Association between echocardiographic manifestations and bacterial infections in patients with infective endocarditis: a cohort study

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Abstract

Abstract Background The diagnosis of infective endocarditis (IE) is based on microbiological analyses and diagnostic imaging of cardiac manifestations. Echocardiography (ECHO) is preferred for direct visualization of IE-induced cardiac manifestations. We investigated correlations between bacterial infections and IE manifestations diagnosed by ECHO. Methods In this cohort study, data from patients aged 18 years or above, with definite or possible IE admitted at the Karolinska University Hospital between 2008-2017 were obtained from Swedish National Registry of Endocarditis. Bacteria registered as pathogen were primarily selected from positive blood culture and for patients with negative blood culture, bacteria found in culture or PCR from postoperative material was registered as pathogen. Patients with negative results from culture or PCR were excluded. IE manifestations diagnosed by ECHO and risk factors were obtained from the registry. Chi-squared test and two-sided Fisher's exact test was used for comparisons between categorical variables, and student's ttest was used for continuous numerical variables; two-sided and skewed variables were log-transformed before these analyses. Multivariable analyses were performed using logistic regression. Associations and the strength between the variables were estimated using odds ratios (ORs) with 95% confidence intervals (CIs). $P< 0.05$ was considered significant. Results The most common bacteria were Staphylococcus aureus(n= 268, 47%) and viridans group streptococci (n= 127, 22%). The most common manifestations were vegetation in the mitral (n = 222, 36%), aortic (n = 214, 34%), and tricuspid valves (n = 117, 19%). Correlations were seen between aortic valve vegetation and coagulase-negative staphylococci (CoNS) and Enterococcus faecalis, between mitral valve vegetation and group B streptococci, tricuspid valve vegetation, andS.aureus, and between perivalvular abscesses and CoNS (all $P< 0.05$). Conclusions Correlations were found between certain bacteria and specific ECHO manifestations. Our study contributes to a better understanding of IE manifestations and their underlying bacterial etiology, which pathogens can cause severe infections and might require close follow-up and surgical treatment.

Background

Infective endocarditis (IE) is a serious infectious condition causing heart valve destruction, perivalvular abscesses, aneurysms, and fistulas, and can be lethal [1-3]. The diagnosis of IE is based on microbiological analyses and diagnostic imaging of cardiac manifestations. Echocardiography (ECHO) is the method of choice for direct visualization of vegetations, morphological valve abnormalities/dehiscence, septal defects or fistula formation, and for the evaluation of hemodynamic consequences [4]. ECHO can be performed as transesophageal (TEE) or transthoracic (TTE) examinations [2]. Because TEE provides better image quality and has higher sensitivity and specificity for IE than TTE, it is recommended for all cases of prosthetic valves and intracardiac devices, and if a prior TTE had been negative but the clinical suspicion of IE is high. TEE should also be performed if the TTE is of low quality and is positive for IE, to rule out the possibility of local complications [1, 2].

Because bacteremia is common among patients with IE, microbiological analysis is an important step in the diagnosis of those with suspected IE. Bacteria causing bacteremia are most often considered as

pathogens causing IE. If the patients undergo cardiac surgery for IE, biological material can be taken directly from the focus of infection, for microbiological analysis with culture and 16S rRNA sequencing, which has a value especially for patients with blood culture-negative endocarditis [5]. This is recommended by the European guidelines for management of IE to optimize the choice of antibiotic treatment [2]. However, a positive culture confirming bacteremia is not sufficient to establish the diagnosis of IE [2, 6]. Further diagnostic criteria should be fulfilled, for example, one or more infectious manifestations verified by ECHO [2, 7].

Recommendations for the treatment of IE depend on the results from blood cultures, if the patients have native or prosthetic valves or cardiovascular implantable electronic devices (CIEDs), and are based on current evidence status [8]. Antibiotic treatment is recommended in clinically suspected cases of IE and if IE manifestations are present on ECHO but the blood cultures are negative [2, 9]. Although identification of causative bacteria and IE specific cardiac manifestations are crucial for the diagnosis and treatment of IE, the studies on associations between microbiological data and ECHO findings are scarce and the published results diverging [10-12]. Therefore, our aim was to analyze whether there were relationships between the bacteria found in blood culture or from sites of infection found during cardiac surgery and specific IE manifestations detected by ECHO in a cohort of IE patients. Furthermore, the aim was also to analyze the associations between bacteria species and ECHO findings in subgroups of patients with risk factors for IE.

Methods

Patients, study design and data selection

We performed a retrospective cohort study based on data from the Swedish National Registry of Infective Endocarditis (SRIE), which was established in 1995. Online reporting by Internet started in 2008 and all Swedish departments for infectious diseases report data from patients treated for possible or definite IE (ICD codes I33.0, I33.9, I38.9, and I39.8). The coverage for patients with IE is estimated to be 70–80% [13]. The SRIE includes variables such as gender, age, blood cultures, microbiological findings from samples taken during cardiac surgery, ECHO findings, as well as risk factors such as IV drug abuse, prosthetic heart and bicuspid aortic valves, antibiotics prescribed, duration of antibiotic treatment, and in-hospital mortality (defined as death during hospital stay). For this study, data from the SRIE were analyzed to identify a cohort of patients with IE treated at the Karolinska University Hospital (KUH), Stockholm, Sweden, a tertiary referral center for IE. All patients aged ³18 years admitted to the Department for Infectious Diseases at KUH with possible or definite IE between January 1, 2008 and December 31, 2017 were obtained from the SRIE, giving a total of 591 patients. The ECHO investigations (TTE and TEE) were performed at the Department of Clinical Physiology in accordance with existing guidelines [2].

Data management

Bacteria registered as possible infectious pathogens were primarily selected from positive blood culture results in 565 patients. For an additional five patients having negative blood cultures, the registered pathogens were found in culture or by polymerase chain reaction (PCR) amplification from material sampled during cardiac surgery. In total, 21 patients had negative results from both blood cultures and cultures or PCR from material sampled during cardiac surgery and were excluded from the study.

Thus, 570 patients were included in the study. Among the patients with positive blood culture results, 23 were registered with more than one bacterial strain, or bacteria plus fungi; for these patients, the first pathogen listed was chosen for the statistical analysis. Of all the included patients who had positive results from both blood culture and culture or PCR from heart valve material, all but one were positive for the same bacterium in blood culture as in culture or PCR amplification from heart valve material. That patient had blood culture positive for *S. aureus* and a PCR test from postoperative material positive for viridans group streptococci. For this patient, the bacterial strain found in blood culture was chosen for the statistical analysis. Coagulase-negative staphylococci (CoNS) were grouped including *Staphylococcus lugundensis* and *Staphylococcus epidermidis* and the following bacteria were grouped as HACEK: *Haemophilus* species, Aggregatibacter species, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella kingae*. The IE manifestations were detected during TEE or TTE ECHO studies. If more than one ECHO finding was registered for the same patient, all manifestations were analyzed both separately and together. Data from the patient cohort were analyzed for age, gender, history of any IV drug abuse, presence of prosthetic heart valves, and for in-hospital mortality.

Statistical analyses

Analyses were performed using STATA software (version 15.1 Stata Corp., College Station, Texas, USA). Frequencies and percentages were calculated for categorical variables and numeric variables are presented as the mean and standard deviation (SD) or median and 25th and 75th percentiles, when appropriate. For comparisons between categorical variables, the chi-squared test was conducted for values ³5 and the two-sided Fisher's exact test for values <5. Student's *t* test was used for continuous numerical variables; two-sided and skewed variables were log-transformed before these analyses. Multivariable analyses were performed using logistic regression. Associations and the strength between the variables were estimated using odds ratios (ORs) with 95% confidence intervals (CIs). $P < 0.05$ was considered significant.

Results

Clinical characteristics

Of the 570 patients included in our study, 513 (90%) had definite IE according to modified Duke's criteria for IE and 57 (10%) had possible IE [2, 14]. The clinical characteristics of the included patients are presented in Table 1. There were no differences in mean age between male and female patients. The most common bacterial pathogens were *S. aureus*, present in 268 (47%) patients, followed by viridans group streptococci in 127 (22%) and *Enterococcus faecalis in* 54 (9%). There were no differences in

etiology between male and female patients. Most of the patients with possible or definite IE (547; 96%) underwent ECHO during hospital stay: TEE was performed in 481 patients (84%) and 68 (12%) underwent TTE only. The most frequent ECHO manifestations were mitral valve vegetation (*n* = 222, 36%), aortic valve vegetation (*n* = 214, 34%), and tricuspid valve vegetation (*n* = 117, 19%). Among all patients who underwent ECHO, 421 (74%) had one IE manifestation, 95 (17%) had more than one, 10 (2%) had more than two and 44 (8%) had no IE manifestation detected by ECHO. The most commonly combined IE manifestations were aortic valve vegetation and mitral valve vegetation (42 patients) and aortic valve vegetation and abscess (28 patients). Total in-hospital mortality was 7% (41 patients). The distributions of IE manifestations found with ECHO are presented in Figure 1.

Table 1 should be inserted here.

Bacterial strain and ECHO manifestations

Distributions and correlations between etiology and IE manifestations detected by ECHO are presented in Table 2. Patients with *S. aureus* infection were more likely to have tricuspid valve vegetation but less likely to have aortic valve vegetation. There were correlations between the incidences of patients with *S. aureus* and IE or pulmonary valve vegetation, although few patients had pulmonary valve vegetation (*n* = 9, 2%). Significant correlations were seen between CoNS and ECHO findings of aortic valve vegetation, abscesses, and the incidence of patients with more than one IE manifestation. Patients with *E. faecalis* etiology were more likely to have aortic valve vegetation. There were significant correlations between aortic valve vegetation and CoNs or *E. faecalis*, both among patients with prosthetic aortic valve IE and native aortic valve IE. Patients with group B streptococci were more likely to have mitral valve vegetation. Patients with viridans group streptococci in blood cultures were less likely to have tricuspid valve vegetation or CIED-associated IE. Patients with HACEK multiple infections were more likely to have CIED-associated IE.

Table 2 should be inserted here.

Risk factors related to microbiology data and ECHO manifestations

Patients with IV drug abuse were more likely to have an etiology of *S. aureus* infection but less likely to have CoNS or viridans group streptococcal-related IE. Furthermore, such patients were more likely to have tricuspid valve IE and pulmonary valve IE but less likely to have aortic and mitral valve vegetations. Of the 268 patients with *S. aureus*-linked IE, 129 had a history of IV drug abuse and 139 did not. The associations between *S. aureus* and tricuspid valve vegetation when adjusted for IV drug abuse and *S. aureus* IE were correlated with tricuspid valve vegetation both among patients with IV drug abuse and those who did not (OR 3.0, 95% CI 1.7–5.3; $P < 0.01$).

In our cohort, 110 patients (19%) had prosthetic heart valves, and 10 (9%) of these patients had two prosthetic heart valves. Such patients were more likely to have *E. faecalis*-linked IE, but they were less likely to have IE caused by *S. aureus*. There was no correlation between the incidence of prosthetic heart

valves and perivalvular abscesses (no specific locations were registered). Correlations were seen between in-hospital mortality rates and *S. aureus* infections (*n* = 26, OR 2.06, 95% CI 1.02–4.27; *P* = 0.03) as well as between in-hospital mortality and an ECHO finding of a perivalvular abscess (*n* = 6, OR 3.46, 95% CI 1.08–9.37; *P* < 0.01). Among patients with *S. aureus*-linked IE, in-hospital mortality was more common among patients with left-sided valve IE (n = 17, 14%) compared with patients with right-sided valve IE (*n* = 1, 1%; OR 11.1, 95% CI 1.66–469.63; *P* < 0.01). Among patients with *S. aureus*-linked IE, those with left-sided valve IE were significantly older than those with right-sided valve IE (mean age for right-sided valve IE was 38.1 years, mean age for left-sided valve IE was 60.6 years; *P* < 0.01). Furthermore, prosthetic valve IE was not associated with in-hospital mortality (OR 1.81, 95% CI 0.81–3.83; *P* = 0.09). There was no significant association between more than one IE manifestation on ECHO and in-hospital mortality (OR 1.9, 95% CI 0.8–4.2; *P* = 0.07). The distributions and correlations between etiology and ECHO manifestations among patients with IE and risk factors are presented in Tables 3 and 4, respectively.

Table 3 and 4 should be inserted here.

Surgical treatment

In total, 157 (28%) patients were treated with cardiac surgery. There was no difference in age between patients who did or did not undergo surgical treatment for IE (surgery mean age was 56 years, non-surgery mean age was 59 years; 95% CI 0.64–6.12; *P* = 0.11). Of patients who underwent surgery, 32 had a prosthetic valve IE and 124 had a native valve IE. There was no difference in surgical treatment between these two groups (OR 1.11, 95% CI 0.68–1.79; *P* = 0.66). Patients with a history of IV drug abuse were treated less frequently with cardiac surgery than patients who did not (OR 0.41, 95% CI 0.25–0.66; *P* < 0.01). Surgical treatment was more common among patients with aortic valve IE, perivalvular abscess, and CIED endocarditis and less common among patients with tricuspid valve IE. There were no significant differences in in-hospital mortality between patients who had surgical treatment for IE (*n* = 14, 9%) and those who did not (*n* = 27, 7%; OR 1.41; 95% CI 0.66–2.88; *P* = 0.31). In total, 28 patients had aortic root abscesses of whom 19 (68%) were treated with cardiac surgery; of these 19, three died during hospital stay. Among the remaining nine patients for whom surgery was not performed, two died during hospital stay. In patients presenting with an aortic root abscess, there was no significant association between surgical treatment and in-hospital mortality (OR 0.66, 95% CI 0.06–9.65; *P* = 1.00), nor between nonsurgical treatment and death (OR 1.52, 95% CI 0.10–16.45; *P* = 1.00).

Gender differences

There were no significant differences in bacterial species between male and female patients, although male patients were more likely to have aortic valve vegetation than female patients (OR 1.57, 95% CI 1.06–2.31; *P* = 0.02). In addition, bicuspid aortic valves were more common in male than in female patients (OR 4.91, 95% CI 1.16–43.81; *P* = 0.02,). There were no differences between male and female patients in terms of history of IV drug abuse or in the incidences of prosthetic heart valves, in-hospital mortality, or surgical treatment for IE (Table 1).

Differences over time

During the first 5 years of the study period (2008–2012), IV drug abuse was more common among IE patients than in the later 5 years (2013–2017) (OR 1.56, 95% CI 1.07–2.29; $P = 0.02$). Mitral valve IE became significantly more common during the latter period (OR 1.66, 95% CI 1.16–2.38; $P < 0.01$), while the presence of aortic, tricuspid, and pulmonary valve IE, CIED-associated IE, prosthetic valve IE, perivalvular abscess, and in-hospital mortality did not change between the two periods. The distributions of IE manifestations over time are presented in Figure 2.

Discussion

To our knowledge, this is the first and to date the largest study showing significant correlations between causative bacteria and IE manifestations detected by ECHO. In this cohort of 570 patients from the SRIE, we found that patients with *S. aureus* were more likely to have tricuspid valve vegetation but less likely to have aortic valve vegetation. Furthermore, *S. aureus*-linked IE was more common among patients with a history of IV drug abuse but less so among patients with prosthetic valves. Correlations were found between CoNS and the presence of a perivalvular abscess and aortic valve vegetation. CoNS as an agent was more common among patients with more than one manifestation on ECHO, but less common among patients with a history of IV drug abuse, although it should be noted that there were relatively few patients with CoNS ($n = 29$, 5%). Patients with *E. faecalis* infections were more likely to have aortic valve vegetation. Patients with CoNS or *E. faecalis* infections were also more likely to have aortic valve vegetation, regardless of whether they had native or prosthetic aortic valves. Significant correlations were seen between group B streptococcal infections and mitral valve vegetation and between HACEK- and CIED-associated IE.Correlations between specific bacterial infections and IE manifestations detected by ECHO have been reported previously [10, 11]. Trifunovic et al. could not show any correlations between specific IE manifestations and certain etiologies in their study of 246 patients with IE, even though their main findings were that *S. aureus* and gram-negative bacteria caused large vegetations, CoNS caused destructive leaflet lesions, CoNS and gram-negative bacteria caused perivalvular extension of the infective process, and that gram-negative bacteria were correlated with multiple manifestations in the same patient [11]. Those results were consistent with our findings that CoNS infections were correlated with perivalvular abscesses (extension of the infective process). Furthermore, we found that *S. aureus* infections were correlated with tricuspid valve IE, which is supported by Bonetti et al. in their study of 274 patients with IE [10].

Microbiological findings

In our analysis of the most common bacteria causing IE, *S. aureus* was present in 47% of all patients and was also the only strain that was significantly correlated with in-hospital mortality. These findings are in line with studies showing that *S. aureus* is the most common bacterium causing IE in industrialized countries, and that it has higher mortality rates than IE caused by other pathogens [3, 12, 15, 16]. Furthermore, in our study, *Streptococcus* species were also common (28%), as was seen in studies

presenting a high and increasing prevalence of streptococci in general, but more specifically viridans group streptococci and *S. bovis* [17, 18]. In addition, we found that the presence of a perivalvular abscess, a serious IE manifestation of tissue destruction, was correlated with in-hospital mortality. Similar results were reported by Lauridsen et al. who showed that perivalvular abscess and valve perforation independently predicted 1-year mortality in patients with left-sided native valve *S. aureus*-linked endocarditis [19].**Surgery**In our study, 28% of patients underwent surgical treatment, slightly less than the 31% of Swedish patients with IE who underwent surgical treatment in 2017 [10]. This lower percentage in our cohort might be explained by the large proportion of patients with a history of IV drug abuse (29%). Patients with aortic or mitral valve vegetation, CIED-associated endocarditis, or a perivalvular abscess more often underwent surgical treatments. None of the bacteria in our analyses were correlated with surgical treatment of IE. It has been argued whether *S. aureus* should be listed as an absolute indication for surgical treatment, as it often causes severe IE with the presence of emboli or abscesses, and/or severe valvular engagement, but the current recommendations promote individual evaluation of patients for decisions on using surgical treatments [6, 20, 21]. This individualized approach was adopted in decision-making at KUH.

Prosthetic valves and CIED-linked IE

It has been reported that prosthetic valve IE and CIED-linked IE are becoming more frequent [17]. In our study, there was no difference in the prevalence of CIED-associated IE and prosthetic valve IE between the two 5-year periods, although it should be noted that there were only a few patients with CIED-linked IE and prosthetic valve IE. These cases can be challenging to diagnose, especially with TTE because of its relatively low resolution and shading from the prosthesis or chordae tendinae; thus, TEE is highly recommended [2, 17, 22]. The respective sensitivities for diagnosing native IE and prosthetic valve IE are approximately 96% and 70% with TTE and 96% and 92% for TEE, respectively [2]. The correlations between the incidences of prosthetic valve IE and *E. faecalis* infection found in our study differ from previous reports. *S. aureus* and CoNS infections have been described as common etiological factors for prosthetic valve IE [18].**IV drug abuse**KUH has a special ward for addicts with infections, with an uptake area covering Stockholm County Council (approximately 2.3 million inhabitants), which might contribute to the relatively high presence of IV drug abuse among endocarditis patients at KUH. Studies of patients with IE in the USA in 2012–2013 showed a lower incidence of IV drug abuse among IE patients (6.5–7.8% of the IE patients had IV drug abuse) than in our results (29% of the patients had a history of IV drug abuse), although recent US and European studies have noted that the presence of IV drug abuse is generally increasing among patients with IE [23, 24]. *S. aureus* was the most common bacterial strain among patients with IE and a history of IV drug abuse, which is consistent with previous studies [23-25].

Gender differences

Although there were significantly more men than women in our study (~2:1), we found no gender differences in IE etiology, which is consistent with earlier studies in which the ratio of men to women was typically higher than 2:1 [26, 27]. Previous work has evaluated the differences in etiology and

manifestations, but with ambiguous results. For instance, Aksoy et al. showed that women were more likely to have vegetations on CIED and men were more commonly infected with CoNS [26], while Sambola et al. showed that mitral valve IE and aortic valve IE were more common among men, but the etiology did not differ between genders [27]. In our study, men were more likely to have aortic valve IE, which could possibly be explained by the higher presence of bicuspid aortic valves among men, and the known higher risk of developing IE in bicuspid versus tricuspid aortic valves [28]. The rates of in-hospital mortality and surgical treatment for IE in our study did not differ between men and women, which does not accord with previous reports indicating that women have higher mortality and receive surgical treatment to a lesser extent compared with men [10]. In our cohort, the in-hospital mortality rate was low (7%), which contrasts with previously reported rates of 15–20% [29, 30]. This might be explained by the relatively low age of the patients (mean age 58.2 years) in our study.

Diagnosis of IE manifestations

TEE has been reported to have high sensitivity for the diagnosis of IE, ranging between 90% and 100%, as well as a high negative predictive value of 86–97% [22, 31]. Moreover, it has been shown that ECHO findings did not differ between patients who underwent ECHO early (<2 days) or late (³2 days) after starting antibiotic treatment for IE [12]. We found IE manifestations most frequently on the mitral valve (*n* = 222, 36%), followed by the aortic valve (*n* = 214, 34%) and the tricuspid valve (*n* = 117, 19%). Our results resemble those of a study involving 68 autopsies of patients with IE, which reported that 35% of patients had mitral valve IE, 26% had aortic valve IE, and 5% had tricuspid valve IE [32]. Our results are also consistent with a multicenter study of 1055 patients in Europe and the USA, showing that the most common ECHO manifestations among patients with IE were on the mitral valve followed by the aortic valve [33].

Limitations

The SRIE includes variables on IE manifestation, such as vegetation localization, but not the size or numbers of vegetations. Nor does it include detailed information on comorbidity, for example, a history of heart failure, other diseases, or results from blood tests such as glucose and brain natriuretic peptide levels, which are valuable for the analysis of predisposition for bacteria or specific IE manifestations. Furthermore, we could not assess how many days after initiating antibiotic treatment ECHO was conducted. In addition, it would be interesting to analyze patients with IE with a more unusual etiology, such as infections with gram-negative bacteria and fungi; however, this was not possible in our cohort as there were very few cases with these infective agents.

Conclusions

Significant correlations were found between the incidence of certain bacterial strains and specific IE manifestations detected by ECHO, such as aortic, mitral, tricuspid, or pulmonary valve vegetations, abscess formation, and CIED-associated IE. Correlations were found between infections with certain bacterial strains and more than one IE manifestation. Correlations were also found between certain

bacterial strains and IE manifestations among patients with a history of IV drug abuse, those with prosthetic heart valves, and those with in-hospital mortality. Aortic valve vegetations were more common among male patients, but there were no differences between genders with respect to which bacterial strain was the cause of IE. In current practice, ECHO is known to contribute to the diagnosis of IE and its lesions. However, the challenge for the future is to come closer to identifying which specific bacterial strain is involved in the pathogenesis of IE, where ECHO might have a role. We believe that the results of the present study contribute useful information about which pathogens can cause severe infections, on which valves, and that might require close follow-up with ECHO and surgical treatment.

Abbreviations

CI confidence interval

CIED cardiovascular implantable electronic device

CoNS coagulase negative staphylococci

ECHO echocardiography

IE infective endocarditis

IV intravenous

HACEK Haemophilus species, Aggregatibacter species, Cardiobacterium hominis, Eikenella corrodens and Kingella kingae

KUH Karolinska University Hospital

OR odds ratio

PCR polymerase chain reaction

PET-CT positron emission tomography–computed tomography

SRIE the Swedish national registry of infective endocarditis

TEE transesophageal echocardiography

TTE transthoracic echocardiography

Declarations

Ethics approval

The study was approved by the Regional Ethics Review Board, Stockholm, Sweden (diary number K 2018-6018).

Consent for publication

Not applicable.

Availability of data and materials

The data that support the findings of this study were taken from the SRIE, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not available publicly. However, data are available from the first author upon reasonable request and with permission of the SRIE.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

AD, EM, KC, CSL and MJE designed the study. AD analyzed the data and AD, KW and MJE interpreted it. AD was a major contributor in writing the manuscript, all authors revised it. All authors read and approved the final manuscript.

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Tables

Table 1

Descriptive data of the 570 patients included in the study of infective endocarditis (IE) at the Karolinska University Hospital (KUH) in 2008–2017.

	Patients *n* (% of all patients)	Women *n* (% of all women)	Men *n* (% of all men)	Age mean (± SD); medians (25th and 75th percentiles)
Women	189 (33)			59.4 (21.0); 64 (44, 78)
Men	381 (67)			57.6 (17.0); 58 (46, 71)
All patients	570 (100)	189 (100)	381 (100)	58.2 (18.4); 59 (45, 73)
History of IV drug abuse	165 (29)	54 (29)	111 (29)	41.9 (11.8); 44 (31, 50)
Bicuspid aortic valve	21 (4)	2 (1)	19 (5)	48.7 (14.4); 51 (40, 57)
Prosthetic cardiac valve	110 (19)	34 (18)	76 (20)	61.7 (16.5); 65 (48, 75)
In-hospital mortality	41 (7)	16 (8)	25 (7)	67.9 (17.3); 67 (53, 84)

Abbreviations: IV, intravenous; SD, standard deviation.

Table 2

Distribution of echocardiography (ECHO) manifestations and bacterial strains accounting for 90% of the etiologies among patients with IE at KUH in 2008–2017.

	Aortic valve vegetation *n* (%), OR, 95% CI; *P*	Mitral valve vegetation *n* (%), OR, 95% CI; *P*	Tricuspid valve vegetation *n* (%), OR, 95% CI; *P*	Pulmonary valve vegetation *n* (%), OR, 95% CI; *P*	CIED-associated IE *n* (%), OR, 95% CI; *P*	Perivalvular abscess *n* (%), OR, 95% CI; *P*	Total *n* (%)
Number of patients	214 (38)	222 (39)	117 (21)	9 (2)	24 (4)	31 (5)	570 (100)
Staphylococcus aureus	**77 (14), 0.49, 0.34–0.70; < 0.01**	95 (17), 0.76, 0.53-1.08; 0.11	**94 (17), 6.55, 3.93–11.23; < 0.01**	**8 (1), 9.26, 1.22–412.22; 0.01**	9 (2), 0.66, 0.25-1.65; 0.34	12 (2), 0.70, 0.30-1.55; 0.34	268 (47)
CoNS	**18 (3), 2.88, 1.26-6.88; 0.01**	8 (1), 0.58, 0.22-1.40; 0.20	2 (0), 0.27, 0.03-1.12; 0.09	0 (0)	4 (1), 4.17, 0.96-13.75; 0.03	**5 (1), 4.13, 1.13–12.25 ; < 0.01**	29 (5)
Viridans group streptococci	53 (9), 1.25, 0.82-1.91; 0.27	59 (10), 1.49, 0.99-2.26; 0.05	**6 (1), 0.15, 0.05–0.35; < 0.01**	0 (0)	**1 (0), 0.14, 0.00–0.91; 0.02**	6 (1), 0.83, 0.27-2.13; 0.69	127 (22)
Group B streptococci	4 (1), 0.83, 0.18-3.14; 1.00	**10 (2), 8.16, 1.71–77.03; < 0.01**	0 (0)	0 (0)	0 (0)	1 (0), 1,60, 0.04-11.69; 0.49	12 (2)
Group D streptococci	3 (1), 1.25, 0.18-7.47; 1.00	4 (1), 2.11, 0.35-14.52; 0.44	0 (0)	0 (0)	0 (0)	1 (0), 2.96, 0.06-25.57; 0.33	7 (1)
Group G streptococci	4 (1), 1.68, 0.31-9.09; 0.48	3 (1), 0.94, 0.14-4.88; 1.00	1 (1), 0.55, 0.01-4.35; 1.00	0 (0)	0 (0)	0 (0)	8 (1)
Enterococcus faecalis	**31 (5), 2.45, 1.34-4.54; < 0.01**	19 (3), 0.84, 0.44-1.55; 0.55	8 (1), 0.65, 0.26-1.44; 0.27	0 (0)	2 (0), 0.86, 0.09-3.68; 1.00	2 (0), 0.65, 0.07-2.68; 0.76	54 (9)
HACEK	6 (1), 0.83, 0.25-2.42; 0.71	3 (1), 0.30, 0.06-1.09; 0.05	2 (0), 0.48, 0.05-2.07; 0.55	1 (0), 4.00, 0.09-32.72; 0.25	**4 (1), 7.60, 1.66–27.06; 0.01**	1 (0), 1.02, 0.02-6.98; 1.00	18 (3)

Abbreviations: CI, confidence interval; CIED, cardiovascular implantable electronic device; CoNS, coagulase-negative staphylococci; HACEK, *Haemophilus* species, *Aggregatibacter* species, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella kingae*; IE, infective endocarditis; OR, odds ratio. Statistically significant correlations ($P < 0.05$) are shown in bold.

Table 3

Distribution of risk factors and etiologies among patients with IE at KUH in 2008–2017.

	All patients *n* (%)	>1 ECHO manifestation *n* (%), OR, 95% CI; *P*	Surgical treatment for IE *n* (%), OR, 95% CI; *P*	Prosthetic heart valve *n* (%), OR, 95% CI; *P*	IV drug abuse *n* (%), OR, 95% CI; *P*	In-hospital mortality *n* (%), OR, 95% CI; *P*
All patients	570 (100)	95 (100)	157 (100)	110 (100)	165 (100)	41 (100)
Staphylococcus aureus	268 (47)	42 (44), 0.87, 0.55-1.39; 0.55	68 (43), 0.81, 0.55-1.20; 0.27	**34 (31), 0.43, 0.27–0.69; < 0.01**	**129 (78), 6.86, 4.42–10.76; < 0.01**	**26 (63), 2.06, 1.02–4.27; 0.03**
CoNS	29 (5)	**11 (12), 3.32, 1.36–7.73; <0.01**	11 (7), 1.65, 0.69-3.80; 0.20	8 (7), 1.64, 0.61-3.99; 0.25	**2 (1), 0.17, 0.02–0.70; 0.01**	3 (7), 1.53, 0.28-5.34; 0.42
Viridans group streptococci	127 (22)	16 (17), 0.66, 0.35-1.21; 0.16	38 (24), 1.16, 0.75-1.87; 0.50	19 (17), 0.68, 0.37-1.19; 0.16	**10 (6), 0.16, 0.07–0.31; < 0.01**	7 (17), 0.70, 0.26-1.66; 0.41
Group B streptococci	12 (2)	2 (2), 1.00, 0.10-4.80; 1.00	3 (2), 0.87, 0.15-3.57; 1.00	2 (2), 0.83, 0.09-3.99; 1.00	0 (0)	1 (2), 1.18, 0.03-8.48; 0.57
Group D streptococci	7 (1)	1 (1), 0.83, 0.02-6.98; 1.00	4 (3), 3.57, 0.60–24.61; 0.10	3 (3), 3.20, 0.46-19.14; 0.14	0 (0)	0 (0)
Group G streptococci	8 (1)	0 (0)	1 (1), 0.37, 0.01-2.94; 0.46	2 (2), 1.40, 0.14-7.97; 0.66	1 (1), 0.35, 0.01-2.74; 0.45	0 (0)
Enterococcus faecalis	54 (9)	11 (12), 1.32, 0.59-2.73; 0.44	10 (6), 0.57, 0.25-1.19; 0.12	**19 (17), 2.56, 1.31–4.79; < 0.01**	17 (10), 1.14, 0.58-2.26; 0.67	2 (5), 0.47, 0.05-1.91; 0.56
HACEK	18 (3)	4 (4), 1.45, 0.34-4.75; 0.52	8 (5), 2.16, 0.73-6.21; 0.10	6 (5), 2.15, 0.65-6.36; 0.13	0 (0)	1 (2), 0.75, 0.02-5.06; 1.00

Abbreviations: CI, confidence interval; CoNS, coagulase-negative staphylococci; ECHO, echocardiography; HACEK, *Haemophilus* species, *Aggregatibacter* species, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella kingae*; IE, infective endocarditis; KUH, Karolinska University Hospital; IV, intravenous; OR, odds ratio. Statistically significant correlations ($P < 0.05$) are shown in bold.

Table 4

Distribution of risk factors and ECHO manifestations among patients with IE at KUH in 2008–2017.

	All patients *n* (%)	Surgical treatment for IE *n* (%), OR, 95% CI; *P*	IV drug abuse *n* (%), OR, 95% CI; *P*	In-hospital mortality *n* (%), OR, 95% CI; *P*
All patients	570 (100)	157 (27)	165 (29)	41 (7)
Aortic valve vegetation	214 (38)	**78 (14), 2.01, 1.36–2.97; < 0.01**	**33 (6), 0.31, 0.20–0.48; < 0.01**	19 (3), 1.48, 0.74-2.94; 0.23
Mitral valve vegetation	220 (39)	71 (12), 1.46, 0.99-2.16; 0.05	**47 (8), 0.53, 0.35–0.80; < 0.01**	12 (2), 0.63, 0.29-1.31; 0.19
Tricuspid valve vegetation	117 (21)	**20 (4), 0.48, 0.27–0.81; < 0.01**	**90 (16), 16.80, 9.97–28.61; < 0.01**	**3 (1), 0.29, 0.06-0.93; 0.03**
Pulmonary valve vegetation	9 (2)	1 (0), 0.32, 0.01-2.46; 0.46	**7 (1), 8.93, 1.67–88.58; < 0.01**	0 (0)
CIED IE	29 (5)	**22 (4), 9.45, 3.77–26.66; < 0.01**	**2 (0), 0.17, 0.02-0.63; 0.01**	3 (1), 1.47, 0.27-5.11; 0.42
Perivalvular abscess	31 (5)	**19 (3), 4.60, 2.05–10.65; < 0.01**	0 (0)	**6 (1), 3.46, 1.08–9.37; 0.01**
VSD	2 (0)	0 (0)	0 (0)	0 (0)
Prosthetic heart valve	110 (19)	32 (6), 1.11, 0.68-1.80; 0.65	**12 (2), 0.24, 0.12–0.47; < 0.01**	12 (2), 1.81, 0.81–3.83; 0.09

Abbreviations: CI, confidence interval; CIED, cardiovascular implantable electronic device; IE, infective endocarditis; IV, intravenous; OR, odds ratio, VSD, ventricular septal destruction caused by IE. Statistically significant correlations ($P < 0.05$) are shown in bold.

Figures

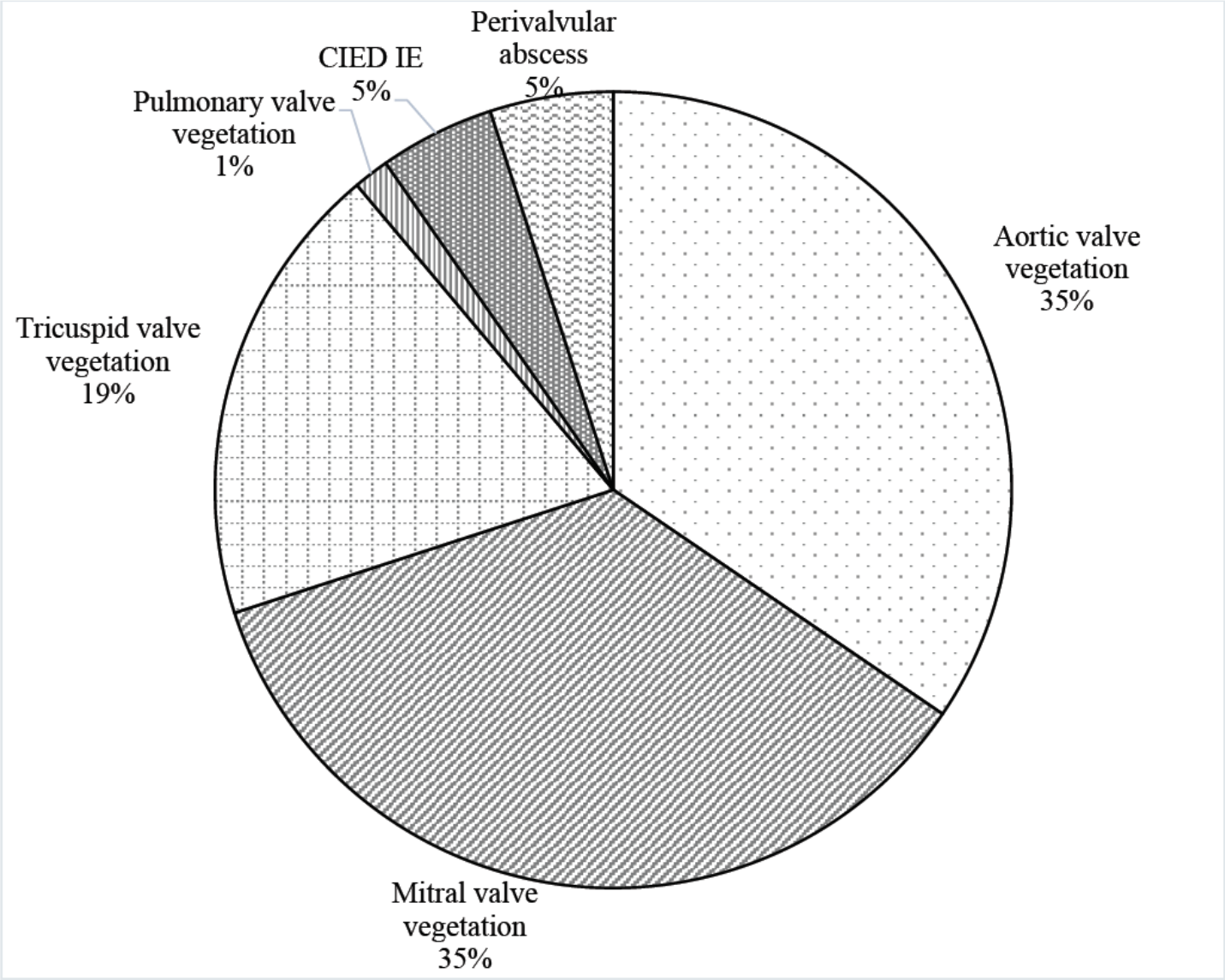

Figure 1

Echocardiographic manifestations among patients with infective endocarditis in 2008–2017. Legend Abbreviations: CIED, cardiovascular implantable electronic device; IE, infective endocarditis.

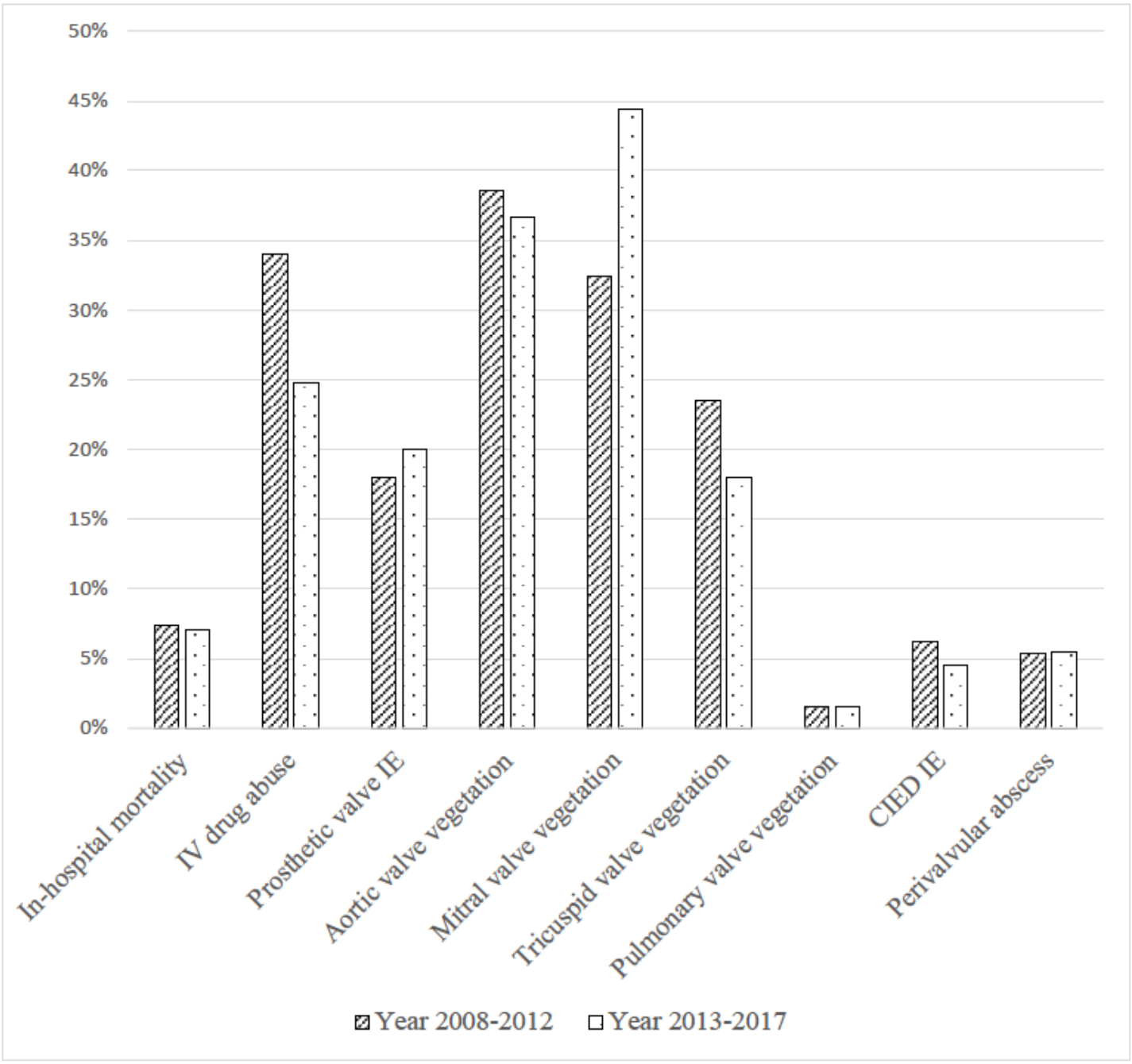

Figure 2

Echocardiographic manifestations and risk factors among infective endocarditis patients in 2008–2012 and 2013–2017. Legend Abbreviations: CIED, cardiovascular implantable electronic device; IE, infective endocarditis, IV, intravenous.