



Risks of Bloodstream Infection and Infective Endocarditis Following Cardiac Valve Repair: A Population-Based Study

Jack W. McHugh M.B. B.Ch. B.A.O.¹, Khawaja M. Talha M.B. B.S.², Larry M. Baddour M.D.^{2,3} Jennifer St. Sauver, MPH Ph.D.⁴, Karen M. Fischer M.P.H.⁵, Juan A. Crestanello, MD⁶, Arman Arghami, MD⁶, Daniel C. DeSimone, MD^{2,3}

¹Division of Internal Medicine, ²Division of Infectious Diseases, Department of Medicine and ³Department of Cardiovascular Disease, ⁴Division of Epidemiology, ⁵Division of Biomedical Statistics and Informatics, ⁶Division of Cardiovascular Surgery, Mayo Clinic College of Medicine and Science

ABSTRACT

BACKGROUND

Bloodstream infections (BSI) confer an increased risk of infective endocarditis (IE) in patients with a prosthetic cardiac valve. This relationship has received limited investigation in patients who have previously undergone valve repair. We therefore conducted a retrospective population-based study to determine the incidence of BSI following valve repair, risk factors associated with the development of BSI, and the incidence of IE as a complication of BSI.

METHODS

The expanded Rochester Epidemiology Project (E-REP) data linkage system was used to identify all persons who underwent valve repair in a 7-county region in Southeastern Minnesota between January 1, 2010 and December 31, 2018. Medical records were screened for BSI from date of the repair procedure until May 15, 2020. Patients were classified as having BSI only, BSI with IE at outset, or BSI with subsequent development of IE. IE at outset was defined as cases where IE was diagnosed at the time of initial positive blood culture. To identify risk factors associated with BSI, case-control matching with a 1:3 ratio was conducted for the variables of sex, Charlson Co-Morbidity index (CCI), and residency in one of the following counties: Olmsted, Wabasha, Mower, Steele, Freeborn, Waseca, and Dodge.

RESULTS

Overall, 385 patients underwent valve repair surgery and 28 (7.2%) patients subsequently developed BSI. Gram negative rods (GNRs) accounted for 17 (61%) of 28 cases of BSI; the most common portal of entry was gastro-intestinal/genitourinary (GI/GU) (13/28, 46%). Median time to development of BSI was 280 days. Annual incidences of BSI and IE were 1,464 per 100,000 person-years, and 209 per 100,000 person-years, respectively. CCI was associated with subsequent risk of BSI; median CCI was 3 in the control group and 5 in the BSI group; HR 1.78 (1.21, 1.88), p<0.001). Of 28 patients with BSI, 4 had BSI with IE at outset, and all cases occurring within one year of surgery. Enterococcus spp. was responsible for 3 cases of IE, and MSSA for 1. No cases of BSI with subsequent development of IE were identified.

CONCLUSIONS

Elevated baseline CCI conferred an increased risk of subsequent BSI, and could be a consideration when selecting patients for some type of valve surgery. It is notable that all cases of IE occurred within one year of surgery. Recognizing that endothelialization of device surfaces occurs over several months, it is tempting to speculate that the risk of IE may be time dependent and could conceivably decline over time. Subsequent investigation of this theory is underway.

INTRODUCTION

BACKGROUND

While it is well established that post-surgical BSI confers an increased risk of IE in patients with a prosthetic valve¹, the incidence of BSI following valve repair and subsequent risk of IE, along with specific risk factors associated with the development of BSI, are less established.

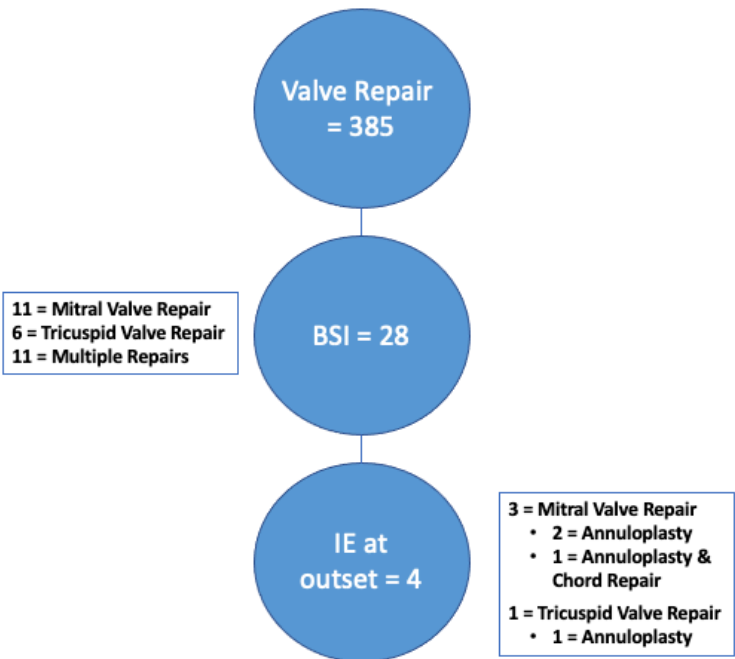
Understanding risk factors associated with BSI and defining the incidence of both BSI and IE in this cohort is a question of clinical import; for example, the American Heart Association continues to recommend antimicrobial prophylaxis for certain dental procedures following valve repair with implantation of prosthetic material²

OBJECTIVES

To clarify this issue, 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 an 8-year period were examined to determine:

1. The incidence and clinical characteristics of patients who developed BSI following valve repair surgery,
2. The incidence of IE in this cohort, and
3. Risk factors associated with the development of BSIs following valve repair

FIGURE 1: BSI & IE POST-VALVE REPAIR



METHODS

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 in a 7-county region in southern Minnesota. The combined population size, according to 2018 US census data, was 345,751. Olmsted County consists of a major urban center, the other six counties are predominantly rural.

CASE IDENTIFICATION

The E-REP database was used to pull all current procedure terminology codes corresponding to valve repair procedures between January 1st 2010 - December 31st 2018. Patients were classified as having BSI only, BSI with IE at outset, or BSI with subsequent development of new IE. IE was defined as either definite or possible using the modified Duke criteria². Early IE was defined as that occurring <12 months following valve repair, with subsequent cases defined as Late IE.

DATA RECORDING AND ANALYSIS

Chart review was conducted to identify cases with BSI post-valve repair. Salient data were extracted for cases of BSI and entered into a REDCap database. To identify risk factors associated with BSI, case-control matching on a 1:3 basis was conducted for the variables of sex, Charlson Co-Morbidity index (CCI) and residency in Olmsted County, as compared to Wabasha, Mower, Steele, Freeborn, Waseca, and Dodge counties. Chi-square and Kruskal-Wallis p-values were calculated, with a Cox model used to generate hazard ratios.

RESULTS

- A total of 385 patients underwent valve repair and 28 (7.2%) patients developed BSI. Four had BSI with IE at onset (1%) (Figure 1).
- The median follow-up time was 4.81 years, with median time to development of BSI of 280 days.
- Annual incidence of BSI was 1,464 per 100,000 person-years, annual incidence of IE was 209 per 100,000 person-years.
- 22 of 28 (79%) patients were male, one patient was Asian and the other 27 were non-Hispanic white. Median age at time of BSI was 69.
- GNRs accounted for 17/28 (61%) cases of BSI. E. Coli was the most common pathogen (Table 1).
- The most common portal of entry was GI/GU (13/28, 46%).
- Four patients with BSI had IE at outset. Gram positive bacteria accounted for all four cases; Enterococcus spp. in three and MSSA in one (Table 2). In all four cases the portal of entry was undetermined. No patient developed IE subsequent to BSI.
- All four cases of IE occurred within one year of surgery; three of four occurred within six months of surgery (Table 2). In 2 cases where there was concomitant valve replacement IE occurred in the repaired valve. 2 of 4 patients had history of previous IE
- CCI was positively associated with subsequent risk of BSI; sex and residency in Olmsted County, Wabasha, Mower, Steele, Freeborn, Waseca, and Dodge counties were not associated with increased risk of BSI (Table 3, Table 4)

BSI & IE CHARACTERISTICS

Table 1: BSI Microbiology

Organism	BSI Only (n=24)	IE at outset (n=4)
<i>S. aureus (MSSA)</i>	1	1
<i>Coagulase-negative staphylococci</i>	1	
<i>S. pyogens</i>	2	
<i>Viridans group streptococci</i>	1	
<i>Enterococcus spp.</i>		3
<i>C. striatum</i>	1	
<i>K. pneumoniae</i>	3	
<i>E. coli</i>	7	
<i>P. aeruginosa</i>	2	
<i>S. marcescens</i>	2	
<i>Other GNR</i>	4	
<i>C. albicans</i>	1	
Total	25*	4

*One patient had polymicrobial bacteremia with 2 organisms isolated

Table 2: IE Characteristics

Age	Sex	Surgical Procedure	Organism	Early vs Late
57	M	TV annuloplasty & MV replacement	<i>E. faecalis</i>	Early
31	M	MV annuloplasty & NeoChord repair	MSSA	Early
75	M	MV annuloplasty & AV replacement	VRE	Early
61	M	MV annuloplasty & AV replacement	<i>E. faecalis</i>	Early

BSI RISK FACTORS

Table 3: BSI Risk Factors, Descriptive Statistics

	Control (N=110)	Case (N=28)	Total (N=138)	p-value
Sex, n (%)				0.0386 ¹
0	47 (42.7%)	6 (21.4%)	53 (38.4%)	
1	63 (57.3%)	22 (78.6%)	85 (61.6%)	
CCI				0.0001 ²
Mean (SD)	3.1 (1.94)	5.4 (2.95)	3.6 (2.36)	
Median	3.0	5.0	3.0	
Range	0.0, 8.0	0.0, 11.0	0.0, 11.0	
Olmsted County, n (%)				0.9363 ¹
No	58 (52.7%)	15 (53.6%)	73 (52.9%)	
Yes	52 (47.3%)	13 (46.4%)	65 (47.1%)	

¹Chi-Square p-value; ²Kruskal-Wallis p-value

Table 4: Cox Model with matches included as strata

	Hazard Ratio (95% CI)	p-value
CCI	1.51 (1.21, 1.88)	<0.001
Sex	1.78 (0.70, 6.38)	0.182

DISCUSSION

- This is the first study that has examined risk factors for BSI following valve repair, and the first study that has examined incidence of IE following valve repair at a population-level
- The incidence of BSI following valve repair in this cohort is significantly higher than rates of BSI previously established in Olmsted County (156 per 100 000 person-years for females and 237 per 100 000 person-years for males)⁴
- Elevated baseline CCI conferred increased risk of subsequent BSI, and could be a consideration when selecting patients for intervention
- Although the cohort size is limited, it is notable that the prevalence of IE was relatively low at 1%; and that all cases occurred within one year following surgery

CONCLUSIONS

- All cases of IE occurred within one year of surgery. Although the number of IE cases is small, the observation that all BSI cases due to Enterococcus species also caused IE at onset deserves further study with a larger cohort. Subsequent investigation of this theory in a larger cohort is underway

REFERENCES

1. Fang G, Keys TF, Gentry LO, et al. Prosthetic valve endocarditis resulting from nosocomial bacteremia: A prospective, multicenter study. Ann Intern Med. Published online 1993. doi:10.7326/0003-4819-119-7_part_1-199310010-00003
2. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Fleisher LA, Jneid H, Mack MJ, McLeod CJ, O'Gara PT, Rigolin VH, Sundt TM 3rd, Thompson A. 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2017 Jun 20;135(25):e1159-e1195. doi: 10.1161/CIR.0000000000000503. Epub 2017 Mar 15.
3. Li JS, Sexton DJ, Mick N, et al. Proposed Modifications to the Duke Criteria for the Diagnosis of Infective Endocarditis. Clin Infect Dis. Published online 2000. doi:10.1086/313753 Lorem ipsum dolor sit amet, consectetur adipiscing elit. Duis eu sapien metus. Duis vestibulum tincidunt felis, at euismod dolor aliquam duis vesti.
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(8):834-839. doi:10.1001/archinte.167.8.834