Author/s:
Yaftian, N;Buratto, E;Ye, XT;Wilson, A;Darby, J;Newcomb, A

Title:
Long-term outcomes of mitral valve endocarditis: improved survival through collaborative management

Date:
2020-05-01

Citation:
Yaftian, N., Buratto, E., Ye, X. T., Wilson, A., Darby, J. & Newcomb, A. (2020). Long-term outcomes of mitral valve endocarditis: improved survival through collaborative management. ANZ Journal of Surgery, 90 (5), pp.757-761. https://doi.org/10.1111/ans.15814.

Persistent Link:
https://hdl.handle.net/11343/275544

Yaftian Nima (Orcid ID: 0000-0002-2976-0666)

Long-term outcomes of mitral valve endocarditis: improved survival through collaborative management.

Authors:

Nima Yaftian MD[1], Edward Buratto MBBS[1,2] , Xin Tao Ye MD[1], Andrew Wilson MBBS PhD[3], Jonathan Darby MBBS[4], Andrew Newcomb MBBS[1, 2]

Affiliations:

1. Department of Cardiothoracic Surgery, St Vincent's Hospital Melbourne, Australia

2. Department of Surgery, University of Melbourne, Australia

3. Department of Cardiology, St Vincent's Hospital Melbourne, Australia

4. Department of Infectious Diseases, St Vincent's Hospital Melbourne, Australia

Presented at the AATS Mitral Conclave on 27-28 April, 2017 at New York, USA

Key words: Infective Endocarditis, Multidisciplinary, Mitral Valve

Corresponding author:

Nima Yaftian, MD

St Vincent's Hospital Melbourne

41 Victoria Parade, Fitzroy, Victoria, 3065, Australia

Tel 61 3 9231 2211

E-mail: nimayaftian@gmail.com

Abstract

Background: Infective Endocarditis (IE) of the mitral valve is an illness associated with significant morbidity and mortality. We describe the long-term outcomes of mitral valve endocarditis at a single-centre.

Methods: All patients who presented with IE to the study institution between 2000 and 2015 were included. Data was obtained by retrospective review of the medical records.

Results: There were 163 patients who presented with mitral valve IE. Mean age was 58 ± 16.8 years. A history of intravenous drug use was present in 18% (30/163) of patients. The most common infective agents were *Staphylococcus aureus* in 42% (69/163) (7% [5/69] were methicillin resistant), *Streptococcus* Viridans species in 15% (25/163) and *Enterococcus faecalis* in 10% (17/163). Surgery was performed in 29% (47/163) of patients. Hospital mortality was 23% (38/163). Survival was 71% (95%CI: 63.1–77.6%) at 1-year, 56% (95%CI: 46.0–64.9%) at 5-years and 44 % (95%CI: 36.4–59.7%) at 10-years follow-up. There was no survival difference between medical and surgical management (p=0.55). On multivariate Cox regression analysis, need for renal replacement therapy (RRT) (p=0.003) and increasing age

(p=0.014) were found to be risk factors while Infectious Diseases consult during index admission (p=0.007) was found to be protective.

Conclusions: Mitral valve endocarditis is associated with survival of less than 50% at 10 years follow-up. Surgical and medical management were associated with similar outcomes. increasing age and need for RRT were associated with mortality, Infectious Diseases consultation was associated with improved survival.

Introduction

Infective endocarditis (IE) is a serious cause of hospitalisation which has a population incidence of between 1.7 – 6.2/100,000 person-years (1). Mitral valve endocarditis is the most common form of native valve endocarditis, accounting for up to 50% of all cases (2, 3). Mortality rates for mitral valve endocarditis remain very high, up to 25% at some centres (4). Long-term survival of endocarditis is poor with 10-year mortality rates of 53 – 58%(5, 6). There is a lack of literature concerning the long-term outcomes of surgical and medical consultation and management of mitral valve endocarditis. Hence, we conducted a retrospective review of all the patients that were diagnosed with IE of the mitral valve at a single institution in order to determine outcomes and risk factors.

Methods

Patients

Our institutional endocarditis database was retrospectively analysed and all cases with mitral endocarditis from 2000 – 2015 were included. Surgical cases were cross-referenced with our national dataset (Australia and New Zealand Society of Cardiac and Thoracic Surgeons) for completeness. The patients and public were not involved in the design, conduct and reporting of the research.

Definitions

Endocarditis was diagnosed according to the modified Duke criteria (7). Operative

mortality was defined as mortality occurring during the admission for surgical management of endocarditis or within 30 days of surgery. Late mortality was defined as mortality occurring 30 days after discharge from hospital. Urgency of surgery was defined as elective, urgent, emergency and salvage. Cardiology, Cardiothoracics (CTS) and Infectious Diseases (ID) consult was defined as a consultative review by the respective teams during the index admission for infective endocarditis. Renal replacement therapy (RRT) was defined as the need for haemofiltration or peritoneal dialysis.

Statistical analysis

Data were analysed with STATA version 15 (Stata Corp, College Station, TX, USA). Unless otherwise stated, continuous data were summarised as mean ± standard deviation. The time dependant end point was all-cause mortality. Cox proportional hazards analysis was used to examine risk factors for mortality. Univariate analysis was performed and variables with moderate evidence against the null hypothesis ($P < 0.1$) were included in the multivariate model. ab

Ethics

Research ethics was attained via study institutions Research Governance Unit (QA 016/13)

Results

A total of 163 patients were admitted for management of mitral valve endocarditis between January 2000 and January 2015. Mean patient age at the time of presentation was 58 ± 16.8 years. A history of IVDU was present in 18% (30/163) of the patients (**Table 1)**. Hepatitis C infection was present in 15% (24/163) of patients. A history of smoking was present in 62% (101/163) of the patients. A total of 23% (37/163) of the patients had previously had heart valve surgery. Concomitant infection of other heart valves occurred in 26% (43/163) of the patients with 24% (39/163) involving the aortic valve, 6% (10/163) involving the tricuspid valve and 0.5% (1/163) involving the pulmonary valve.

Surgical management

Indications for surgical intervention were based on the American Heart Association (AHA) guidelines for management of IE (8). Surgical management of endocarditis during index admission occurred in 29% (47/163) of patients with 71% (116/163) of patients undergoing medical management at index admission (**table 1**). Of the medically managed patients, 6.9% (8/116) returned for elective surgery after discharge. There was no difference in long-term survival between medically and surgically managed patients (p = 0.55) (**Figure 1**). Of the patients who underwent surgical management, 68.1% (32/47) had mitral valve replacement while 31.9% (15/47) had repair of the mitral valve.

Causative organisms

Microbiological diagnoses are summarized in **Table 2.** The most common causative organism was *Staphylococcus aureus* which accounted for 42% (69/163) of all endocarditis infections. Of these patients, 7% (5/69) had methicillin resistant *Staphylococcus aureus* (MRSA). The other most common causative organisms were Viridans *Streptococcus* species in 15% (25/163) of the patients and *Enterococcus faecalis* in 10% (17/163) of the patients. The only other infective agents of note were coagulase negative *Staphylococcus* species in 4% (7/163) and *Streptococcus bovis* in 2% (4/163). A total of 7% (12/163) of the patients were culture negative. There were no recorded cases of *Haemophilus* species, *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corodens* and *Kingella kingae* (HACEK) endocarditis.

Specialist review at index admission

Most patients at index admission had a review by CTS, Cardiology or ID specialty services. ID consultations were performed for 94% (154/163) patients, Cardiology consultations were performed for 78% (127/163) patients and CTS consultations were performed in 56% (91/163) of the patients. All three specialist services consultations were performed in 52% (84/163) of the patients. A summary of the 9 patients who did not undergo ID review can be found in **table 3**.

Prosthetic valve endocarditis

A total of 18% of patients (30/163) had prosthetic valve endocarditis. Management of

prosthetic valve endocarditis was based upon the AHA guidelines (8). Of the patients with prosthetic valve endocarditis, 30% (9/30) underwent surgery during index admission. Hospital mortality was 28.6% (6/21) among the non-operative group and 22.2% (2/9) among the operative group.

Mortality and follow-up

Total hospital mortality was 23% (38/163) (**Table 1)**. Hospital mortality amongst patients undergoing medical management of IE was 24% (28/116) and 21% (10/47) for patients undergoing surgical management (p = 0.55). Follow-up was 92% complete with 10 patients lost to follow-up. Mean follow-up time was 3.1 ± 3.0 years (range 1 month – 14.9 years). Late mortality occurred in 18% (22/125) of patients. Survival was 71% (95%CI: 63.1 – 77.6%) at 1-year, 56% (95%CI: 46.0 – 64.9%) at 5-years and 44% (95%CI: 36.4 – 59.7%) at 10-years follow up (**Figure 2)**.

Risk factors

On univariate analysis (**Table 4**) the need for renal replacement therapy (RRT) (P = 0.0001) and increasing age (P = 0.008) were significant risk factors for mortality. ID consultation (P = 0.0001, HR = 0.24) and IVDU (P = 0.046, HR = 0.42) was found to be protective against mortality. Cardiology consultation demonstrated a trend towards being protective against mortality but it did not reach statistical significance (P = 0.092, HR = 0.63). Other factors that were not statistically significant on univariate analysis have been outlined in ***Table 4***.

On multivariate analysis (***Table 4***) need for RRT (P = 0.003) and increasing age (P = 0.014) were both risk factors for mortality. ID consultation was protective against mortality (P = 0.007, HR = 0.31).

Discussion

Mitral valve endocarditis remains associated with poor short- and long-term survival outcomes. Several studies have published the long-term outcomes of surgical intervention for infective endocarditis of the mitral valve (2, 3, 5, 9-14), however, there is a lack of literature regarding the long-term outcomes of both medically and surgically managed mitral valve IE. To our knowledge, this is the largest single centre report of mitral valve IE.

Amongst our cohort of patients, there were a higher proportion of patients who received medical management compared to patients who received surgical management (approximately 2:1). This was similar to Greason and colleagues (10) who reported 37% of their mitral valve IE patients receiving surgical therapy while 63% received medical therapy alone. The hospital mortality rate they reported for the surgical cohort was 13% and 5-year survival was 48%, both of which were similar to our cohort. However, they did not describe the medically managed cohort of patients in this particular study (10). Verhuel and colleagues (6) reported a rate of 30%

surgical management and 70% medical management for their cohort of 130 IE patients. They reported similar early mortality rates of 26% and 27% for the surgical and medical management groups respectively. In the long-term both groups had a 5-year survival of 84%, however at 10-years they diverged significantly with 53% survival among surgical patients and 77% survival among medically managed patients. These outcomes were very similar to our outcomes (hospital mortality of 20% and 25% for surgical and medically managed patients respectively and no difference in survival at 5 years). However, where we showed there was no significant difference in long-term survival for our respective groups there was a significant difference in 10-year survival amongst their patient population. However, they included patients with IE of all valves in their analysis limiting the possibility of directly comparing the cohorts (6).

The commonest causative organism among our study cohort was *Staphylococcus aureus* (42% of all cases). The other common causative organisms were Viridans species *Streptococci* (15% of all cases) and *Enterococcus faecalis* (10% of all cases). Amongst all the literature these findings are consistent with *Streptococci, Staphylococcus aureus and Enterococci* being reported as the three most common causative organisms (in that order) (1, 15, 16). Coagulase negative *Staphylococcus* and *Streptococcus bovis* were the only other organisms of note among our population (4% and 2% respectively). There were also a significant number of patients that were culture negative (7%), which is consistent with current literature (1, 10). Other rare

causative organisms such as the HACEK group have been reported as rare causes of endocarditis (1). However, there were no cases of HACEK endocarditis within our cohort.

Currently, to the best of our knowledge there is no literature assessing the impact of input from different medical subspecialties. In our institution, all patients with IE will have their management driven by Cardiology or CTS. Commonly, these teams, along with ID, will also consult and offer advice on the management of patients under the care of the other teams. Amongst our cohort 94% had ID input, 78% had Cardiology input, 56% had CTS input and 52% had input from all three subspecialty teams. This disparity reflects the 2:1 ratio in medical vs. surgical management and the reality that all surgical patients will require concomitant medical management. On multivariable analysis ID consultation was the only statistically significant protective factor against mortality that was identified. The reasons why ID consultation may affect long-term survival are multiple. Among our cohort of patients who did not get an ID review the majority (7/9, **table 3**), were transferred from an external facility. Patients transferred from external facilities may have had delayed ID review due to an unclear diagnosis or the timing of admission and presentation. Patients who are diagnosed when in a critical condition may die prior to review by the ID team. Other patients who are culture negative may have a delay in being discussed with ID and this may impact on survival. Finally, expert advice regarding antibiotic management may impact on survival of patients. Taking these data into account we believe they support the early

routine referral of all patients with suspected IE to cardiology, ID and CTS units for review. We have adopted this multidisciplinary approach at our centre.

The only two statistically significant risk factors for mortality on multivariable analysis were increasing age and need for RRT (P = 0.003 and 0.014 respectively). Once again, these findings are concordant with the existing literature with de Kerchove and colleagues (3) reporting both of these (amongst others) as univariable risk factors for mortality, Sheikh and colleagues (5) reporting pre-operative renal failure as a statistically significant risk factor for early mortality and Greason and colleagues (10) reporting age > 65 as the only risk factor for operative mortality.

The greatest limitation of this study was that it was a retrospective cohort analysis. While our analysis found that there was no difference in long-term survival between surgically and medically managed patients this does not take into account the severity of the infection. Our study does not suggest any equivalence in medical or surgical management of endocarditis of the mitral valve.

Conclusions

Mitral valve endocarditis is associated with substantial hospital mortality and survival of less than 50% at 10 years follow-up. Surgical and medical management of mitral valve endocarditis were associated with similar outcomes both in the short and long-term. Increasing age and need for renal replacement therapy were associated with

mortality, while Infectious Diseases specialist consultation was associated with improved survival. Early multidisciplinary involvement is essential in all cases of endocarditis.

Tables

Table 1. Patient characteristics

Table 2. Causative organisms

Table 3: Outcomes among patients who did not undergo ID review

Table 4: Cox-hazards model for mortality

CTS = cardiothoracics, ID = infectious diseases, IVDU = intravenous drug use, RRT = need for renal replacement therapy, 3 consults = ID, CTS and cardiology consult, CCF = congestive cardiac failure, MI = myocardial infarction, MSSA = methicillin sensisitve Staphylococcus *aureus*, MRSA = methicillin resistant Staphylococcus *aureus*.

Figure legend

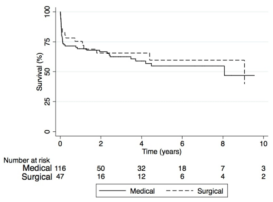
Figure 1: Kaplan-Meier medical vs. surgical intervention survival estimates

Figure 2: Kaplan-Meier survival estimates

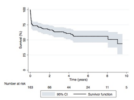
References:

1. Mylonakis E, Calderwood SB. Infective Endocarditis in Adults. New England Journal of Medicine. 2001;345(18):1318-30.
2. Doukas G. Mitral valve repair for active culture positive infective endocarditis. Heart. 2005;92(3):361-3.
3. de Kerchove L, Price J, Tamer S, Glineur D, Momeni M, Noirhomme P, et al. Extending the scope of mitral valve repair in active endocarditis. The Journal of thoracic and cardiovascular surgery. 2012;143(4):S91-S5.
4. Feringa HHH, Shaw LJ, Poldermans D, Hoeks S, van der Wall EE, Dion RAE, et al. Mitral Valve Repair and Replacement in Endocarditis: A Systematic Review of Literature. The Annals of thoracic surgery. 2007;83(2):564-70.
5. Sheikh AM, Elhenawy AM, Maganti M, Armstrong S, David TE, Feindel CM. Outcomes of surgical intervention for isolated active mitral valve endocarditis. The Journal of thoracic and cardiovascular surgery.137(1):110-6.
6. Verheul HA, van den Brink RBA, van Vreeland T, Moulijn AC, Düren DR, Dunning AJ. Effects of changes in management of active infective endocarditis on outcome in a 25-year period. American Journal of Cardiology.72(9):682-7.
7. Li JS, Sexton DJ, Mick N, Nettles R, Fowler JVG, Ryan T, et al. Proposed Modifications to the Duke Criteria for the Diagnosis of Infective Endocarditis. Clinical Infectious Diseases. 2000;30(4):633-8.
8. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP, 3rd, Guyton RA, et al. 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 Practice Guidelines. J Am Coll Cardiol. 2014;63(22):e57-185.
9. Ragnarsson S, Sjogren J, Stagmo M, Wierup P, Nozohoor S. Clinical Presentation of Native Mitral Valve Infective Endocarditis Determines Long-Term Outcome after Surgery. J Card Surg. 2015;30(9):669-76.
10. Greason KL, Thomas M, Steckelberg JM, Daly RC, Schaff HV, Li Z, et al. Outcomes of surgery in the treatment of isolated nonnative mitral valve infective endocarditis. The Journal of thoracic and cardiovascular surgery. 2014;147(1):349-54.
11. Wang TK, Oh T, Voss J, Gamble G, Kang N, Pemberton J. Valvular repair or replacement for mitral endocarditis: 7-year cohort study. Asian cardiovascular & thoracic annals. 2014;22(8):919-26.

12. Zegdi R, Debieche M, Latremouille C, Lebied D, Chardigny C, Grinda JM, et al. Long-term results of mitral valve repair in active endocarditis. Circulation. 2005;111(19):2532-6.
13. Shimokawa T, Kasegawa H, Matsuyama S, Seki H, Manabe S, Fukui T, et al. Long-term outcome of mitral valve repair for infective endocarditis. The Annals of thoracic surgery. 2009;88(3):733-9; discussion 9.
14. Kanemitsu H, Nakamura K, Fukunaga N, Koyama T. Long-Term Outcomes of Mitral Valve Repair for Active Endocarditis. Circulation journal : official journal of the Japanese Circulation Society. 2016;80(5):1148-52.
15. Hoen B, Alla F, Selton-Suty C, et al. Changing profile of infective endocarditis: Results of a 1-year survey in france. JAMA. 2002;288(1):75-81.
16. Wallace SM, Walton BI, Kharbanda RK, Hardy R, Wilson AP, Swanton RH. Mortality from infective endocarditis: clinical predictors of outcome. Heart. 2002;88(1):53-60.



ANS_15814_Figure 1.tiff



ANS_15814_Figure 2.tiff

Variable	Number of patients (%)
Total	163
Male/Female	98 (60.0%)/65 (40.0%)
Age at admission	58 +/- 16.8 years
Medically managed at index admission	116 (71.2%)
Surgically managed at index admission	47 (28.8%)
Hospital mortality	38 (23.3%)
Late mortality	22 (17.6%)
Prosthetic valve infective endocarditis	25 (15.3%)
Mean follow-up time	3.1 +/- 3.0 years
Cardiology consult	127 (77.9%)
Infectious diseases consult	154 (94.5%)
Cardiothoracic surgery consult	91 (55.8%)
All three consults	84 (51.5%)
IVDU	30 (18.4%)
Smoking history	101 (61.9%)

Organism	**Number affected (%)**
Staphylococcus aureus (MSSA)	64 (39%)
Staphylococcus aureus (MRSA)	5 (3%)
Viridans Streptococci	25 (15%)
Enterococcus faecalis	17 (10%)
Coagulase negative Staphylococcus	7 (4%)
Enterococcus faecium	5 (3%)
Streptococcus anginosus	4 (2%)
Streptococcus bovis	4 (2%)
Group G Streptococcus	3 (2%)
Streptococcus agalactiae	3 (2%)
Other organism	14 (9%)
Culture negative	12 (7%)

Patient	Index admission date	Peripheral hospital admission date	Date of empirical antibiotic commencement	Time to antibiotics	Outcomes	Time from admission to death (days)	Organism
1	21/05/02	19/05/02	19/05/02	0	Hospital mortality	10	MSSA
2	15/08/05	14/08/05	14/08/05	0	Hospital mortality	1	Culture negative
3	24/04/06	15/04/06	23/04/06	8	Late mortality		Viridans Streptococcus
4	11/06/06	07/06/06	08/06/06	1	Hospital mortality	4	MRSA
5	11/11/06	10/11/06	10/11/06	0	Hospital mortality	1	MSSA
6	31/12/06		31/12/06	0	Alive at last follow-up		Culture negative
7	21/08/07		21/08/07	0	Late mortality		MSSA
8	13/05/09	03/05/09	05/05/09	2	Alive at last follow-up		MSSA
9	13/12/11	12/12/11	14/12/11	2	Hospital mortality	14	MSSA

Variable	**Univariate analysis**	**Multivariate analysis**		
	P value	**P value**	**Hazards ratio**	**95% CI**
IVDU	0.046	0.771	1.18	0.39 – 3.49
CTS consult	0.355			
Cardiology consult	0.092	0.747	1.11	0.60 – 2.06
ID consult	0.0001	0.007	0.31	0.13 – 0.72
3 consults	0.204			
RRT	0.001	0.003	3.15	1.49 – 6.67
Smoking	0.349			
Diabetes	0.161			
Previous endocarditis	0.56			
Prosthetic valve endocarditis	0.173			
Previous MI	0.543			
CCF	0.202			
Increasing Age	0.008	0.014	1.03	1.01 – 1.05
Multivalve involvement	0.325			