Infective endocarditis: trends in the disease and how we study them

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Infective endocarditis (IE) has long fascinated medical students, physicians and surgeons. Unfortunately, unlike many areas in cardiology where large scale randomised trials have helped to shape our management, such studies have not been performed in IE for a number of reasons. These include the infrequency of the disease, difficulties in making a definitive diagnosis, and variability in presentation.

In the most recent European Society of Cardiology Infective Endocarditis Guidelines\(^1\) there are no recommendations based on Level of Evidence A, i.e. multiple randomised clinical trials. Evidence to guide changes in treatment and outcomes has therefore come predominantly from observational studies of increasing sophistication. As in other areas of medicine these have evolved from single centre experiences to larger, multi-centre, national and international cohort studies.

In New Zealand there are a series of cohort studies spanning the last 50 years. In 1981 John Ormiston, John Neutze, Trevor Agnew, Jim Lowe and Alan Kerr reported the Green Lane Cardiology experience (n=177 with mean age 36y) from 1959 to 1976.\(^2\) Subsequently further single centre experiences were reported from South Auckland (n=78)\(^3\), Dunedin (n=62)\(^4\) and Tauranga (n=47).\(^5\)

The first multi-centre New Zealand (NZ) cohort is reported in this edition of the NZMJ by Genevieve Walls, David Murdoch, and colleagues.\(^6\) They participated in the International Collaboration on Endocarditis Prospective Cohort Study (ICE-PCS) which prospectively enrolled 2781 patients at 58 sites in 25 countries between 2000 and 2005 and reported in 2009.\(^7\)

The current study in the Journal reports on the 336 patients (median age 60y) in this study who were enrolled in Auckland, Counties Manukau, Waitemata, Capital and Coast and Canterbury District Health Board hospitals. Notably this is only slightly fewer patients than the sum of all prior NZ cohorts, and when combined with the ICE-PCS procedures to ensure consistent and comprehensive capture, it represents the best snapshot of this disease performed to date in NZ. There is a wealth of clinically relevant data presented.

Although most patients were hospitalised within a month of symptom onset only a minority were hospitalised within a week. Presentation was varied and non-specific with 76% having fever >38°C and only 36% with a new or worsening murmur. Splinter haemorrhages were seen in 19% but other classic manifestations (Osler’s nodes, Janeway lesions) were rare, a finding relevant for teaching medical students. Two thirds had a predisposing abnormal (37%) or prosthetic heart (31%) valves, which is relevant for both prevention and early diagnosis strategies.

Prior rheumatic heart disease was surprisingly uncommon. Blood cultures and confirmatory echocardiography were the mainstay of diagnosis. Blood cultures were
positive in 94% of those cultured. Viridans streptococci were the most common organism closely followed by *Staphylococcus aureus*. No data on antibiotic treatment is available, but a third had surgery. In-hospital mortality was lower than in prior series or in the remaining ICE-PCS cohort at 6%, but 14% of patient had strokes and 17% other systemic emboli.

What has changed? When compared with the historical NZ cohorts several broad trends emerge although these comparisons are limited by several considerations including variable cohort inclusion criteria and changing definitions. Patients with IE are older with more pre-existing degenerative valve disease or prosthetic valve disease. They are more likely to have recent health care exposure (a quarter in ICE-PCS), be diagnosed earlier, and have *Staphylococcus aureus* as the causative organism.

Where we need to know more:

- Are outcomes in IE improving? The in-hospital mortality rate of 6% is lower than in the older NZ series where it was around 20%. Whilst this may represent an improvement in outcomes, the relative roles of earlier diagnosis, improved diagnostic tools (e.g. echocardiography)/treatment or selection bias is unclear. Notably the in-hospital mortality in the international ICE-PCS cohort of 18% was similar to the rate of 16% reported in a review of 26 reports published between 1993 and 2003, suggesting that internationally in-hospital mortality is unchanged. At this time there is not sufficient evidence to conclude that in-hospital mortality has reduced in NZ.

- How is the incidence of IE changing? The current report is the best available multicenter NZ data for the period 2000 to 2005, but it is not comprehensive and there are no other data to allow us to assess temporal trends reliably. If we are to improve outcomes we need more up to date and regular data regarding presentation, treatment variables and outcome.

- Would more aggressive prevention help? Are patients with high risk of IE, in particular those with prosthetic valves getting recommended antibiotic prophylaxis? Are at risk patients getting recommended regular dental reviews?

- What treatment? Recommended treatment is based mostly on prior observational data and clinical “common sense” and embedded in international guidelines. These include considerations such as duration of antibiotic therapy, when to operate in patients with mobile vegetations to prevent stroke, when to operate after embolic stroke has occurred, what valve types to use, how long to treat with antibiotics prior to surgery. Are these recommendations correct and are they being adhered to?

We believe that there is an opportunity to move beyond periodic audits of practice to take a more systematic registry approach to IE. In NZ, under the auspices of the Ministry of Health, electronic national cardiac registries have been implemented in 2013 at all NZ public hospitals which now collect data on all patients having cardiac procedures, including coronary angiography and percutaneous coronary intervention, and will soon include most patients having heart attacks, cardiac surgery and receiving devices to treat cardiac arrhythmias.
These registries are linked to comprehensive NZ national and regional data collections, which include diagnosis, outcomes, laboratory and pharmaceutical data. This combination of registry and national collection data will be a powerful tool to better understand and improve patient management.

Although it is conceivable that IE cases may be able to be identified from national collections through ICD10 codes, it is likely that a registry approach to prospectively collect a core data set on these patients, with linkage to national data sets would be most useful. Such a registry could then serve to monitor incidence, management and outcome across NZ and serve as a source for more in-depth and representative audits.

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**References:**


