Bloodstream Infection Following Cardiac Valve Repair: A Population-Based Study

Jack W. McHugh,[1] Khawaja M. Talha,[2] Larry M. Baddour,[2,3] Karen M. Fischer,[4] Juan Crestanello,[5] Arman Arghami,[5] and Daniel C. DeSimone[2,3]

[1]Department of Internal Medicine, Mayo Clinic School of Medicine and Science, Rochester, Minnesota, USA, [2]Division of Infectious Diseases, Department of Medicine, Mayo Clinic School of Medicine and Science, Rochester, Minnesota, USA, [3]Department of Cardiovascular Disease, Mayo Clinic School of Medicine and Science, Rochester, Minnesota, USA, [4]Department of Biomedical Statistics and Informatics, Mayo Clinic School of Medicine and Science, Rochester, Minnesota, USA, and [5]Division of Cardiovascular Surgery, Mayo Clinic School of Medicine and Science, Rochester, Minnesota, USA

Background. The aim of this study was to determine the incidence, epidemiology, and associated risk factors of bloodstream infection (BSI) in patients who had previously undergone cardiac valve repair.

Methods. A population-based study that included 7 counties in southeastern Minnesota using the expanded Rochester Epidemiology Project (e-REP) for adults (≥18 years) who underwent valve repair between 1 January 2010 and 31 December 2018 was conducted. Electronic health records were screened for development of BSI and infective endocarditis (IE) from the date of valve repair through 30 July 2020. A 1:4 nested case-control analysis was performed to determine an association, if any, of male sex, Charlson comorbidity index (CCI), and county of residence with BSI.

Results. A total of 335 patients underwent valve repair, of whom 28 (8.3%) developed an index case of BSI, with 14 episodes occurring within 1 year of surgery. The median age of patients with BSI was 70 years, and 79% were male. The crude incidence of BSI was 1671 cases per 100 000 person-years and *Escherichia coli* was the most common pathogen. Case-control analysis demonstrated a significant correlation between CCI and incidence of BSI ($P < .001$). Only 4 (14.3%) patients developed IE concurrent with the onset of BSI, and no patients developed IE subsequent to BSI.

Conclusions. The crude incidence of BSI following valve repair was higher in our e-REP cohort than previous population-based studies, and half of the BSI cases occurred within 1 year of surgery. Patients with a higher CCI at baseline were at increased risk of subsequent BSI.

Keywords. bloodstream infection; cardiac; incidence; infective endocarditis; mortality; population-based; valve repair.

Among the various illnesses associated with aging, valvular heart diseases are present in >10% of patients aged 75 years and older [1]. Mitral valve (MV) regurgitation is the most common valve disease in the United States, and MV repair for regurgitation is the most frequently performed MV surgery [2], with rates of tricuspid valve repair also increasing [3].

The incidence of bloodstream infection (BSI) increases with age [4], and outcomes have been linked to number of underlying comorbidities [5]. Patients undergoing valve repair are older and have poorer health overall than the general population [6], and may therefore be at higher risk of BSI subsequent to surgery. They may also suffer increased rates of complications associated with BSI; for instance, BSI confers an increased risk

of infective endocarditis (IE) in patients with a prosthetic heart valve [7, 8]. At present few, if any, studies have examined the relationship between valve repair and subsequent BSI.

METHODS

To investigate the relationship between valve repair and BSI, we conducted a retrospective population-based study encompassing a 7-county region in southern Minnesota. Medical records of all patients who underwent valve repair procedures during a 9-year period were examined to determine (1) the incidence and clinical characteristics of patients who developed BSI following valve repair surgery; (2) risk factors associated with the development of BSI following valve repair; and (3) the incidence and characteristics of patients who developed IE.

Study Setting

The expanded Rochester Epidemiology Project (e-REP) data linkage system was used to identify persons who underwent valve repair between 2010 and 2018. The e-REP is a research infrastructure that links medical records of persons residing in 27 counties in southeastern Minnesota and southwestern Wisconsin for research studies. The REP originally included only 1 county—Olmsted County, Minnesota—and has previously

been used to study specific infectious disease syndromes using a population-based approach [4, 9, 10]. To minimize selection bias we limited our investigations to persons living in counties where data were available for >90% of the population [11]. This led to the inclusion of 7 counties: Wabasha, Olmsted, Steele, Waseca, Freeborn, Mower, and Dodge (Supplementary Figure 1). The combined population size, according to 2018 US census data, was 345 751, and was predominantly non-Hispanic white.

Study Population

The e-REP database was used to identify all current procedure terminology codes corresponding to valve repair procedures conducted between 1 January 2010 and 31 December 2018. This included procedures involving placement of annuloplasty rings or bands, mitral clip placement and chord repairs, procedures where concomitant valve repairs were performed, and procedures where there was concomitant repair and replacement of another valve. Isolated valve replacement via open or transcatheter techniques was excluded. Among persons who received the aforementioned procedures, we used *International Classification of Diseases* (*ICD-9* and *-10*) codes to identify persons with BSI up to 30 July 2020. A detailed list of the BSI and IE diagnosis codes has been provided in the Supplementary Data. Persons under the age of 18 years and persons undergoing valve repair in the context of active IE were excluded. Medical records of all persons with BSI and IE codes were fully reviewed.

Case Identification

Cases were classified as BSI if the patient had positive bacterial or fungal blood cultures associated with a systemic inflammatory response resulting in alteration of patient's clinical, laboratory, or hemodynamic parameters [12]. In patients who had multiple episodes of BSI, the index case was used in the analyses; of note, additional episodes were recorded in our database.

A blood culture contaminant was defined if 1 or more of the following organisms were identified in a single set of blood cultures: coagulase-negative staphylococci, *Cutibacterium acnes*, *Micrococcus* spp, *Corynebacterium* spp, viridans group streptococci, or *Bacillus* spp [13], and these cases were excluded from the analysis. Where multiple cultures identified an organism usually considered a contaminant, clinical judgment was used to determine whether or not to include the patient in our cohort. A primary focus of infection was identified when cultures obtained from a specific site (eg, urine) were consistent with blood culture results. Pulmonary and intra-abdominal infectious syndromes were identified where there was appropriate positive radiological findings and clinical features of disease, in tandem with a plausible pathogen on blood culture. Primary BSI was defined as cases for which no source was identified.

Patients were classified as having BSI only, as having IE concurrent with onset of BSI, or as having BSI with subsequent development of new IE. IE concurrent with onset of BSI was defined as cases where IE was diagnosed at the time of initial positive blood culture. Patients in whom BSI was complicated by the subsequent development of IE were classified as having new IE [7]. IE was defined as either definite or possible using the modified Duke criteria [14]. Early IE was defined as that occurring <12 months following the valve repair procedure, with cases >12 months defined as late IE.

Patient Characteristics

Pertinent clinical and laboratory data were collected through medical record review by J. W. M. and K. M. T. and entered into a REDCap database [15]. Clinical data were collected retrospectively from the date of valve repair for all patients. For each case, demographic data including age, sex, and county of residence were collected. Perioperative patient data, including the site and type of valve repair (including procedures where a concurrent valve replacement was performed), reason for the procedure, and postoperative regurgitation were recorded. Purported risk factors were recorded at the time of surgery and included history of previous IE, history of prior valve surgery, presence of cardiac implantable electronic device, intravenous drug use, chronic hemodialysis, immunosuppression (defined as patient with any immunodeficiency syndrome or taking systemic corticosteroids), diabetes mellitus, Charlson comorbidity index (CCI) score at time of valve repair, and degree of congestive cardiac failure, if present, according to New York Heart Association classification [16]. Date of first positive blood culture, causative pathogen, source of infection, and duration of BSI were recorded. Date of diagnosis and location of IE based on echocardiogram or blood culture results was recorded.

Controls

A maximum of 4 controls per case, where possible, were selected from the population of persons who had undergone valve repair but did not develop BSI. Controls were matched to cases by age (± 1 year) and approximate date of residence in the 7-county region.

Data Analysis

A case-control analysis was conducted to determine the relationship, if any, between male sex, CCI score, and residency in Olmsted County and BSI post–valve repair. Male sex was chosen as it has previously been associated with higher rates of BSI [17], CCI has been associated with poorer outcomes in selected cases of BSI [18], and we theorized that there may be differences in socioeconomic factors that could influence BSI rates in the 7-county survey. Olmsted County, an affluent urban center, was compared to the 6 other counties where there are differences in socioeconomic factors that include the percentage of persons living below the poverty line, non-White race, college education, and rural vs urban designation. In addition, the

latter socioeconomic factors may be more representative of the United States as a whole.

Univariate analysis between the cases and controls was conducted using either the Kruskal-Wallis test for continuous variables or the χ^2 test for categorical variables. Multivariate conditional logistic regression models were utilized to evaluate the association of male sex and CCI with subsequent risk of BSI. A P value of <.05 was considered statistically significant. All analyses were done in SAS statistical software version 9.4 (SAS Institute, Cary, North Carolina).

RESULTS

A total of 335 patients underwent valve repair surgery. The median age at time of surgery was 70 years, and the interquartile range (IQR) was 58–78 years. Follow-up data were available on all patients; the median length of follow-up from time of surgery to end of the study period was 5.0 years and the IQR was

Table 1. Site and Type of Valve Repair

Repair Site	Repair Type				
	Band	Band and Chord	Suture	Clip	Concurrent Valve Replacement
Mitral valve	15	2	0	1	2
Tricuspid valve	7	…	2	…	5
Dual mitral and tricuspid valve	1	…	…	…	1

2.5–8.0 years. A total of 28 (8.3%) patients developed an index case of BSI, with a cumulative, nonadjusted crude incidence of post–valve repair BSI of 1671 (95% confidence interval, 287.1–3056.2) episodes per 100 000 person-years (PY). Site and types of valve repair surgery in patients who developed BSI are included in Table 1.

The median age at time of BSI was 72.6 years, 22 (79%) patients were male, and 4 patients had a history of IE (Table 2).

Table 2. Demographic and Clinical Characteristics of Patients With Bloodstream Infection Post–Valve Repair

Characteristic	BSI Only (n = 24)	IE With Concurrent BSI at Onset (n = 4)	Total (N = 28)
Sex			
Male	18 (75)	4 (100)	22 (79)
Female	6 (25)	…	6 (21)
Age, y, median (IQR)	74 (19.8)	60 (22.2)	70 (20.0)
White race	23 (96)	4 (100)	27 (96)
County of residence			
Olmsted	12 (50)	2 (50)	14 (50)
Mower	3 (13)	…	3 (11)
Steele	4 (17)	…	4 (14)
Dodge	1 (4)	…	1 (4)
Freeborn	1 (4)	…	1 (4)
Waseca	3 (11)	1 (4)	4 (14)
Wabasha	…	1 (25)	…
Past medical history			
History of IE	2 (8)	2 (50)	4 (14)
Presence of CIED	8 (29)	1 (25)	9 (32)
Hemodialysis	3 (13)	1 (25)	4 (14)
IVDU	…	1 (25)	1 (4)
Immunosuppression	2 (8)	…	2 (8)
CHF at baseline	15 (54)	3 (75)	18 (64)
NYHA I	3 (13)	…	3 (11)
NYHA II	3 (13)	…	3 (11)
NYHA III	5 (21)	3 (75)	8 (29)
NYHA IV	5 (21)	…	5 (18)
CCI, median	5	6	5
Port of entry			
CLABSI	2 (7)	…	2 (7)
Urinary tract infection	6 (21)	…	6 (21)
SSTI	5 (18)	2 (7)	7 (25)
Pneumonia	3 (11)	…	3 (11)
Intra-abdominal infection	8 (29)	…	8 (29)
Primary BSI	…	2 (7)	2 (7)

Data are presented as No. (%) unless otherwise indicated.

Abbreviations: BSI, bloodstream infection; CCI, Charlson comorbidity index; CHF, congestive heart failure; CIED, cardiovascular implantable electronic device; CLABSI, central line–associated bloodstream infection; IE, infective endocarditis; IQR, interquartile range; IVDU, intravenous drug user; NYHA, New York Heart Association; SSTI, skin and soft tissue infection.

The median time to development of BSI after valve repair was 280 days (IQR, 70–1486 days). Of 28 cases of BSI, 14 (50%) occurred within 1 year of surgery, and 6 (21%) occurred within 1 month of surgery (Supplementary Figure 2). Two patients had a subsequent episode of BSI after the index case. The mortality rate within 3 months of BSI was 18%, and at 1 year was 28%. Of 28 patients with BSI, 17 (60%) had died at the end of the study period, as compared with 19 of 110 patients (17%) in the control group.

Microorganisms responsible for BSI are listed in Table 3. Gram-negative bacilli accounted for 17 (61%) cases of BSI. The most common organisms were *Escherichia coli* (7 cases), and *Enterococcus* spp (3 cases). One patient had candidemia and 1 patient had polymicrobial infection (*Klebsiella pneumonia, Citrobacter freundii*). All 4 cases of BSI with IE at onset were due to gram-positive cocci infection, and *Enterococcus* spp accounted for 3 of 4 cases. Primary foci of infection associated with BSI are listed in Table 2. The most common portal of entry for BSI was intra-abdominal. In cases of IE with concurrent BSI at the onset, skin and soft tissue infection accounted for 2 cases and the portal of entry was undetermined in the remaining 2 cases.

A 1:4 nested case-control univariate analysis demonstrated a significant association between male sex (P = .0386) and higher CCI score (P = .0001) with subsequent risk of BSI. There was no association between county of residence and BSI (Table 4). Multivariate conditional logistic regression models that included sex and CCI score as predictor variables were also performed. In these analyses, higher CCI score was significantly associated with risk of BSI (P < .001); however, no significant association was observed for male sex and BSI (P = .182; Table 4).

Of 28 patients, 4 had IE concurrent with onset of BSI, and no patients developed IE subsequent to BSI. The crude incidence of IE was 239 cases per 100 000 PY. All 4 cases of IE are detailed further in Table 5. Three of 4 cases were categorized as definite

IE. In 1 case, IE was presumed based on increased MV thickness and regurgitation seen on transesophageal echocardiography (TEE). Of note, 3 patients had concurrent prosthetic valve implantation at the time of valve repair, although in all cases TEE showed involvement of the repaired valve only. The rate of complicating IE in those who underwent valve repair and concurrent valve replacement was 27% compared to 6% in those undergoing valve repair only (Fisher exact test P value = .30). Median time to development of BSI with IE at onset was 110 days. One of the 4 patients died within 2 months of BSI diagnosis, and another patient died after developing a subsequent episode of IE in the context of intravenous drug use; the 2 remaining patients were cured with antibiotic therapy alone.

Table 3. Cause of Bloodstream Infection Post–Valve Repair

Organism	BSI Only	IE With Concurrent BSI at Onset	Total
Staphylococcus aureus	1	1	2
Coagulase-negative staphylococci	1	…	1
β-hemolytic streptococci	2	…	2
Viridans group streptococci	1	…	1
Enterococcus spp	…	3	3
Corynebacterium striatum	1	…	1
Klebsiella pneumoniae	3	…	3
Escherichia coli	7	…	7
Pseudomonas aeruginosa	2	…	2
Serratia marcescens	2	…	2
Haemophilus influenzae	1	…	1
Raoultella planticola	1	…	1
Citrobacter freundii	1	…	1
Capnocytophaga canimorsus	1	…	1
Candida albicans	1	…	1
Total	25[a]	4	29[a]

Abbreviations: BSI, bloodstream infection; IE, infective endocarditis.

[a]One case of polymicrobial BSI; 2 organisms isolated.

Table 4. Bloodstream Infection Post–Valve Repair: Risk Factor Analysis

Risk Factor	Controls (n = 110)	Cases (n = 28)	Total (N = 138)	P Value
Univariate analysis				
Sex, No. (%)				.0386[a]
Female	47 (42.7)	6 (21.4)	53 (38.4)	
Male	63 (57.3)	22 (78.6)	85 (61.6)	
CCI				.0001[b]
Mean (SD)	3.1 (1.94)	5.4 (2.95)	3.6 (2.36)	
Median (range)	3.0 (0.0–8.0)	5.0 (0.0–11.0)	3.0 (0.0–11.0)	
County of residence				.9363[a]
Olmsted	58 (52.7)	15 (53.6)	73 (52.9)	
Other	52 (47.3)	13 (46.2)	65 (47.1)	
Multivariate analysis, HR (95% CI)				
CCI (unit =1)	1.51 (1.21–1.88)			<.001
Male sex	1.78 (.70–6.38)			.182

Abbreviations: CCI, Charlson comorbidity index; CI, confidence interval; HR, hazard ratio; SD, standard deviation.

[a]χ^2 test.

[b]Kruskal-Wallis test.

Table 5. Characteristics of 4 Patients With Infective Endocarditis and Concurrent Bloodstream Infection at Onset

Age, y	Sex	History of IE	CIED	Surgical Procedure	Organism	IE Location	Postoperative Day	Management	Outcome
75	M	No	No	MV annuloplasty, AV replacement	*Enterococcus faecium*	MV	82	Antibiotics	Death
31	M	Yes	No	MV annuloplasty, chord repair	MSSA	TV	95	Antibiotics	Recovery
57	M	Yes	Yes	TV annuloplasty, MV replacement	*Enterococcus faecalis*	MV	125	Antibiotics, TV replacement	Recovery
61	M	No	No	MV annuloplasty, AV replacement	*E faecalis*	MV	223	Antibiotics	Recovery

Abbreviations: AV, aortic valve; CIED, cardiovascular implantable electronic device; IE, infective endocarditis; MSSA, methicillin-sensitive *Staphylococcus aureus*; M, male; MV, mitral valve; TV, tricuspid valve.

DISCUSSION

To our knowledge, this is the first population-based investigation to define the incidence of BSI following cardiac valve repair. The crude incidence of BSI in our cohort was high—1671 cases per 100 000 PY. A population-based study conducted between 2003 and 2005 examining BSI rates in Olmsted County, one of the counties included in our study, demonstrated a BSI rate of 189 cases per 100 000 PY [4]. Similar rates were observed in a population-based study conducted in England between 2004 and 2008 [19].

Why was the BSI rate higher in our cohort than in the general population? The most likely explanation is the older age of our cohort—the median age at time of surgery was 70 years. It has previously been established that older age is a risk factor associated with BSI [4]. This may not account for the totality of the observed difference; however; the median age in the Olmsted County study was 63 years, and the aforementioned English study reported a BSI rate of 857 cases per 100 000 PY in those aged ≥75 years [19].

To further address this question, we conducted an age-matched, case-control study to examine additional purported risk factors of male sex, burden of illness at baseline calculated via the CCI, and residency in Olmsted County. Importantly, a significant association was identified between preoperative CCI and risk of BSI. While there has been limited investigation into the relationship between CCI and BSI, Bonnet et al conducted a propensity-matched study and found an association between burden of illness at baseline and postoperative morbidity following MV repair [6]. It is plausible that sicker patients have increased health care contact, which predisposes to higher rates of health care-associated infection. One risk factor that we could not control for was the index hospitalization itself, which may predispose to development of BSI [20]. In our case, 1 in 5 cases of BSI was acquired during the index hospitalization.

The mortality rates and timing associated with BSI in this cohort deserve further comment. The mortality rate in the BSI cohort through the end of the study period was significantly higher than that of the control group (60% vs 17%). This reflects the higher rate of comorbidities in the BSI cohort, but is also directly attributable to mortality associated with BSI—just under 1 in 5 patients died within 3 months of BSI. It is also notable that 20% of BSI cases occurred within 1 month of surgery, and half of cases occurred within 1 year of surgery. Clinicians should be aware that risk of BSI and associated mortality is high in the early postoperative period following valve repair. Empiric antibiotic therapy should be avoided in patients presenting with undifferentiated fever in this time frame, unless the clinical condition (eg, sepsis) warrants it. Patients should have a thorough evaluation and blood cultures should be obtained, an approach endorsed in the 2015 American Heart Association guidelines that address the diagnosis and management of IE [21].

While it is difficult to generate robust hypotheses given the low number of IE cases in our cohort, several findings deserve further attention. First, the rate of complicating IE in our cohort was lower than that of a previous landmark study. Fang et al examined a cohort of patients with BSI following cardiac valve replacement and noted an overall progression rate to IE of 43% at 1 year in a cohort of 171 patients; valve repair, however, was not examined [7]. In another related study [22], Karavas et al documented a rate of IE of 0.7% post-MV repair. While the latter was not a population study and loss to follow-up is therefore difficult to assess, it is tempting to speculate that the IE risk among patients who undergo valve repair is less than that for patients with prior placement of prosthetic valves who develop BSI.

It is also noteworthy that (1) all IE cases occurred within 1 year of surgery; (2) all cases occurred in men; and (3) while gram-negative rods accounted for the majority of BSI cases, gram-positive cocci were implicated in all 4 cases of IE, with *Enterococcus* spp present in 3 cases. It has previously been established that men are at heightened risk of infection with gram-positive cocci [4], and endothelialization of prosthetic valve material has previously been noted in animal models after approximately 6 months in situ [23]. It is plausible that lack of complete endothelialization of prosthetic material used in cardiac valve repair could predispose to development of IE in patients. Of course, intraoperative contamination could also account for early cases of IE. Thus, more investigation is warranted as we consider infection pathogenesis of this syndrome.

There are limitations to the current investigation. This includes a retrospective approach to patient identification and diagnoses, and the use of *ICD* codes as opposed to laboratory databases for case identification. The limited number of BSI cases among valve repair patients prevents a thorough characterization of BSI complications, including IE, and associated risk factors. A nested case-control analysis was conducted to assess this issue, which included patient sex and CCI as purported risk factors associated with the development of post–valve repair BSI. The study cohort included a diverse range of valve repair procedures, and included procedures where concomitant valve replacement was undertaken; a similar study that focuses on a single type of valve repair, for example, isolated MV repair, would be useful to determine whether there are specific risk factors associated with type of valve repair. An important strength is the population-based aspect of this investigation, which provides a realistic example of the incidence of BSI among valve repair patients, alleviating referral bias introduced by single or multicenter tertiary care experiences.

CONCLUSIONS

The incidence of BSI following cardiac valve repair was higher in our e-REP cohort than in previous population-based studies, and BSI carried a poor prognosis. Patients with a higher CCI at baseline were at increased risk of subsequent BSI. Half of all cases of BSI, and all cases of complicating IE, occurred within 1 year of surgery. Clinicians should be aware of the high rate of BSI following valve repair, especially in the early postoperative period when the risk of complicating IE is highest. Prompt evaluation of patients in this cohort who develop fever is warranted, with a minimum of obtaining blood cultures and an attempt to define the primary site of infection.

References

1. Nkomo VT, Gardin JM, Skelton TN, et al. Burden of valvular heart diseases: a population-based study. Lancet **2006**; 368:1005–11.
2. Vemulapalli S, Grau-Sepulveda M, Habib R, et al. Patient and hospital characteristics of mitral valve surgery in the United States. JAMA Cardiol **2019**; 4:1149–55.
3. Kilic A, Saha-Chaudhuri P, Rankin JS, Conte JV. Trends and outcomes of tricuspid valve surgery in North America: an analysis of more than 50,000 patients from the Society of Thoracic Surgeons database. Ann Thorac Surg **2013**; 96:1546–52; discussion 1552.
4. Uslan DZ, Crane SJ, Steckelberg JM, et al. Age- and sex-associated trends in bloodstream infection: a population-based study in Olmsted County, Minnesota. Arch Intern Med **2007**; 167:834–9.
5. Artero A, Zaragoza R, Camarena JJ, et al. Prognostic factors of mortality in patients with community-acquired bloodstream infection with severe sepsis and septic shock. J Crit Care **2010**; 25:276–81.
6. Bonnet V, Boisselier C, Saplacan V, et al. The role of age and comorbidities in postoperative outcome of mitral valve repair: a propensity-matched study. Medicine **2016**; 95:e3938.
7. Fang G, Keys TF, Gentry LO, et al. Prosthetic valve endocarditis resulting from nosocomial bacteremia. A prospective, multicenter study. Ann Intern Med **1993**; 119:560–7.
8. Garrido RQ, Pessanha B, Andrade N, et al. Risk factors for early onset prosthetic valve endocarditis: a case-control study. J Hosp Infect **2018**; 100:437–43.
9. Crane SJ, Uslan DZ, Baddour LM. Bloodstream infections in a geriatric cohort: a population-based study. Am J Med **2007**; 120:1078–83.
10. Tleyjeh IM, Steckelberg JM, Murad HS, et al. Temporal trends in infective endocarditis: a population-based study in Olmsted County, Minnesota. JAMA **2005**; 293:3022–8.
11. Rocca WA, Grossardt BR, Brue SM, et al. Data resource profile: expansion of the Rochester Epidemiology Project medical records-linkage system (E-REP). Int J Epidemiol **2018**; 47:368–368j.
12. Viscoli C. Bloodstream infections: the peak of the iceberg. Virulence **2016**; 7:248–51.
13. Bekeris LG, Tworek JA, Walsh MK, Valenstein PN. Trends in blood culture contamination: a college of American pathologists Q-tracks study of 356 institutions. Arch Pathol Lab Med **2005**; 129:1222–5.
14. Li JS, Sexton DJ, Mick N, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. Clin Infect Dis **2000**; 30:633–8.
15. Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform **2009**; 42:377–81.
16. White P, Myers M. The classification of cardiac diagnosis. JAMA **1921**; 77:1414–15.
17. Cohen B, Choi YJ, Hyman S, et al. Gender differences in risk of bloodstream and surgical site infections. J Gen Intern Med **2013**; 28:1318–25.
18. Vaquero-Herrero MP, Ragozzino S, Castaño-Romero F, et al. The Pitt bacteremia score, Charlson comorbidity index and chronic disease score are useful tools for the prediction of mortality in patients with *Candida* bloodstream infection. Mycoses **2017**; 60:676–85.
19. Wilson J, Elgohari S, Livermore DM, et al. Trends among pathogens reported as causing bacteraemia in England, 2004–2008. Clin Microbiol Infect **2011**; 17:451–8.
20. Aliyu S, Cohen B, Liu J, Larson E. Prevalence and risk factors for bloodstream infection present on hospital admission. J Infect Prev **2018**; 19:37–42.
21. Baddour LM, Wilson WR, Bayer AS, et al. Infective endocarditis in adults: diagnosis, antimicrobial therapy, and management of complications. Circulation **2015**;132:1435–86.
22. Karavas AN, Filsoufi F, Mihaljevic T, et al. Risk factors and management of endocarditis after mitral valve repair. J Heart Valve Dis **2002**; 11:660–4.
23. Jana S. Endothelialization of cardiovascular devices. Acta Biomater **2019**; 99:53–71.