Chapter

Infective Endocarditis in Aortic Valve Disease

Juan Bustamante-Munguira, Eva María Aguilar Blanco and Angels Figuerola-Tejerina

Abstract

Although infective endocarditis is a rare disease, its incidence has increased over the last years and, despite improved diagnosis and treatment, it has a poor prognosis. The left side is compromised in most cases and underlying valvular heart disease is present in a substantial proportion of cases. We review the incidence, main clinical features and indications for surgery in left-sided native valve infective endocarditis, focusing on the aortic valve.

Keywords: epidemiology, incidence, left-sided endocarditis, surgery

1. Introduction

Infective endocarditis (IE) is an infectious disease generally caused by bacteria that affect the endocardium, mostly the left chambers. Right-sided endocarditis is a different, much less prevalent entity with other clinical and epidemiological characteristics. In this chapter, we analyse left-sided endocarditis, focusing on aortic valve involvement to ascertain frequency of presentation, normal signs and symptoms, treatment and prognosis. Endocarditis frequently develops on a pathological valve. In the western world, the most common valve involvement is aortic sclerosis, that is, a certain degree of stenosis from age-associated valve degeneration. It is important to point out that aortic stenosis is the most prevalent western-world valvular heart disease that requires surgical or interventionist treatment. At 65 years of age, 2–7% of the population present some degree of aortic valve sclerosis, and the condition progresses over time [1–5].

Infective endocarditis is diagnosed based on modified Duke criteria. Their application means that there is an overlap with previously established criteria in large series. In addition, the European Society of Cardiology (ESC) in their Clinical Practice Guides have recently included some changes with respect to the criteria [6, 7], giving more importance to echocardiographic findings and the role of blood cultures. These findings are supported by new radiological tests, mainly CT scan, F-FDG PET/CT and radiolabelled leucocyte single-photon emission CT (SPECT)/CT, and there are a major criteria.

The incidence of IE is known to vary according to the series analysed. This finding might be due to multiple factors. Various epidemiological cohort studies covering prolonged time periods have recently been published, providing key updates to clinical and epidemiological knowledge about IE. What is observed in these series is an increase in IE incidence, greater comorbidity in the patients and a

morbidity-mortality prognosis that has remained substantially the same during the last decades in spite of advances in diagnosis and therapy [8].

2. Incidence

As indicated earlier, infective endocarditis (IE) is a rare disease of poor prognosis, whose incidence has been growing during the last two decades. Various clinical pictures are found within it; fundamentally, it can be divided into endocarditis on native valve or prosthesis, and right- or left-sided endocarditis according to location [1–5]. Another entity has recently appeared that, due to its frequency and severity, is considered separate: health care-associated endocarditis.

Data on the incidence of the disease have been updated in the last few years by the publication of various studies of an epidemiological nature. The most recent ones report an incidence of 3–10 cases per 100,000 inhabitants/year, but there is great geographical variability in the data [1–5, 9]. Over the last few years, several groups have published incidences from local studies that give us a geographical view of the current IE situation. In a study carried out in Spain, Olmos et al. observed an increase in incidence, rising from 2.72 cases to 3.49 cases per 100,000 inhabitants/year during the period analysed (2003–2014) [10]. Likewise, Bustamante Munguira et al. reported increased IE incidence in Spain, which rose from 3.17% in 1997 to 5.56% in 2014 [9]. In Denmark, Erichsen et al. also observed a rise in incidence during 1994–2011, going from 3.93 to 7.55 cases per 100,000 inhabitants a year [11]. In Italy, Cresti et al. found 4.6 cases per 100,000 during the study period 1998–2014 [12]. Representing the Spanish Group Collaboration on Endocarditis (*Grupo de Apoyo al Manejo de Infective Endocarditis en España, GAMES*), Muñoz et al. estimated an annual incidence of 3.5 cases per 100,000 inhabitants during 2008–2012 [13].

The increase in the incidence of the disease is consequently perfectly documented in the different studies mentioned. One of the motives justifying this increase is the appearance of clinical practice-associated endocarditis, as we have pointed out. This type of endocarditis is becoming more and more frequent, reaching up to 25% depending on the series analysed. Other causes of increased IE incidence are population ageing and growth in patient comorbidity. As we indicated earlier, associated with ageing of the population, there is an increase in the prevalence of valvular heart disease, predominantly in the development of degenerative aortic sclerosis and degenerative mitral insufficiency.

Published records from different European countries reveal both increased IE incidence and increased fragility and comorbidity in patients presenting IE. In a study in France, Hoen et al. reported an incidence of 3.1 cases per 100,000 inhabitants a year [14]. In their study on an English population, Dayer et al. analysed the impact that the change in antibiotic prophylaxis recommendations had on the incidence of endocarditis in the United Kingdom. Their study results showed that IE incidence increased from the start of the study in 2000 until its end in 2013. The authors attributed this growth in incidence (as other authors have) to ageing of the population, increased comorbidity and the rise in invasive measures associated with health care attention. However, they also indicated that one of the determining factors in the sample analysed was the change in antibiotic prophylaxis recommendations instituted in March 2008 [15]. In the series reported by Erichsen et al., analysing the population in Denmark, incidence rose throughout the study period, from 3.93 per 100,000 inhabitants a year in 1994–1996 to 7.55 per 100,000 inhabitants a year in 2009–2011 **Table 1**.

Author	Country	Study period	No. of patients	Incidence	Rate of indication for surgery	Reference
Bustamante Munguira	Spain	1997–2014	34,399	3.17% in 1997 and 5.56% in 2014	11.7% in 1997 to 17.8% in 2014	[8]
Erichsen	Denmark	1994–2011	5486	3.93 in 1994–1996 to 7.55 in 2009–2011	None	[10]
Olmos	Spain	2003–2014	16,867	2.72 in 2003 3.49 in 2014	23%	[9]
Fedeli	Italy	2000–2008	1873	4.1 in 2000–2002 to 4.9 in 2006–2008	23%	[15]
Cresti	Italy	1998–2014	167	4.6/100,000	46.5%	[11]
Hoen	France	1999	390	3/100000	49%	[13]
Dayer	England	1 January 2004 to 31 March 2013	19,804	0.11 cases per 10 million people per month	None	[14]
Muñoz	Spain	1 January 2008 to 31 December 2012	1804	3.5 cases per 100,000 inhabitants	44.2%	[12]
Ilhão Moreira	Portugal	2006 and 2014	233		36.9%	[20]

Table 1.
Main epidemiological studies on endocarditis.

These epidemiological studies obtain the information from data in administrative databases gathered when patients are admitted. They are administrative coding systems used for management of both public and private hospitals. This method makes it possible to analyse broad population samples over long period of time, but the fact that it lacks clinical content is a decided weakness. This is the case with the Spanish series, in which the minimum basic data set of the National Surveillance System for Hospital Data in Spain provided by the Spanish Ministry of Health was used [9]. In Italy, Cresti et al. used the Health Care System Hospital Discharge Records database with a primary or secondary International Classification of Diseases 9th Revision IE diagnosis code [12]. The Danish registry published by Reichsen et al. was based on an analysis of the Danish National Patients Registry, which was set up in 1968 [11].

The data published in these studies should be interpreted with certain caution, given the limitations such analyses have. What is clear, and agreed upon in most of the studies, is that the incidence of endocarditis on both native and prosthetic valves has increased.

3. Left-sided endocarditis, with aortic compromise

When we analyse valve involvement, we see that endocarditis is found on left cavities in 90–95% of the cases, while right-side involvement is rare. Native valve endocarditis is far more common (70–80% of the cases) than prosthetic

endocarditis [16]. Multiple valve involvement is infrequent, ranging up to 15–20% of the cases according to the series consulted [17].

According to the majority of authors, the frequency of distribution of mitral and aortic valve compromise follows a similar proportion. There are almost no studies that analyse aortic involvement individually [18]. This is not the case with native mitral valve endocarditis; some authors have analysed it independently, alleging that the embolism rate is greater and that surgical treatment for these patients can be based on valve repair with good short-, medium- and long-term clinical results. However, the majority of the studies do not discriminate according to location, making a global analysis. Nevertheless, there are certain discrepancies in the studies published.

In one of the most numerous series published, with 2781 patients attended in 58 centres from 25 countries, Murdoch et al. observed that the mitral valve was compromised in 41.1% of the cases, while the aortic valve was in 37.6% [19]. In a series of 945 consecutive episodes, Olmos et al. found no statistically significant differences between the two locations [20], while Muñoz et al. observed that the mitral valve was involved in 44.8% of the cases and the aortic in 47.2% [13].

There are discrepancies in the literature. In a French study with 303 patients with left-sided endocarditis, Lung et al. found a higher incidence of mitral valve compromise than of aortic (49.2 vs. 32.3%) [17]. At the opposite extreme, we find the results of the study by Ilhão Moreira et al.; in a series of 233 patients followed for 8 years, they observed that aortic involvement was more frequent (55.7%) than mitral (38.2%) [21].

As we have pointed out, it is important to remember that endocarditis develops on pathological valves in one-fourth of the cases, with valve degeneration being the most frequent underlying condition [10, 13, 19]. In some series, this percentage is even higher than 35% [12]. It bears repeating that epidemiological aspects are important in interpreting study results.

4. Specific clinical profile of left-sided infective endocarditis with aortic valve compromise

Independently of valve involvement, IE presents a shared clinical picture characterised by symptoms of systemic infection. Some of these are more frequent based on the location involved. The most common symptom is fever, which can be present in 90% of the patients. Heart failure is also highly frequent. Associated constitutional symptoms, such as weight loss, asthenia and anorexia, are also found. There are differences in the percentage of presentation in some of the complications.

4.1 Embolism

Aortic valve compromise does not involve embolic risk greater than that of the compromise of other valves. Its incidence depends on the size of the vegetation and of the microorganism causing the infection. The frequency of embolism in aortic endocarditis is, if anything, less than that of mitral endocarditis. Systemic embolism is estimated to occur in 22–50% of the cases; most embolisms affect the central nervous system, while other locations such as the spleen or kidney are less common [7, 22].

There is a certain variability in the results reported by different authors. Vilacosta et al., in a series of 211 patients with left-sided endocarditis, found a correlation between vegetation size and embolism for the patients with mitral valve endocarditis but not in the case of the aortic valve [23]. However, Hubert et al., in

their study analysing 1022 patients, found no correlation with location, but did find a statistically significant association with vegetation size [24]. Likewise, in their study including 1456 patients, Rizzi et al. found no association with location but did find ones with vegetation size and with the causal agent being *S. aureus* [25].

When the relationship between microorganism and embolism is analysed, it can be observed that the results reported are also different according to the series considered. Vilacosta et al. indicated that they did not observe any differences based on the type of microorganism. This aspect is controversial, given that clinical practice guidelines and some authors point out that there is a relationship between endocarditis caused by specific microorganisms and the likelihood of developing embolic phenomena.

Various risk scores have been developed in relation to this complication for calculating the probability of developing embolisms. Among these, the Italian and French scales are the most utilised. In a study on 167 patients, Cresti et al. did not observe any differences between aortic and mitral locations in the case of native valve endocarditis [12]. Hubert et al., in a sample of 1022 patients, likewise found no relationship with location; however, they did observe an association with vegetation size and when the endocarditis was caused by *S. aureus* [24].

4.2 Atrioventricular block

Aortic valve compromise can progress with symptoms of aortic insufficiency. It may trigger heart failure if inception is acute, while other common symptoms are embolism and rhythm disorders. Within rhythm alterations, the most frequent complication is atrioventricular block from conduction system disruption; its incidence ranges from 1 to 15% depending on the series. This complication worsens the prognosis, principally because it is the consequence of an annular compromise reflecting the extension of the infection. It is more frequent when staphylococci are involved. In these cases, it is important to delay the pacemaker implantation and always be sure that the infectious process is under control, in order to avoid the risk of infection of the pacemaker. There are also differences in the literature as to the involvement of the aortic valve compared with the mitral, although some authors report similar figures [26].

4.3 Heart failure

Heart failure is the most frequent complication of patients with IE. It is the main factor that predicts mortality at 30 days [18]. The presence of heart failure is more common when the valve compromise is aortic. The mechanism that explains its appearance is the occurrence of valve dysfunction. It is currently the most common cause for indicating surgery [27, 28].

5. Indication for surgery in left-sided aortic valve endocarditis

The reported rate for indication for surgery also varies considerably according to the studies published. Surgery indication is influenced by the characteristics of the centre, which are basically determined by the availability of multidisciplinary teams in patient assessment. The range is very wide, going from very low figures of 9.6% of the patients with endocarditis [12] up to the rates of indication reported by Lung et al. of 73% of the patients attended (with surgery being performed in 46% of the cases) [17]. Analysed by location, aortic endocarditis required surgery in 38.2% of the cases, when aortic valve compromise was 17% lower.

Very few authors study surgery of the aortic valve independently of that of the mitral valve. The majority of the series combine the two in their analyses, considering them the same process, left-sided endocarditis. It should be remembered that there are some differences between the two locations with respect to clinical repercussion, the possibility of generating embolism and the appearance of rhythm disorders.

Bustamante Munguira et al., analysing the Spanish series during the time period 1997–2014, found that the percentage of patients requiring surgery increased over the course of the study, reaching 15.7% of the patients [9]. These figures are much lower than those of the European registry, in which the Euro Heart Survey reported a rate of 58.7% [29]. Once again, the most logical explanation for this finding lies in the establishment of protocols for and in the treatment of endocarditis with the attention of these patients being given by units of reference.

There are intermediate ranges between these figures. One example is the study by Murdoch et al. (with 2781 patients attended in 58 centres in 25 countries), in which 48.2% of the patients underwent surgery [19]. In this study, important differences based on the type of centre were also observed in the percentage of patients that received an indication for surgery, with ranges of 63.4–37.1% ($P < 0.001$). In the series reported by Olmos et al., 23% of the patients required surgery [10]; the percentage was greater in the case of the centres with cardiac surgery (35.5%). A limitation of this study was that it did not analyse the percentage of aortic patients compared with other patients having problems in different locations.

In the study published by Moreira et al. (analysing 233 patients for 8 years), 57% of the patients received the indication for surgery, and the patients were operated in 36.9% of the cases. In that study, the frequency of indication for surgical treatment was analysed according to location. It was found that operations were performed in 64% of the cases of aortic endocarditis, while the percentage was only 31% in the cases of mitral endocarditis [21].

6. Conclusions

Infective endocarditis has increased its frequency of appearance as a consequence of ageing of the population and of the number of invasive procedures giving rise to the appearance of the condition called health care-associated endocarditis. Left-sided cavities are compromised far more frequently than right-sided ones. However, there is no clear difference between the percentage of aortic and mitral valve involvement. Indications for surgery have gradually increased, but the result considered in terms of morbidity-mortality has not improved despite advances in techniques and postoperative care. It is hard to find studies in which aortic valve compromise is analysed individually, because most studies focus on studying left-cavity endocarditis and consequently produce a global evaluation.

Conflict of interest

None declared.

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