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Letter to the Editor

Infective endocarditis in patients with cardiac implantable electronic devices: Impact of comorbidities on outcome☆

We read with interest the paper by Armiñanzasa et al., recently published in the European Journal of Internal Medicine [1]. The authors provided an important analysis of a large, prospectively collected, cohort of patients with possible/definite infective endocarditis enrolled in the Spanish Collaboration on Endocarditis—Grupo de Apoyo al Manejo de la Endocarditis infecciosa en España (GAMES) registry maintained by 39 Spanish hospitals from January 2008 to April 2015. According to this analysis an age ≥ 80 years, a Charlson Comorbidity Index score ≥ 3, and absence of surgical reparation, were independent predictors of mortality. Consequently, the authors suggest to carefully consider these parameters in each patient at the time of multidisciplinary evaluations targeted to a proper assessment of the patient-specific risk/benefit ratio of interventions directed to treat infective endocarditis.

Notably, the authors reported that a significant proportion of the included patients (12%) presented a cardiac implantable electrical device (CIED), and in many of them this was the only site of infection. Actually, these patients represent a peculiar population, not only for the different type of prosthesis (aimed at treating arrhythmias and heart failure) but also in view of the pathophysiology of the infection (mainly related to CIED re-interventions) [2] and in view of the need for a specific therapeutic invasive management, based on percutaneous removal of all the CIED system (i.e. the device and all the leads). For this reason, we believe that this topic deserves a series of specific considerations. Indeed, CIED-related infections are an emerging clinical problem in the last years, leading to an high burden of mortality and morbidity [3]. As reported by current guidelines [4,5], the cornerstone for the treatment of CIED-related endocarditis is the complete extraction of the device system (along with optimal antimicrobial therapy), usually performed via a percutaneous approach. This approach is based on data indicating that a conservative management with medical therapy alone is associated with worse and severe outcomes [4]. In the paper by Armiñanzasa et al., it has been reported that a significant percentage of patient with endocarditis and an indication for surgery did not undergo the invasive treatment (in view of comorbidity or operator judgement) [1]. However, it is not clear if the lack of an interventional approach included CIED carriers, who have a specific indication for hardware removal in case of endocarditis, or if it was limited to patients who were potential candidates to surgery for valvular heart disease. In view of this, we would be really interested to have further details on the overall percentage of patients with CIED-related endocarditis actually treated with lead extraction and on associated patient outcomes.

Notably, also in the specific setting of CIEDs we previously reported that comorbidities beyond infection were significant predictors of long term survival, also independently on effective removal of all the implanted hardware [6]. Chronic kidney disease, in particular, seems to play the principal role as promoter of both CIED infections and post-extraction mortality. As reported in a prospective study, chronic kidney disease (defined as a glomerular filtration rate < 60 ml/min) is an independent predictor of mortality after percutaneous lead extractions performed for CIED-related infection, with an hazard ratio of 4.7 (1.7–12.5) [7]. Consistent findings were previously reported in a larger, retrospective cohort where chronic kidney disease resulted associated with outcome at multivariate analysis (hazard ratio 1.94; 1.37 to 2.74) [8]. For this reason we agree with Armiñanzasa et al., that comorbidities should be taken into account in any risk stratification for adverse outcomes, either before implantation of any prosthesis or after development of an infection related to an implanted device/prosthesis. At this regard, the stratification of patients with CIED-related infection, prior to CIED removal, according to a different comorbidity scale proposed and validated by Shariff et al. [9], allowed to identify patients at higher risk of mortality after lead extraction [6], and therefore should play a role in the assessment of predictors of mortality in this population.

Echocardiography represents the gold standard and the most widely adopted imaging technique for the diagnosis of endocarditis, as confirmed in the cohort analysed by Armiñanzasa et al. [1]. Previously confirmation of the suspect of endocarditis by means of echocardiographic techniques (transoesophageal echocardiogram) was found to have prognostic implications [10] and to be a cornerstone for the follow-up after intervention [11]. However, there is a growing interest in the adoption of ^{18}F-FDG PET for the diagnostic work-up of endocarditis, particularly for the evaluation of patients with prosthetic valves and cardiac devices. In the study reported by Armiñanzasa et al. it is noteworthy the adoption of ^{18}F-FDG PET and the role of modified Duke criteria in predicting long term mortality [1]. We previously described a poor association between the Duke classification (negative, possible and definite endocardial infection) and long-term prognosis after extraction of infected CIEDs. However, the different scenario of valve-related endocarditis versus CIEDs-related infections could provide different results, especially in view of the different mechanisms of infection. Notably, we described a different prognostic profile of patients with CIED infection comparing patients with vs. without involvement of CIED pocket as documented by visual inspection or ^{18}F-FDG PET scan [12]. In our view this seems to reflect a different

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pathophysiologic mechanism: metastatic infection rather than infection spreading from the pocket.

According to the abovementioned considerations we think that in the group of patients reported by Armiñanzasa et al. [1] it could be useful to assess the impact of the treatments specifically applied in CIEDs- associated endocarditis with respect to the remaining cohort and consider the specific contribution of the different items included in the Charlson Comorbidity Index along with the overall score. Moreover, the adoption of ^{18}F-FDG PET scan for diagnostic purposes should be object of consideration.

Conflict of interests

No conflicts of interest to declare for all the authors.

References

[1] Arminanzas C, Farinas-Alvarez C, Zarauza J, Munoz P, Gonzalez Ramallo V, Martinez Selles M, et al. Role of age and comorbidities in mortality of patients with infective endocarditis. Eur J Intern Med 2019;64:63–71. https://doi.org/10.1016/j.ejim.2019.03.006. Epub 2019 Mar 21.

[2] Diemberger I, Parisi Q, De Filippo P, Narducci ML, Zanon F, Potenza DR, et al. Detect long-term complications after ICD replacement (DECODE): rationale and study design of a multicenter Italian registry. Clin Cardiol 2015;38:577–84.

[3] Diemberger I, Biffi M, Martignani C, Boriani G. From lead management to implanted patient management: indications to lead extraction in pacemaker and cardioverter-defibrillator systems. Expert Rev Med Devices 2011;8:235–55.

[4] Habib G, Lancellotti P, Antunes MJ, Bongiorni MG, Casalta JP, Del Zotti F, et al. ESC Guidelines for the management of infective endocarditis: the task force for the management of infective endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). Eur Heart J 2015;2015(36):3075–128.

[5] Kusumoto FM, Schoenfeld MH, Wilkoff BL, Berul CI, Birgersdotter-Green UM, Carrillo R, et al. HRS expert consensus statement on cardiovascular implantable electronic device lead management and extraction. Heart rhythm. 2017 2017;14:e503–51.

[6] Diemberger I, Migliore F, Biffi M, Cipriani A, Bertaglia E, Lorenzetti S, et al. The "subtle" connection between development of cardiac implantable electrical device infection and survival after complete system removal: an observational prospective multicenter study. Int J Cardiol 2018;250:146–9.

[7] Diemberger I, Biffi M, Lorenzetti S, Martignani C, Raffaelli E, Ziacchi M, et al. Predictors of long-term survival free from relapses after extraction of infected CIED. Europace. 2018;20:1018–27.

[8] Habib A, Le KY, Baddour LM, Friedman PA, Hayes DL, Lohse CM, et al. Predictors of mortality in patients with cardiovascular implantable electronic device infections. Am J Cardiol 2013;111:874–9.

[9] Shariff N, Eby E, Adelstein E, Jain S, Shalaby A, Saba S, et al. Health and economic outcomes associated with use of an antimicrobial envelope as a standard of Care for Cardiac Implantable Electronic Device Implantation. J Cardiovasc Electrophysiol 2015;26:783–9.

[10] Vicent L, Saldivar HG, Bouza E, Munoz P, Cuerpo G, de Alarcon A, et al. Prognostic implications of a negative echocardiography in patients with infective endocarditis. Eur J Intern Med 2018;52:40–8.

[11] Garcia-Granja PE, Lopez J, Vilacosta I, Sarria C, Ladron R, Olmos C, et al. Surgery changes prognosis in infective endocarditis: the importance of post-surgical clinical evolution. Eur J Intern Med 2018;55:52–6.

[12] Diemberger I, Bonfiglioli R, Martignani C, Graziosi M, Biffi M, Lorenzetti S, et al. Contribution of PET imaging to mortality risk stratification in candidates to lead extraction for pacemaker or defibrillator infection: a prospective single center study. Eur J Nucl Med Mol Imaging 2019;46:194–205.

Igor Diemberger[a], Stefano Lorenzetti[a], Marco Vitolo[b], Giuseppe Boriani[b,*]

[a] *Institute of Cardiology, Department of Experimental, Diagnostic and Specialty Medicine, University of Bologna, S.Orsola University Hospital, Bologna, Italy*

[b] *Cardiology Division, Department of Biomedical, Metabolic and Neural Sciences, University of Modena & Reggio Emilia, Modena University Hospital, Modena, Italy*

E-mail address: giuseppe.boriani@unimore.it (G. Boriani).

[*] Corresponding author.