Aorto-cavitary fistulae in infective endocarditis: understanding a rare complication through collaboration

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This editorial refers to 'Aorto-cavitary fistulous tract formation in infective endocarditis: clinical and echocardiographic features of 76 cases and risk factors for mortality'† by I. Anguera et al., on page 288

Even in the modern era of antimicrobial chemotherapy and advanced diagnostic imaging, infective endocarditis continues to surprise, frustrate, and perplex, and remains an evolving disease with a persistently high mortality and morbidity. Almost all aspects of the disease, including its natural history, pre-disposing factors, sequelae, and causative organisms are virtually unrecognizable compared with Osler’s initial descriptions from the nineteenth century. In particular, chronic rheumatic heart disease is now an uncommon antecedent, whereas mitral valve prolapse, prior valve replacement, intravenous drug use, and preceding vascular instrumentation have become increasingly frequent, coinciding with an increase in staphylococcal infections and those due to fastidious or atypical organisms. Clinical studies have been slow to adapt to these shifting epidemiological patterns, partly on account of the relative scarcity of infective endocarditis, contemporary series indicating a current incidence of 1.7–6.2 cases per 100 000 patient years. Knowledge of the clinical features and natural history of the disease has therefore relied largely on small, uncontrolled, outdated studies; modern, well-designed studies reflecting current disease patterns are long overdue.

Anguera et al. report a large case series of 76 patients with surgically or autopsy proven aorto-cavitary fistulous tract formation, identified from a multi-centre clinical database of infective endocarditis over a 10 year period. Previously, data on aorto-cavitary fistulae were limited to isolated reports and small case series, and despite its retrospective nature, the study contributes substantially to knowledge of this rare but important complication of infective endocarditis. Within the study, aorto-cavitary fistulae occurred with a prevalence of 1.7%, rising to 5.8% in those with prosthetic valve endocarditis. Fistulae occurred uniquely in aortic valve endocarditis, usually in association with identifiable peri-valvular abscess formation, and with equal distribution between all three coronary sinuses and all four cardiac chambers. Almost all fistulae were successfully identified echocardiographically, though transthoracic imaging appeared unreliable in this regard, and the diagnosis was frequently only made after transoesophageal assessment. Fistulae were identified a median of 25 days after initial symptom onset, and 5 days after hospitalization, by which time moderate or severe aortic regurgitation and significant heart failure were present in over 60% of patients. Surgical correction was undertaken in 87% of the patients, largely in conjunction with aortic valve replacement, and in-hospital post-operative mortality was high at 42%. This adverse outcome was independently related to the pre-operative presence of moderate or severe heart failure and the need for urgent or emergency surgery. In surviving patients, late post-operative prognosis was substantially worse in the presence of residual fistulae.

Although the present study does not demonstrate a major survival advantage associated with surgery, the findings suggest that aorto-cavitary fistulae are a surrogate for severe and extensive tissue destruction and support the need for early intervention. In general, fistulae appear to be associated with peri-valvular abscess...
formation, this being relatively common in aortic valve endocarditis, arising in 10–40% and 56–100% of patients with native and prosthetic valve disease, respectively. Abscesses arise by direct spread of infection, usually into mitral-aortic inter-valvular fibrous tissue, and are often associated with severe valvular regurgitation, congestive heart failure, local aneurysms, and a substantially impaired clinical outcome. In a recent study, Choussat et al. highlighted the excess mortality associated with peri-valvular abscess formation, reporting a mean 3 month actuarial survival of 75% in 233 patients enrolled over a 5 year period from 1989 onwards, the majority of whom underwent surgical treatment. Outcome was independently worse in older patients, and in those with staphylococcal infection, pre-operative renal failure, and concomitant fistula formation.

These findings emphasize the importance of early detection of peri-valvular abscess formation and aorto-cavitary fistulae both in terms of determining the need for early surgical management, and assessing short- and medium-term prognoses. These complications should be suspected in all patients with prosthetic aortic valve endocarditis and in those with native aortic valve endocarditis associated with continuing unexplained sepsis or acute haemodynamic deterioration. Recent guidelines of the European Society of Cardiology emphasize the importance of transoesophageal echocardiography to detect peri-annular extension of infection, allied with subsequent early surgical intervention. The present study of Anguera et al. does not allow estimation of the true screening characteristics of transoesophageal echocardiography for detection of aorto-cavitary fistulae, since transoesophageal imaging was not performed in every patient. Furthermore, it is unclear whether some cases of aorto-cavitary fistulae may have been undetected in surviving medically treated patients. It is fair to conclude, however, that transthoracic imaging alone appears to be inadequate for this purpose, detecting only 53% of proven aorto-cavitary fistulae, compared with a detection rate of 97% by means of transoesophageal imaging. On this basis, transoesophageal echocardiography should be undertaken in all patients with suspected prosthetic valve endocarditis, and in all patients with aortic valve endocarditis associated with staphylococcal infection, haemodynamic instability, or evidence of persistent infection after 7 days of appropriate antibiotic treatment.

The valuable information provided by this study would not have been possible without the establishment of a large multi-centre database—consisting of 4681 episodes of infective endocarditis collated over a 10 year period—and it is likely that further insights into the natural history of infective endocarditis will be gained from this and other collaborations. In this respect, the International Collaboration on Endocarditis (ICE) will almost certainly contribute significantly to both our current and future knowledge of infective endocarditis, allowing the development of new diagnostic and therapeutic strategies. This initiative was devised primarily to unite a worldwide network of investigators in the development of a collaborative database, allowing both the prospective study of infective endocarditis and the undertaking of adequately sized randomized clinical trials. Since its inception in July 1999, 39 sites in 16 countries have become involved in this project headed by an International Steering Committee. The initial merger of existing databases has yielded a primary group of 2200 well-characterized patients with definite infective endocarditis by the Duke criteria, allowing the assessment of regional differences in infective endocarditis. Although databases from specialized units have the potential for referral bias and over-representation of seriously ill patients or those with uncommon disease manifestations, ICE has established an infrastructure which will allow the subsequent prospective recording of all new cases of infective endocarditis, including a minimum standardized clinical dataset, with re-analysis of microbiological samples and echocardiographic studies in core laboratory facilities. This collaboration will provide the platform to allow our understanding of infective endocarditis to expand further and keep pace with changing disease patterns, and to test new pharmacological and surgical approaches to treatment with sufficient power to allow reasoned decision making.

In conclusion, the clinical outcome of patients with aorto-cavitary fistulae is poor, either with medical or surgical therapy. Fistula formation is associated with such extensive peri-valvular damage that even appropriate antibiotic therapy and an early surgical strategy is insufficient to cure infective endocarditis in a high proportion of these patients. The study of Anguera et al. further emphasizes the need to consider early surgery in high-risk patients, particularly those with prosthetic valve endocarditis and abscess formation, and highlights the need for appropriate antibiotic prophylaxis in those at high clinical risk.

References