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ORIGINAL ARTICLE

A Retrospective Review: Significance of Vegetation Size in Injection Drug Users with Right-Sided Infective Endocarditis

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Background Previously described prognostic markers in right-sided infective endocarditis (RSIE) include vegetation size ≥1cm, fever for more than three weeks, cardiac failure and severe sepsis. This study aimed to evaluate effectiveness of medical therapy for vegetations ≥1cm and explore determinants of outcome in a representative population of intravenous drug users (IDUs) at a metropolitan Australian health service.

Methods Retrospective review of consecutive IDUs presenting to our institution with native-valve RSIE (by modified Duke criteria) over seven years (2005-2011). Data recorded included echocardiographic estimation of maximal vegetation diameter (classified as < or ≥1cm). Relationships between vegetation size and specified outcomes of death, septic shock, recurrence and relapse were examined by Chi-squared testing.

Results Of 49 episodes five (10%) were managed surgically and a further four (8%) were lost to follow-up and excluded from the analysis. Of the remaining 40 evaluable medically treated patients (median age 28, range 20-55), 37 (93%) cultured methicillin-sensitive *S. aureus* and all had tricuspid valve involvement. Of 24 with vegetations ≥1cm, three died (mortality 13%) compared with one (6%) in 16 medically treated patients with vegetations <1cm (p=0.63). A Pittsburgh (PITT) bacteraemia score of ≥4 at presentation was associated with a mortality of 24% (four of 17 patients died) compared with 0 in 23 patients with PITT scores <4 (p=0.026).

Conclusion Medical therapy alone can be effective for RSIE when large vegetations are present. However a high sepsis score at presentation may increase risk of death. Larger studies are required to determine optimal indications for early surgical intervention.

Keywords Infective endocarditis • Right-side • Injection-drug-use • Vegetation

Background

Determining optimal management of infective endocarditis in intravenous drug users (IDU) is challenging [1,2]. Poor health-seeking behaviour, non-compliance, economic and psychosocial factors impact not only on outcomes, but also make this a difficult population to study in prospective clinical trials [1–3]. Right-sided infective endocarditis (RSIE) accounts for 10% of all episodes of endocarditis [4,5] but more than 70% of those in IDUs [6] and has a highly specific clinical, epidemiologic, and prognostic profile that differs notably from left-sided endocarditis [7]. Surgery is less

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frequently needed and shorter antibiotic courses have been used [8]. Mortality and morbidity from RSIE are generally lower than from left-sided endocarditis [6,9].

Two previous studies of RSIE in IDUs have suggested vegetation size as a poor prognostic factor, prompting suggestions that it be considered an indicator for early surgical intervention [6,10]. The first was a prospective cohort that evaluated 21 patients presenting to two New York hospitals between 1979 and 1982 [6]. After pooling data from a further 25 patients from previous studies, they showed a higher rate of surgical intervention in those with maximal vegetation diameters ≥1cm (37%) versus those <1cm (0%, p =0.02). However, the use of a therapeutic decision (whether to proceed to surgery or not) as the primary outcome in this study was seriously flawed, being subject to obvious sources of bias (including clinicians potentially basing their decision to proceed to surgery on the size of the vegetation), a methodological flaw described as ''incorporation bias'' [6,11]. More objective clinical endpoints (including mortality, relapse and recurrence) are less subject to this bias. Notably, in the 45 patient presentations described in this study there was only one death (who had vegetation diameter <1cm). A further large retrospective study from a single centre in Spain (1985-1999) demonstrated a higher mortality (odds ratio 10.2, p=0.014) with large vegetations using a cut-off of >2cm. However only 111 out of 220 cases (50%) had evaluable echocardiographic data necessary for study inclusion, raising the possibility of selection bias influencing these results [10].

Given the lack of a robust evidence-base to inform management of RSIE and widespread anecdotal reports of successful medical management of RSIE with large vegetations, we performed a retrospective study of outcomes in management of RSIE in IDU at our institution. We hypothesised that medical treatment can be successful even in those with larger vegetations (≥1cm) and sought to explore associations between other putative prognostic factors and clinical outcomes.

Methods

Study Site

This study was undertaken at Western Health, a network of three hospitals servicing the inner west of Melbourne, a region with the highest rates of IDU in metropolitan Melbourne [12]. Cardiac surgery is not performed at any of the study hospitals, requiring transfer to a quaternary referral centre when this is deemed necessary. At our centre the practice is to administer the entire duration of prescribed intravenous antibiotic therapy under direct supervision in hospital rather than through hospital in the home.

Ascertainment and Data Collection

We used international classification of diseases (ICD)-10 2010 codes I38 and I39 to identify all patients with a diagnosis of infective endocarditis over seven years (January 2005 to December 2011). Following review of the medical record, we included only those with a documented recent history of IDU and who fulfilled the modified Duke's Criteria for ''definite endocarditis'' [13]. Those with concurrent or isolated left-sided endocarditis were excluded. Demographics (including age, sex and ethnicity) clinical (including vital signs at presentation), microbiological (blood culture results) and echocardiography data were recorded from retrospective review of patient records. Data extracted from echocardiography reports included the number of vegetations, their diameter (in two dimensions) and the maximal diameter of the largest vegetation (dichotomised as < or ≥1 for the purposes of analysis). For all patients a PITT bacteraemia score, previously validated tool was calculated based on first-recorded blood pressure, temperature, conscious state, presence of cardiac arrest and whether mechanical ventilation was used [14]. For the purposes of analysis, all patients were dichotomised using a PITT score cut-off of ≥4, where a score of ≥4 has been validated to be associated with poor outcome [14].

Outcomes and Definitions

The primary outcome was all-cause in-hospital mortality. Secondary outcomes included septic shock (SS), relapsed and recurrent endocarditis. Septic shock was defined as hypotension persisting despite adequate fluid resuscitation (defined as infusion of 30ml/kg of crystalloids / albumin equivalent) [15]. ''Relapse'' was defined as any confirmed episode of infective endocarditis within six months of the initial episode where the same organism was isolated on both occasions. [16] ''Recurrence'' was defined as either an episode occurring more than six months after a previous IE (even when the same organism was isolated) or less than six months when a different organism was cultured [16]. The remaining surviving patients who had neither recurrence nor relapse and in whom clinical and microbiological features of endocarditis had resolved at the time of discharge were defined as having achieved successful cure. We also noted whether patients defaulted (left hospital prior to completion of prescribed therapy) and those who underwent cardiac surgery.

Statistical Analysis

Data were recorded in Microsoft Excel and described as proportions, means (±SD) or median (range). Univariate analysis of associations between putative prognostic variables and specified outcome variables were tested using Chi-Squared and Fisher's Exact testing (with P values determined by two-sided testing) or, for continuous variables, Mann-Whitney U test (SPSS v 19.0). Relapses or recurrence occurring in the same individual were treated as separate episodes for the purposes of this analysis. Patients receiving medical therapy and those who had surgery were analysed as separate groups.

Ethical Approval

The study was approved by the Western Health Human Research Ethics Committee (QA2012.23).