Cardiac magnetic resonance left atrial volumes and function to predict appropriate device therapy and death

Ming-Yen Ng^{1,2} · Jessica Poon^{1,3} · Andrew Li⁴

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Editorial Commentary

Sudden cardiac death (SCD) remains an important cause of mortality worldwide. Several landmark trials [1–3] have shaped current guidelines [4, 5] to recommend the implantation of implantable cardioverter defibrillator (ICD) in patients with reduced left ventricular ejection fraction (LVEF) < 35% for primary prevention. However, LVEF being the sole determinant of guiding ICD implantation has proven to be inadequate in multiple subsequent studies. Studies have shown the majority of patients experiencing SCD have LVEF > 35% [6, 7], and a high proportion of patients implanted with ICDs do not receive an ICD shock even before death [8]. In terms of patient outcomes, the 2016 DANISH trial [9] showed that prophylactic ICD implantation in patients with symptomatic non-ischaemic heart failure and LVEF < 35% was not associated with a significant reduction in mortality. Thus the search for additional parameters to LVEF to better guide ICD placement is ongoing.

In recent years, cardiac magnetic resonance (CMR) has been established as the gold standard for left ventricular volume and systolic function due to its high reproducibility amongst observers and lack of geometric assumptions in volume and LVEF quantification [10]. Therefore, CMR quantification of left atrial size/volume and left atrial emptying fraction is regarded as an accurate tool for left atrial size and function assessment. Previous CMR studies have

demonstrated associations between left atrial size/ function with atrial arrhythmias, impaired LV diastolic function, abnormal left ventricular filling pressures and adverse cardiovascular outcomes [11, 12]. In two CMR studies performed by Rijnierse et al. [13] and Lydell et al. [14], left atrial ejection fraction (LAEF) were both shown to be predictive of appropriate device therapy for ventricular arrhythmia with or without sudden cardiac death. However, both papers had relatively small numbers of primary end-points (ie. 62 and 35 end-points respectively). Furthermore, both papers did not have multivariable Cox regression models that incorporated LVEF. In Rijnierse et al.'s [13] paper, one of the multivariable models included LGE with both LAEF and LGE remaining statistically significant. Therefore, there is a lack of clarity whether LA volume and function replaces or is additive in value to LVEF and LGE as independent determinants of ventricular arrhythmias following ICD implantation.

This issue has been partly addressed by Gong et al. [15]. The authors conducted a retrospective, multi-centre observational cohort study of 392 patients with ischaemic and non-ischaemic cardiomyopathy who underwent CMR prior to primary or secondary prevention ICD implantation. The primary outcome was a composite of independently adjudicated appropriate ICD shock or all-cause death. During a median follow-up time of 61 months, 140 (35.7%) experienced an appropriate ICD shock or death. Higher maximum LA volume index (maxLAVi), higher minimum LA volume index (minLAVi), and lower LAEF were associated with greater risk of appropriate ICD shock or death in univariate analysis. However, in multivariable analysis, LAEF and maxLAVi were not independent predictors of the primary outcome.

The apparent differences in concluding the usefulness of LA volume and function to predict appropriate ICD shock or mortality of this study in contrast to the previously mentioned publications might stem from three intrinsic differences. Firstly, all three studies [13–15] agree that LAEF

✉ Ming-Yen Ng
myng2@hku.hk

¹ Department of Diagnostic Radiology, The University of Hong Kong, Hong Kong, SAR, China

² Department of Medical Imaging, The University of Hong Kong-Shenzhen Hospital, Shenzhen, China

³ Department of Medicine, Ruttonjee and Tang Shiu Kin Hospitals, Hong Kong, SAR, China

⁴ Department of Medicine, United Christian Hospital, Hong Kong, SAR, China

and maxLAVI are statistically significant for predicting appropriate device therapy. However, in Gong, et al.'s study [15], additional variables such as age, primary/ secondary prevention, LVEF and LGE were incorporated into the multivariable regression analysis providing further detail that LAEF and maxLAVI are unlikely to be significant predictors of appropriate ICD therapy or death when included with more established variables. Secondly, this study was different from the previous two studies by including patients with ICD inserted for secondary prevention in addition to those inserted for primary prevention. The lack of significance in the multivariate regression of primary or secondary prevention also indicates that LAEF and maxLAVI are unlikely to have a role in patients with secondary prevention ICDs. Thirdly, the primary endpoints of these studies were different. This study included the harder end-point of all-cause mortality which differentiates it from the other two studies. Rijnierse et al. [13] and Lydell et al. [14] used appropriate device therapy for ventricular arrhythmia with or without sudden cardiac death as the primary end-points. Appropriate device therapy as an end-point is influenced by ICD programming as part of standard clinical care. ICD shocks, even in the appropriate context to terminate genuine ventricular arrhythmias, can be effectively and desirably reduced by programming manoeuvres such as prolonged ventricular fibrillation or tachycardia detection and anti-tachycardia pacing. Therefore, appropriate ICD therapy could not be regarded as clinical equivalence of life-threatening arrhythmia or mortality.

Nevertheless, the negative finding in this study has helped further our understanding on potential CMR variables which may help predict which patients would likely receive appropriate device therapy. Further research beckons to better identify which patients would benefit most from ICD implantation.

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Declarations

Conflict of interest Ming-Yen Ng has received funding from Bayer and Circle Cardiovascular Imaging. Jessica Poon and Andrew Li have no conflict of interest to declare.

Ethical approval This editorial comment is compliant with ethical standards. Ethics approval is not applicable to this manuscript.

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