25 años? Medicina (B Aires) 2019;79:257–64.

Casabe JH, Hershson A, Ramos MS, Barisani JL, Pellegrini C, Varini S. Endocarditis infecciosa en la República Argentina: complicaciones y mortalidad. Rev Argent Cardiol 1996a;64:39–45.

Casabe JH, Pellegrini CD, Hershson AR, Ramos MS, Vidal L, Sampó EA, et al. Endocarditis infecciosa en la República Argentina (Estudio E.I.R.A.): resultados generales. Rev Argent Cardiol 1996b;64:9–19.

Cecchi E, Chirillo F, Castiglione A, Faggiano P, Cecconi M, Moreo A, et al. Clinical epidemiology in Italian Registry of Infective Endocarditis (RIEI): Focus on age, intravascular devices and enterococci. Int J Cardiol 2015;190:151–6. doi:10.1016/j.ijcard.2015.04.123.

Corral J, García MA, Aquilia S, Ferro A. Epidemiología descriptiva de la endocarditis infecciosa en un hospital general. Infectol & Microbiol Clin 1993;5:7–13.

Cremona AR, Ramírez Borga SJ, Losinno JF, Cartasegna LR, Escudero EM, Fernández JL, et al. Variables predictoras de embolias en endocarditis infecciosa. Medicina (B Aires) 2007;67:39–43.

Damasco PV, Ramos JN, Correal JCD, Potsch Mv, Vieira VV, Camello TCF, et al. Infective endocarditis in Rio de Janeiro, Brazil: a 5-year experience at two teaching hospitals. Infection 2014;42:835–42. doi:10.1007/s15010-014-0640-2.

Downes MJ, Brennan ML, Williams HC, Dean RS. Development of a critical appraisal tool to assess the quality of cross-sectional studies (AXIS). BMJ Open 2016;6. doi:10.1136/bmjopen-2016-011458.

Durack DT, Lukes AS, Bright DK. Duke Endocarditis Service. New criteria for diagnosis of infective endocarditis: utilization of specific echocardiographic findings. Am J Med 1994;96:200–9. doi:10.1016/0002-9343(94)90143-0.

Ediap L, Córdova S, Zúñiga E, Usedo P, Muñoz A, Fernández G, et al. Endocarditis infecciosa asociada a catéter de hemodiálisis: hallazgos clínicos y ecocardiográficos. Rev Chil Cardiol 2017;36:221–31. doi:10.4067/S0718-85602017000300221.

Ferreiros E, Nacinovich F, Casabé JH, Modenesi JC, Swieszkowski S, Cortes C, et al. Epidemiologic, clinical, and microbiologic profile of infective endocarditis in Argentina: A national survey. The Endocarditis Infecciosa en la República Argentina–2 (EIRA-2) Study. Am Heart J 2006;151:545–52. doi:10.1016/j.ahj.2005.04.008.

Flores P, González N, Betancourt P, Berho J, Astudillo C, García C, et al. Endocarditis Infecciosa: caracterización clínica de la enfermedad. Revisión de casos de los últimos 5 años. Rev Chil Cardiol 2017;36:34–40. doi:10.4067/S0718-85602017000100004.

Fournier PE, Thuny F, Richet H, Lepidi H, Casalta JP, Arzouni JP, et al. Comprehensive diagnostic strategy for blood culture-negative endocarditis: A prospective study of 819 new cases. Clin Infect Dis 2010;51:131–40. doi:10.1086/653675.

Fragomeni LS de M, Vieira FF, Bajerski JC, de M, Falleiro RP, Hoppen G, Sartori I. Infective endocarditis: surgical therapy. Arq Bras Cardiol 2003;80:424–37. doi:10.1590/S0066-782X2003000400006.

Fránquiz Cuéllar PA, Alvarez Ozambela C. Endocarditis infecciosa en el anciano. Rev Cubana Med 1986;25:99–104.

Giannitsioti E, Pefanis A, Gogos C, Lekkou A, Dalekos GN, Gatselis N, et al. Evolution of epidemiological characteristics of infective endocarditis in Greece. Int J Infect Dis 2021;106:213–20. doi:10.1016/j.ijid.2021.03.009.

Gomes A, Glaudemans AWJM, Touw DJ, van Melle JP, Willems TP, Maass AH, et al. Diagnostic value of imaging in infective endocarditis: a systematic review. Lancet Infect Dis 2017;17:e1–14. doi:10.1016/S1473-3099(16)30141-4.

Habib G, Erba PA, Iung B, Donal E, Cosyns B, Laroche C, et al. Clinical presentation, aetiology and outcome of infective endocarditis. Results of the ESC-EORP EURO-ENDO (European infective endocarditis) registry: a prospective cohort study. Eur Heart J 2019;40:3222–32. doi:10.1093/eurheartj/ehz620.

Habib G, Lancellotti P, Antunes MJ, Bongiorni MG, Casalta J-P, del Zotti F, et al. 2015 ESC Guidelines for the management of infective endocarditis. Eur Heart J 2015;36:3075–128. doi:10.1093/eurheartj/ehv319.

Hoen B, Duval X. Infective Endocarditis. N Engl J Med 2013;368:1425–33. doi:10.1056/NEJMcp1206782.

Holanda LS de, Daher JF de araújo, Costa AFS, Neves dilma C de O, Holanda VBT de. Hospital Evolution of Patients with Infective Endocarditis in Public Hospital in Belém, Pará, Brazil. Int J Cardiovasc Sci 2015;28:496–503. doi:10.5935/2359-4802.20150076.

Holland TL, Baddour LM, Bayer AS, Hoen B, Miro JM, Fowler VG. Infective endocarditis. Nat Rev Dis Primers 2016;2:16059. doi:10.1038/nrdp.2016.59.

Hubers SA, DeSimone DC, Gersh BJ, Anavekar NS. Infective Endocarditis: A Contemporary Review. Mayo Clin Proc 2020;95:982–97. doi:10.1016/j.mayocp.2019.12.008.

Institute of Health Economics (IHE). Quality Appraisal of Case Series Studies Checklist. Edmonton (AB): Institute of Health Economics; 2014 http://www.ihe.ca/research-programs/rmd/cssqac/cssqac-about accessed February 19, 2021.

Jacob Filho W, Pesaro S, Carvalho Filho ET de. Aspectos diagnósticos da endocardite infecciosa em idosos. Arq Bras Cardiol 1988;51:315–20.

Jáuregui Camargo L, García López S, Moreno Sánchez F. Endocarditis infecciosa en el Hospital ABC. An Méd Asoc Méd Hosp ABC 1997;42:46–9.

Kaiser SE, Thevénard RS, Dondici Filho J, Azevedo AC. O ecocardiograma na endocardite infecciosa. Apresentacao de dezesseis casos e revisao da literatura. Arq Bras Cardiol 1984;42:103–15.

Lamas C da C, Ramos RG, Lopes GQ, Santos MS, Golebiovski WF, Weksler C, et al. Bartonella and Coxiella infective endocarditis in Brazil: molecular evidence from excised valves from a cardiac surgery referral center in Rio de Janeiro, Brazil, 1998 to 2009. Int J Infect Dis 2013;17:e65–6. doi:10.1016/j.ijid.2012.10.009.

Lamas CC, Eykyn SJ. Blood culture negative endocarditis: analysis of 63 cases presenting over 25 years. Heart 2003;89:258–62. doi:10.1136/heart.89.3.258.

Leyva Quert AY, Ruiz Camejo T, González Corrig M, Méndez Peralta T, Ramos Emperador C. Perfil clínico, epidemiológico y microbiológico de la endocarditis infecciosa en el Hospital Hermanos Ameijeiras, 2005-2008. Rev Cubana Med 2009;48:1–14.

Li JS, Sexton DJ, Mick N, Nettles R, Fowler VG, Ryan T, et al. Proposed Modifications to the Duke Criteria for the Diagnosis of Infective Endocarditis. Clin Infect Dis 2000;30:633–8. doi:10.1086/313753.

Mahabadi AA, Mahmoud I, Dykun I, Totzeck M, Rath P-M, Ruhparwar A, et al. Diagnostic value of the modified Duke criteria in suspected infective endocarditis —The PRO-ENDOCARDITIS study. Int J Infect Dis 2021;104:556–61. doi:10.1016/j.ijid.2021.01.046.

Marino BC, Reis SP, Reis FB, Rabelo W, Marino RL. Analysis of infectious endocarditis cases in a tertiary hospital. Rev Med Minas Gerais 2014;24:157–62. doi:10.5935/2238-3182.20140047.

Merello L, Salazar MR, Elgueta GF, Gonzalez D, Elton V, Quiroz M, et al. Sobrevida a 10 años de pacientes egresados luego de cirugía por endocarditis infecciosa en un hospital público. Rev Med Chil 2019;147:1535–42. doi:10.4067/S0034-98872019001201535.

Monteiro TS, Correia MG, Golebiovski WF, Barbosa GIF, Weksler C, Lamas CC. Asymptomatic and symptomatic embolic events in infective endocarditis: associated factors and clinical impact. Braz J Infect Dis 2017;21:240–7. doi:10.1016/j.bjid.2017.01.006.

Muñoz P, Kestler M, de Alarcon A, Miro JM, Bermejo J, Rodríguez-Abella H, et al. Current Epidemiology and Outcome of Infective Endocarditis: A Multicenter, Prospective, Cohort Study. Medicine 2015;94:e1816. doi:10.1097/MD.0000000000001816.

Murdoch DR, Corey R, Hoen B, Miró JM, Fowler Jr VG, Bayer AS, et al. Clinical Presentation, Etiology, and Outcome of Infective Endocarditis in the 21st Century. Arch Intern Med 2009;169:463–73. doi:10.1001/archinternmed.2008.603.

Nakatani S, Mitsutake K, Ohara T, Kokubo Y, Yamamoto H, Hanai S. Recent picture of infective endocarditis in Japan: Lessons from cardiac disease registration (CADRE-IE). Circ J 2013;77:1558–64. doi:10.1253/circj.CJ-12-1101.

Negrín Expósito JE, Roselló Silva N, Sánchez Ruiz J, Negrín Villavicencio JA, Roselló Azcanio Y, Domínguez Cervantes JA. Endocarditis infecciosa. Análisis de 5 años (1997-2001) en el Hospital "Hermanos Ameijeiras. Rev Cubana Med 2003;42.

Nieto RD, Rodríguez A, Brown A, González B. Endocarditis infecciosa en el Hospital Santo Tomas, 1974-1984. Rev Med Panama 1985;10:32–40.

Olaya-Sanchez A, Vargas-Vergara D, Montes-Zabala L, Ávila-Cortes Y, Cárcamo-Molina M. Descripción clínica, microbiológica y ecocardiográfica de la endocarditis infecciosa en un hospital de Bogotá durante los años 2013-2017. Acta Med Colomb 2019;44:14–19. doi:10.36104/amc.2019.1223.

de Oliveira JLR, dos Santos MA, Arnoni RT, Ramos A, Togna D della, Ghorayeb SK, et al. Mortality Predictors in the Surgical Treatment of Active Infective Endocarditis. Braz J Cardiovasc Surg 2018;33:32–9. doi:10.21470/1678-9741-2017-0132.

Ortiz J, Grinberg M, Mansur A, Júnior Nero, del E, Barbato A, Matsumoto AY, et al. Confirmacao anatomo-patologica do valor da ecocardiografia no diagnostico da endocartite infecciosa. Arq Bras Cardiol 1983;41:379–84.

Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. Syst Rev 2016;5:1–11. doi:10.1186/s13643-016-0384-4.

Oyonarte G M, Montagna M R, Braun J S, Maiers P E, Rojo S P, Cumsille G JF. Endocarditis Infecciosa: Morbimortalidad en Chile. Resultados del Estudio Cooperativo Nacional de Endocarditis Infecciosa (ECNEI: 1998-2002). Rev Med Chil 2003;131:237–50. doi:10.4067/S0034-98872003000300001.

Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi:10.1136/bmj.n71.

Pérez Zerpa D, Fernández A, Ríos F, Silva E, Lorente M, Arocena MJ, et al. Perfil clínico y etiológico de pacientes operados con endocarditis activa. Seguimiento a diez años. Rev Urug Cardiol 2020;35:169–79. doi:10.29277/cardio.35.2.8.

Pinheiro IL, Goes IA, Massari GAK, Sylos C, Albuquerque L. Endocardite infecciosa em cirurgias valvares: avaliação ecocardiográfica e clínica como preditores de mortalidade em uma série de casos. Rev Soc Bras Clín Méd 2018;16:113–15.

Pivatto Júnior F, Bellagamba CC de A, Pianca EG, Fernandes FS, Butzke M, Busato SB, et al. Analysis of Risk Scores to Predict Mortality in Patients Undergoing Cardiac Surgery for Endocarditis. Arq Bras Cardiol 2020;114:518–24. doi:10.36660/abc.20190050.

Popilovsky SN, Aristimuño GJ, Roldan J, Comisario RM, Parras JI, Bangher MC, et al. Predictores electrocardiográficos de complicaciones de la endocarditis infecciosa. Rev Fed Argent Cardiol 2014;43:188–91.

von Reyn CF, Levy BS, Arbeit RD, Friedland G, Crumpacker CS. Infective endocarditis: an analysis based on strict case definitions. Ann Intern Med 1981;94:505–18. doi:10.7326/0003-4819-94-4-505.

Ris T, Teixeira-Carvalho A, Coelho RMP, Brandao-de-Resende C, Gomes MS, Amaral LR, et al. Inflammatory biomarkers in infective endocarditis: machine learning to predict mortality. Clin Exp Immunol 2019;196:374–82. doi:10.1111/cei.13266.

Romero Flecha JR, Aveiro Figueredo AC. Características clínicas, bacteriológicas y demográficas de las endocarditis infecciosas. Rev Nac (Itauguá) 2020;12:42–54. doi:10.18004/rdn2020.0012.01.042-054.

Roth GA, Mensah GA, CO Johnson, Addolorato G, Ammirati E, Baddour LM, et al. Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019: Update From the GBD 2019 Study. J Am Coll Cardiol 2020;76:2982–3021. doi:10.1016/j.jacc.2020.11.010.

Rudasill SE, Sanaiha Y, Mardock AL, Khoury H, Xing H, Antonios JW, et al. Clinical Outcomes of Infective Endocarditis in Injection Drug Users. J Am Coll Cardiol 2019;73:559–70. doi:10.1016/j.jacc.2018.10.082.

Saito C, Padilla M, Valle A, Castañeda E. Tratamiento quirúrgico de la endocarditis infecciosa en un hospital general: Indicaciones y morbi-mortalidad. Rev Med Hered 2014;25:135–41.

Selton-Suty C, Célard M, le Moing V, Doco-Lecompte T, Chirouze C, Iung B, et al. Preeminence of Staphylococcus aureus in Infective Endocarditis: A 1-Year Population-Based Survey. Clin Infect Dis 2012;54:1230–9. doi:10.1093/cid/cis199.

Siciliano RF, Gualandro DM, Mueller C, da Costa, Seguro LFB, Goldstein PG, Strabelli TMV, et al. Incremental value of B-type natriuretic peptide for early risk prediction of infective endocarditis. Int J Infect Dis 2014a;29:120–4. doi:10.1016/j.ijid.2014.08.017.

Siciliano RF, Mansur AJ, Castelli JB, Arias V, Grinberg M, Levison ME, et al. Community-acquired culture-negative endocarditis: clinical characteristics and risk factors for mortality. Int J Infect Dis 2014b;25:191–5. doi:10.1016/j.ijid.2014.05.005.

Slipczuk L, Codolosa JN, Davila CD, Romero-Corral A, Yun J, Pressman GS, et al. Infective Endocarditis Epidemiology Over Five Decades: A Systematic Review. PLoS ONE 2013;8:e82665. doi:10.1371/journal.pone.0082665.

de Sousa C, Ribeiro RM, Pinto FJ. The burden of infective endocarditis in Portugal in the last 30 years – a systematic review of observational studies. Rev Port Cardiol (Engl Ed) 2021;40:205–17. doi:10.1016/j.repce.2020.07.011.

Stockins B, Neira V, Paredes A, Castillo C, Troncoso A. Perfil clínico-

epidemiológico de pacientes con endocarditis infecciosa, período 2003-2010 en el hospital de Temuco, Chile. Rev Med Chil 2012;140:1304–11. doi:10.4067/S0034-98872012001000010.

Tagliari AP, Steckert GV, Silveira LMV, Kochi AN, Wender OCB. Infective endocarditis profile, prognostic factors and in-hospital mortality: 6-year trends from a tertiary university center in South America. J Card Surg 2020;35:1905–11. doi:10.1111/jocs.14787.

Talha KM, Baddour LM, Thornhill MH, Arshad V, Tariq W, Tleyjeh IM, et al. Escalating incidence of infective endocarditis in Europe in the 21st century. Open Heart 2021a;8. doi:10.1136/openhrt-2021-001846.

Talha KM, Dayer MJ, Thornhill MH, Tariq W, Arshad V, Tleyjeh IM, et al. Temporal Trends of Infective Endocarditis in North America from 2000 to 2017 – A Systematic Review. Open Forum Infect Dis 2021b:1–10. doi:10.1093/ofid/ofab479.

Tleyjeh IM, Abdel-Latif A, Rahbi H, Scott CG, Bailey KR, Steckelberg JM, et al. A Systematic Review of Population-Based Studies of Infective Endocarditis. Chest 2007;132:1025–35. doi:10.1378/chest.06-2048.

Urina-Jassir M, Jaimes-Reyes MA, Martinez-Vernaza S, C Quiroga Vergara, Clinical Urina-Triana M. Microbiological and Imaging Characteristics of Infective Endocarditis in Latin America: A Systematic Review. PROSPERO 2021. 2021 https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021239602.

Vahabi A, Gül F, Garakhanova S, Sipahi H, Sipahi OR. Pooled analysis of 1270 infective endocarditis cases in Turkey. J Infect Dev Ctries 2019;13:93–100. doi:10.3855/jidc.10056.

Vega-Sánchez AE, Santaularia-Tomas M, Pérez-Román DI, Cortés-Telles A. Endocarditis infecciosa. Experiencia de 5 años en un tercer nivel de referencia en Yucatán México. Rev Med Inst Mex Seguro Soc 2016;54:434–8.

Velásquez O, Matar OA, Jaimes F. Tratamiento quirúrgico de la endocarditis mediante cirugía mínimamente invasiva. Rev Colomb Cardiol 2018;25:281 e1-281.e6. doi:10.1016/j.rccar.2018.03.010.

Vogkou CT, Vlachogiannis NI, Palaiodimos L, Kousoulis AA. The causative agents in infective endocarditis: A systematic review comprising 33,214 cases. Eur J Clin Microbiol Infect Dis 2016;35:1227–45. doi:10.1007/s10096-016-2660-6.

Wells G, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses n.d. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp (accessed February 17, 2021).

Wouters LM de, Furnari R, Pandullo F, Maxit MJ. Endocarditis bacteriana en pacientes mayores de 60 años. Medicina (B Aires) 1991;51:33–40.

Yang A, Tan C, Daneman N, Hansen MS, Habib G, Salaun E, et al. Clinical and echocardiographic predictors of embolism in infective endocarditis: systematic review and meta-analysis. Clin Microbiol Infect 2019;25:178–87. doi:10.1016/j.cmi.2018.08.010.

Yang X, Chen H, Zhang D, Shen L, An G, Zhao S. Global magnitude and temporal trend of infective endocarditis, 1990–2019: results from the Global Burden of Disease Study. Eur J Prev Cardiol 2021:1–10. doi:10.1093/eurjpc/zwab184.

Yew H sen, Murdoch DR. Global Trends in Infective Endocarditis Epidemiology. Curr Infect Dis Rep 2012;14:367–72. doi:10.1007/s11908-012-0265-5.

Zalaquett S R, Garrido O L, Casas R F, Morán V S, Irarrázaval Ll MJ, Becker R P, et al. Cirugía valvular reparadora en endocarditis infecciosa. Rev Med Chil 2004;132:307–15. doi:10.4067/S0034-98872004000300005.