

What are the differences in outcomes between right-sided active infective endocarditis with and without left-sided infection?

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Summary

A best evidence topic in cardiac surgery was written according to a structured protocol. The question addressed was: in patients with isolated right-sided infective endocarditis (RSE) is the outcome of surgical management the same as in patients with or without left-sided involvement? Altogether, 419 papers were found using the reported search, six of which represented the best evidence to answer the clinical question. Two studies point towards better outcomes with isolated RSE. In one paper, mortality was significantly lower in isolated RSE patients ($P=0.0093$) for the duration of the follow-up time (median 488 patient-years). Two studies reported early mortality (<30 days) for RSE patients at 3.6 and 3.8%, respectively. Combined right- and left-sided endocarditis (RLSE) patients were found to have a poorer pre-operative clinical presentation than isolated RSE patients with a greater requirement for inotropic support ($P<0.006$) and the likelihood of an emergency operation ($P<0.001$). They had a poorer intra-operative course with a higher incidence of cardiac abscess formation ($P<0.001$). One study suggested that there is no significant difference in in-hospital and long-term mortality between intravenous drug abuse (IVDA) patients and non-IVDA patients. Left-heart involvement in the IVDA group was 61.5%. This was in-line with the published literature, demonstrating a rise in RLSE in IVDA compared with non-IVDA patients. Three articles looking at isolated left-sided endocarditis (LSE) gave mortality rates in the surgical group to be 27.1, 27.8 and 38%, respectively. In one study, the LSE mortality was not different for native vs. prosthetic valve infection (OR 0.65, 95% CI 0.23–1.87). After propensity matching and adjusting for hazards, the complication rate in the LSE group was higher and this translated to a higher mortality rate. We conclude from the literature that outcomes are more favourable with lower early and late mortality for isolated RSE patients over pure LSE or combined RLSE.

Keywords: Infective endocarditis • Right-sided infective endocarditis • Left-sided infective endocarditis • Outcomes

INTRODUCTION

A best evidence topic in cardiac surgery was written according to a structured protocol. This is fully described in Interactive Cardiovascular and Thoracic Surgery (ICVTS) [1].

THREE-PART QUESTION

In patients with isolated [right-sided infective endocarditis (RSE)], is the [outcome of surgery] the same as in patients with [left-sided or combined right- and left-sided infective endocarditis (RLSE)]?

CLINICAL SCENARIO

The cardiologists ask you to see a 30-year old patient who has tricuspid valve infective endocarditis and has septic pulmonary emboli. They ask your surgical opinion and to counsel the patient for risks for surgery. You remember seeing a patient earlier on with native aortic valve infective endocarditis. You

wonder if right- vs. left-sided infection has a difference in operative outcomes. You decide to look up the evidence on the topic.

SEARCH STRATEGY

Medline search 1955–June 2011 using Pubmed interface [surgery.mp] OR [outcomes] AND [right-sided infective endocarditis] OR [left-sided infective endocarditis].

SEARCH OUTCOME

Four hundred and nineteen papers were found using the reported search criteria. Six of which represented the best evidence to answer the clinical question (Table 1).

Case reports and small series of <10 patients were discarded. Studies that did not declare a clear clinical outcome were also excluded. Primary outcomes of interest were in-hospital or early (<30 days) and overall mortality rates for cases with isolated RSE,

Table 1: Best evidence papers

Author, date and country; study type (level of evidence)	Patient group	Outcomes	Key results	Comments
Zhang <i>et al.</i> [2], 2010, China; Retrospective cohort study (level IIb)	Single-centre study over 15 years <i>n</i> = 28; adult patients with isolated RSE	Primary outcome: (1) mortality Secondary outcome: (1) renal dysfunction and (2) post-operative NYHA class	Mortality: 3.6% (one in-hospital death) Renal failure in 3 of 28 (10.7%) NYHA class was reduced in all patients Mild-to-moderate tricuspid regurgitation in 11 of 28 (39.3%); Re-operation for mediastinal bleeding in 2 of 28 (7.1%)	Good outcomes are observed with surgery in the setting of isolated RSE No recurrent infection found
Musci <i>et al.</i> [3], 2007, Germany; Retrospective cohort study (level IIb)	Single-centre study over 20 years <i>n</i> = 79; adult patients undergoing 84 operations for RSE (<i>n</i> = 57) and combined RLSE (<i>n</i> = 27)	Primary outcome: (1) mortality Secondary outcome: (1) freedom from re-operation	Early mortality for isolated RSE at (<30 days) and 1-year post-operation were 3.8 and 11.6%, respectively RLSE: 30-day and 1-year post-operation mortality were 28.0 and 32.2%, respectively (<i>P</i> = 0.0093) Univariate logistic regression analysis showed significant predictors of early mortality to be: priority of surgery (OR 5.13, <i>P</i> = 0.003); age over 40 (OR 3.24, <i>P</i> = 0.009); left-heart involvement (OR 2.54, <i>P</i> = 0.012) There was no statistically significant influence on early mortality by sex, abscess formation, tricuspid valve reconstruction vs. replacement, IVDA and <i>Staphylococcus</i> infection RLSE group: underwent emergency operations more often (40.7 vs. 5.7%, <i>P</i> < 0.001); were on high-dose inotropes pre-operative (22.2 vs. 3.8%, <i>P</i> < 0.006); showed abscess formation intra-operatively in tricuspid (<i>n</i> = 1), aortic (<i>n</i> = 6) and mitral (<i>n</i> = 3) valves. At 30-day and 1-, 5-, 10- and 20-year survival was 97.4, 95.9, 92.2, 88.6 and 88.6%, respectively; Six (<i>n</i> = 6) patients re-operated on (two in RSE, four in RLSE)	Involvement of the left heart with RSE is statistically significant independent predictor of early and late mortality Combined RLSE showed worse pre-operative condition with complications and significantly poorer prognosis post-surgery
Tleyjeh <i>et al.</i> [4], 2007, USA; Prospective observational study (level IIa)	Single-centre prospective study over 18 years <i>n</i> = 546; adult patients with LSE	Primary outcome: (1) mortality	129 of 546 (23.6%) had surgery at <30 days of diagnosis Mortality: 99 of 417 (23.7%) non-surgical group vs. 35 of 129 (27.1%) surgical group 86 cases (93 pairs of surgical vs. non-surgical cases) matched and propensity scored on diagnosis and follow-up time demonstrated no significant association existed between surgery and mortality (adjusted HR 1.3, 95% CI 0.5–3.1) Surgery was not associated with a survival benefit (adjusted HR 0.92, 95% CI 0.48–1.76)	Valve surgery in LSE found to be not associated with a survival benefit (vs. the non-surgical group) and could be associated with increased 6-month mortality

Continued

Table 1: Continued

Author, date and country; study type (level of evidence)	Patient group	Outcomes	Key results	Comments
Carozza <i>et al.</i> [5], 2006, Italy; Retrospective cohort study (level IIb)	Single-centre retrospective study <i>n</i> = 124, adult patients: 39 IVDA and 85 non-IVDA	Primary outcome: (1) mortality	Tricuspid valve (RSE) significantly more frequent in IVDA cases than in non-IVDA ($P = 0.001$) Left-side involvement in both groups (IVDA and non-IVDA) with higher combined RLSE in the IVDA group Worse cardiac function ($P < 0.002$) and higher rate of embolism ($P = 0.04$) characterized the pre-operative status of IVDA patients	Rate of recurrence was higher in IVDA cases Increasing incidence of LSE in IVDA (61.5%) Hospital and long-term survival did not differ between IVDA and non-IVDA patients due to early aggressive surgical treatment with a prolonged post-operative antibiotic regime
Fernández Guerrero <i>et al.</i> [6], 2009, Spain; Retrospective cohort study (level IIb)	Single-centre retrospective study over 22 years <i>n</i> = 133, <i>Staphylococcus aureus</i> endocarditis	Primary outcome: (1) mortality Secondary outcome: (2) complications	(1) Mortality for RSE was 17 vs. 38% for LSE RSE in IVDA had mortality of 3.7% RSE in infected intravenous catheters had mortality of 82% (OR 0.01, 95% CI 0.001–0.07) LSE mortality was not different for native vs. prosthetic valve infection (OR, 0.65, 95% CI 0.23–1.87) 64 of 133 (48.1%) RSE cases vs. 69 of 133 (51.9%) LSE LSE: the mitral valve was more commonly involved than the aortic valve (61 vs. 30%) (2) 74% LSE patients developed one or more cardiac or extra-cardiac complications vs. 23.4% RSE patients 2–3 complications were associated with an increased risk of mortality (OR 5.59, 95% CI 1.08–28.80 and OR 9.25, 95% CI 1.36–62.72 for two vs. one complication and for three vs. two complications)	Valve replacement improves the outcome following infective endocarditis. LSE is associated with higher complication rate and there is a strong correlation between the number of complications and adverse outcomes
Sy <i>et al.</i> [7], 2009, Australia; Retrospective cohort study (level IIb)	Single-centre retrospective study over 10 years <i>n</i> = 223 with LSE	Primary outcome: (1) mortality	62 of 223 (27.8%) surgical patients had lower mortality vs. 161 of 223 (72.2%) medical patients; follow-up 5.2 years (32 vs. 51%, $P = 0.02$, unadjusted HR 0.54, 95% CI 0.33–0.88, $P = 0.01$) After propensity matching and adjustment there remained a significant benefit for surgery (HR 0.50, 95% CI 0.28–0.88, $P = 0.02$) This decreased with time (HR 0.77, 95% CI 0.42–1.40, $P = 0.39$)	Survivor bias may influence the outcomes following surgery

left-sided endocarditis (LSE) and RLSE. Secondary outcomes of interest were surgical complications.

RESULTS

Zhang *et al.* [2] retrospectively analysed data on 28 patients with isolated RSE. Eighteen patients were females (64.3%) and 10 males (35.7%). Early mortality (<30 days) was 3.6% (1 of 28). The remaining patients were discharged and followed up for at least 6 months. New York Heart Association (NYHA) class decreased in all patients. There was no recurrence of infection during the

follow-up. The authors declare favourable outcomes with surgical management of isolated RSE.

Musci *et al.* [3] compared the outcome of isolated RSE with combined RLSE in a retrospective analysis of 79 patients undergoing 84 operations (median age 43.5 years). Fifty-seven (67.9%) operations were for isolated RSE and 27 (32.1%) for RLSE. Follow-up ranged from 6 months to 19.27 years (median 3.59 years), totalling 448 patient years. There was a significant difference in the survival at 30 days and 1, 5, 10 and 20 years following surgery between the two groups (RSE 96.2, 88.4, 73.5, 70.4 and 57.7% and RLSE 72.0, 50.8, 35.6 and 35.6%; $P = 0.0093$). For combined RLSE, early mortality was significantly higher (18%) compared with isolated RSE (3.8%). The RLSE group had a high

incidence of abscesses found during operation and the RSE group had none ($P < 0.001$). They also required high-dose catecholamines pre-operatively (22.2 vs. 3.85%, $P < 0.006$). Thirty-three per cent of patients ($n = 26$) were intravenous drug abuse (IVDA) with 73% ($n = 19$) having isolated RSE and 27% having RLSE ($n = 7$). However, IVDA was not associated with a significant increase in mortality. The study demonstrated that combined RLSE had a significantly poorer clinical outcome. The authors conclude that the surgical treatment of RSE with or without involvement of the left heart can be performed with favourable results. They acknowledged the limitations of a single-centre retrospective cohort study.

Tleyjeh *et al.* [4] conducted a prospective matched cohort study of 546 infective endocarditis patients diagnosed between 1980 and 1998. Ninety-three pairs were matched between the surgical group ($n = 129$) and the non-surgical group ($n = 417$). Propensity matching resulted in no significant differences between the two groups. Ninety-nine of 417 patients (23.7%) in the non-surgical group died compared with 35 (27.1%) of the surgical group. In the propensity-matched subset, 18 of 93 (19.4%) in the non-surgical group died vs. 27 of 93 (29%) in the surgical group. Surgery was associated with a hazard risk (HR) of 1.3 ($P = 0.56$). Valve surgery was associated with increased 6-month mortality (HR 1.9, $P = 0.11$) when it was treated as a time-dependent covariate. In subgroup analyses, LSE with the involvement of the mitral valve and abscess formation had a statistically significant association with mortality ($P = 0.03$ and 0.003, respectively). *Post hoc* subgroup results demonstrated worse outcomes for LSE.

Carozza *et al.* [5] looked at the outcomes of valve surgery in IVDA. A series of 39 IVDA patients were compared with 85 non-IVDA patients for total follow-up of 717.6 years. RSE involving the tricuspid valve was significantly higher in IVDA cases ($P = 0.001$). This is concordant with other published evidence that IVDA have a higher incidence of RSE than non-IVDA ($P = 0.001$). Although the authors found higher than the expected left-heart involvement in IVDA (61.5%), early and long-term survival were not significantly different between the two groups with no effect on the post-operative mortality.

Fernández Guerrero *et al.* [6] conducted a retrospective review of 133 cases. Patients were divided into RSE ($n = 64$) and LSE ($n = 69$). Overall, 74% of patients with LSE and 23.4% of RSE patients developed at least one complication. Mortality was 17 and 38% for RSE and LSE patients, respectively.

Sy *et al.* [7] reviewed 223 patients admitted with LSE between 1996 and 2006 to assess the potential effects of the survivor treatment selection bias and reduction in mortality post-

operatively after adjustment. Although surgical patients ($n = 62$) had lower mortality (32 vs. 51%; $P = 0.02$) during a median follow-up of 5.2 years compared with medical patients ($n = 161$) with an unadjusted HR of 0.54 ($P = 0.01$), time-dependent analysis (HR, 0.50; $P = 0.02$) showed no significant effect on mortality with surgery. The survivor bias effect was confirmed with the conditional Kaplan–Meier analyses. Excess mortality in the medical group before access to surgery created a false apparent benefit of surgery. The authors conclude that evidence for surgical management is inconclusive, although it could be beneficial in high-risk patients, and when it is expedited in this group of patients within the first 2 weeks in hospital.

CLINICAL BOTTOM LINE

The literature suggests a much better outcome in patients with isolated RSE vs. patients with left-sided or combined RLSE. This is reflected in lower early and late mortality along with fewer post-operative complications.

Conflict of interest: none declared.

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