



EDITORIAL COMMENT

Infective endocarditis in Portugal – another piece added to the puzzle



Endocardite infecciosa em Portugal – outra peça adicionada ao *puzzle*

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The reported low incidence of infective endocarditis (IE) ranging between 3 and 10 per 100 000 people¹ is probably underestimated, as a diagnosis is often challenging. A temporal increase has been documented in some European countries such as United Kingdom (UK),² Germany³ or Denmark.⁴ Recently, an analysis on IE in the Portuguese population⁵ over the last decade identified a similar trend. An aging population, an increasing rate of valve prosthesis and intracardiac device carriers, as well as the survival to adulthood of children with congenital heart disease all contribute to explaining the noted trends. Concomitantly, the extraordinary evolution in the imaging and microbiologic medical adjuvant techniques improve diagnostic ability in a clinical setting. Medical progress can also be a drawback, with an increasing rate of invasive medical procedures. Additionally, the impact of antibiotic prophylaxis restrictions defended by scientific guidelines since 2007⁶ and 2009¹ on IE incidence is unclear. Concerns about physician compliance and evidence obtained mainly from retrospective observational studies do not enable a causal association to be

made, even though an association has been found in the UK,⁷ Netherland⁸ and North America.⁹

Despite substantial improvements in its management (including antibiotic regimens and surgical intervention), complications and in-hospital mortality in IE continue to be substantial. This is in clear contrast to the trends observed with other cardiovascular entities such as acute coronary syndromes. Even though a significant variation exists among sites and countries, overall, in-hospital mortality is around 20%.¹⁰

Survival rates are highly dependent on the infectious agent, comorbid and clinical conditions. Onset to diagnosis time as well as onset to antibiotic/surgery time have been shown to have a significant impact on the outcome. Local team experience¹¹ is a keystone, with essential collaboration between different specialties including cardiology, cardiac and non-cardiac imaging, internal medicine, infectious disease, microbiology and cardiac surgery warranted. The effect of an endocarditis team on survival has been shown by several groups and is indicated on the most recent scientific guidelines¹² as an added value to clinical success.

In the last two decades, three major multicentric international prospective registries on infective endocarditis have been conducted – see Table 1. The most recent, EURO-ENDO¹³ was conducted after the publication of the most

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Table 1 Main results from prospective multicentric registries on IE.

	Euro Heart Survey ¹⁴	ICE-Pro prospective ¹⁵	EURO-ENDO ¹³
Period	2001	2000-2005	2016-2018
Centers	92	58	156 (Portugal – 5)
N (patients)	118	2781	3116
Age – average, years old	56	57.9	59.2
Female (%)	NA	32	31.1
Native/Prosthetic/Cardiac	74/26/-	72/21/7	56.6/30.1/9.9
Device-Related IE (%)			
Community/Nosocomial (%)	NA	71/14	65.6/32.9
Most frequent infectious agents	Staphylococcus aureus (33%)	Staphylococcus aureus (31%) Viridans group streptococci – South America	Staphylococcus (44%)
Blood cultures negative (%)	14	11	21
Cardiac surgery (%)	52	48	51
In-hospital death (%)	12.6	18	17.1

ICE: International Collaborative Endocarditis; NA: not available.

recent guidelines by the European Society of Cardiology in 2015. Portugal was a participant country and included 59 patients. When comparing the latter with the first registries, EURO-ENDO displayed older patients, with a higher rate of prosthetic or cardiac device-related IE. The surgical rate was similar and involved half the cohorts. Finally, a higher mortality rate was noted compared to the Euro Heart Survey.

In the last decade, the Journal has published three observational retrospective studies on IE patients hospitalized in Portuguese institutions, all from tertiary centers.^{16–18} Most national published observational studies derive so far from centers with cardiac surgery on site.¹⁹ In addition, all studies failed to address the issue of the impact of antibiotic prophylaxis restrictions.

In the current the Journal, a descriptive and inferential analysis of all patients admitted with IE between 1998 and 2013 at Hospital de Braga (a level II hospital with no cardiac surgery onsite) was undertaken by Apolinário et al.²⁰ One hundred and seventy-three patients were identified. The authors describe the main clinical characteristics including presentation, comorbidities and main complications found, imaging and microbiologic findings as well as a management strategy. The main outcomes considered were cardiac surgery during the index episode and in-hospital all-cause death. They compare all variables in patients admitted before or after 2007, when the issue of antibiotic prophylaxis restrictions was first defended by international scientific guidelines. The first group included 93 patients (53.8% of the total cohort).

The following findings deserve to be highlighted in the present editorial:

1. Patients admitted with IE are older which accounts for a higher rate of comorbidities and structural heart disease – this is a similar result to other international series.
2. A significant proportion had cardiac valve prosthesis or cardiac device-related IE (18% before 2008 and 34.6% in the second group) – aging of the population and the increasing prevalence of degenerative valve disease, particularly aortic stenosis and mitral regurgitation have contributed to a rise in prosthetic cardiac valve and

pacemaker implantations in developed countries with a repercussion on the rate of related IE.

3. Negative blood cultures cases rose reaching up to 23% in the second group, which is an obstacle to an early diagnosis of these patients.
4. *Staphylococcus aureus* is the most prevalent agent as in other contemporary series. Additionally, the emerging role of *Enterococcus* as an important infectious agent.
5. The rate of patients who underwent cardiac surgery significantly increased after 2007 with an overall rate of 34%, which is comparable to the one displayed by Marques et al.²¹ from Hospital Garcia de Orta (32.8%), inferior nonetheless to the ones from level III Portuguese hospitals.^{16,17} Nevertheless, surgical rates in most Portuguese observational series continue to be inferior to the ones reported in the international registries (see Table 1).
6. The in-hospital all-cause mortality (14.5%) is significantly inferior to the ones reported by most Portuguese observational studies.¹⁹ Also, a non-significant increase in in-hospital mortality was noted in the latter group. Hospital clustering levels, with more complex patients being referred to tertiary hospitals, leading to a referral bias could partially account for these findings. Long term all-cause death, on the other hand, revealed a significant rate of 38% and 47% at one and five years follow up. Regardless of all medical progress, IE continues to be a fatal disease.

In Portugal, physician compliance with guidelines regarding IE prophylaxis is in general an undetermined issue. Therefore, the described analysis by the authors serves the purpose of a temporal testimony more than a causal result of antibiotic prophylaxis restrictions on the outcomes.

Regardless of the limitations acknowledged by the authors, this is undoubtedly an important piece being added to the puzzle, on behalf of the less represented national non-tertiary hospital centers. Further national research is needed, particularly in a disease where diagnosis is dependent on local multidisciplinary expertise (clinical, imaging and microbiology) and the complex management should be

individualized and not “a one size fits all”. From my perspective, it is crucial to further understand how early we are diagnosing IE in our centers, where the obstacles are, how functional the referral circuits to expert centers are, as well as access to multidisciplinary input (via IE heart team) and early corrective surgery. This national evidence will certainly reveal points for technical and organizational improvement that we as physicians should use to achieve a better outcome in this complex disease.

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Conflicts of interest

The author has no conflicts of interest to declare.

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