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EDITORIAL

Long-term follow-up of patients with implantable cardioverter defibrillators in Greece: The Cretan Registry



In the current issue of the *Journal*, Kanoupakis, et al.¹ present long-term data on mortality and utilization of device therapies in their cohort of primary and secondary prevention implantable cardioverter defibrillator (ICD) recipients on the island of Crete. This is an important registry including data from the only ICD implantation center in Crete, and these data are sufficiently robust to be considered representative of Greece. Actually, the number of ICD implantations performed at Heraklion University Hospital during the past five years exceeded the respective number of ICD implantations performed per million population in Greece, as evidenced by the published EHRA White Books.² Moreover, the indications, clinical outcomes, delivered therapies and adverse events identified in this cohort of ICD recipients were in accordance with those reported by other international centers.

The ICD is the most effective therapy currently available to prevent sudden cardiac death (SCD).^{3,4} ICD implantation rates are increasing worldwide.⁵ This increase was driven by secondary prophylaxis ICDs until 2006 and primary prevention ICDs thereafter.^{5,6} The Cretan Registry is in accordance with European Guidelines and current cardiovascular practice. Large randomized trials have demonstrated that ICD implantation was associated with improved survival through the achievement of primary and secondary SCD prevention. The long-term efficacy of ICD treatment was supported by the findings of an extended 11-year follow-up of a subgroup of the secondary prevention population included in the Canadian Implantable Defibrillator Study (CIDS), which enrolled patients with sustained ventricular arrhythmias combined with hemodynamic instability or reduced left ventricular ejection fraction (LVEF).⁷ Long-term ICD treatment (8

years of follow-up) was also deemed effective in the primary prevention population included in the second Multicenter Automatic Defibrillator Implantation Trial (MADIT-II).⁸ These randomized trials were performed in defined patient populations and, therefore, may not be representative of everyday clinical practice. The few long-term survival outcomes that have been reported in patients outside the clinical trial setting include those identified in a cohort of 270 patients with an ICD implanted for life-threatening arrhythmias in the United States in the early 1980s, and this study reported all-cause mortality rates at 1 and 5 years to be 8% and 26%, respectively.⁹ Similar mortality rates were reported by the ALTITUDE project, which included data from >2,000 centers across the United States, with mortality rates of 8% identified at 1 year (12% for cardiac resynchronization therapy-defibrillator patients) and 32% identified at 5 years among ICD patients.¹⁰ The Australian Registry reported 74% and 53% survival rates at 5 and 10 years, respectively.¹¹ Similar findings were reported by Leiden University,¹² the Danish,⁶ and the current Cretan registry.¹

The incidence of all-cause mortality in the Cretan registry was observed to be significantly higher in the group of secondary prevention patients than the group of primary prevention patients over a mean follow-up period of 11.2 ± 7.8 years.¹ Similar findings were reported by Leiden University after an 8-year of follow-up of their ICD recipients,¹² whereas comparable all-cause mortality trends in the two groups were observed during the first 3 years of follow-up.^{12,13}

Moreover, secondary prevention ICD recipients in Crete were found to have a higher prevalence of appropriately delivered therapies relative to primary prevention ICD recipients.¹ Similar findings have been reported previously.^{12–14} Appropriate ICD therapies (particularly delivered shocks) were identified as significantly

Peer review under responsibility of Hellenic Cardiological Society.

<http://dx.doi.org/10.1016/j.hjc.2016.09.002>

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associated with increased long-term mortality rates in the secondary prevention ICD group. This observation was of considerable significance, as a sizeable proportion of patients with ICDs received appropriate intervention during follow-up. Indeed, data suggest that a total of 20–35% of heart failure (HF) patients who receive an ICD for primary prevention and 35–45% of HF patients who receive an ICD for secondary prevention of SCD are predicted to receive an appropriate shock for a life-threatening arrhythmia within 1–3 years.^{15,16} Until now, efforts have been directed at preventing both appropriate and inappropriate ICD shocks. Several therapeutic options that may be used to achieve a reduction in ICD shocks are available, including medications, ICD reprogramming, and prophylactic catheter ablation before ICD implantation.¹⁷ An important meta-analysis comparing ICD therapy reduction programming and conventional programming reported reduction programming to be associated with a significant reduction in mortality.¹⁸ However, this decrease was mainly driven by a reduction in inappropriate, rather than appropriate, shocks. Nevertheless, the increased mortality observed in association with ICD delivered therapies has been considered to occur independent of the modality of ICD intervention,¹⁹ suggesting a negative effect of ventricular arrhythmia episodes on mortality risk or, alternatively, that ventricular arrhythmias may be a marker of more advanced heart disease. Therefore, we should still seek to reduce unnecessary ICD therapies and their associated adverse psychological effects. However, in the case of increased risk after ICD shock, it is the occurrence of an associated arrhythmia in a vulnerable myocardium or vulnerable patient that likely explains the increased cardiovascular risk and not the shock itself.

Important ICD registries, such as the one described by Kanoupakis, et al.,¹ may significantly enhance our understanding of the validity and limitations of ICDs^{20,21} and serve as a solid basis for the deployment of long-term nationwide reports.

Conflict of interest

The authors have no potential conflict of interest to declare.

Funding

None.

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Available online 17 September 2016