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Non-ischemic cardiomyopathy in the elderly: A shocking conundrum

1. Limitations of the guidelines

The SCD-HeFT trial (Sudden Cardiac Death in Heart Failure Trial) in 2005 randomized patients with ischemic and non-ischemic heart failure to drug therapy with amiodarone and a single chamber implantable cardio-defibrillator(ICD). In a population consisting of 48% non-ischemic cardiomyopathy patients over a median follow-up of 45.5 months, ICDs reduced overall mortality by 23%. This trial along with several landmark randomized controlled trials(RCTs) endorsing the benefits of the ICD in patients with ischemic heart disease with reduced EF with and without electrical dyssynchrony [1,2], form the backbone of ICD implantation in patients satisfying ejection fraction(EF) criteria [3]. An independent advantage of providing protection, with the use of ICDs over and above the improvement in EF by electrical resynchronization, was also noted in patients with ischemic cardiomyopathy(ICM) [4,5]. In patients without this substrate, data from randomized controlled trials(RCT) is limited in addressing the benefits of the ICD independently over resynchronization therapy [6]. Hence a differential indication recommendation for both these substrates has been provided in the guidelines, when ICD implantation is planned for primary prevention (Class I for ischemic cardiomyopathy and Class II a for NICM) [7].

2. Representation of elderly patients in RCT

The elderly population eligible for receiving devices under these guidelines form nearly 40% of all ICDs [8,9] and cardiac resynchronization devices(CRTs). Octogenarians' form around 28% of all these patients [10]. The appropriateness criteria rarely give high recommendations for nonagenarians. However, if the life expectancy is more than a year, it can allow for implantation of an ICD in this population. The average age of patients within the primary prevention trials is 58–66 years [11–13] and the elderly population has been poorly represented or even purposely excluded [4,8,9,14]. The recommendations therefore are a mere extrapolation of available data from younger groups.

This lack of representation is compounded when confronted with the clinical query to ascertain the benefits of ICD in elderly patients with NICM. Even in the DANISH trial where the >68-year subgroup was the largest subgroup (216/560 patients), the mean ages were between 56 and 72 years [15].

3. Ejection fraction as a marker of sudden cardiac death

Our current guidelines are geared to use EF as the single most important determinant of the risk of SCD(7). While it remains specific in identifying patients at risk of sudden cardiac death in patients with structural heart disease, its sensitivity and positive predictive value are not impressive [16]. In NICM and ICM, the reasons for the reduction in EF are varied and as such similar numerical values in EF in both these groups may not indicate similarly diseased myocardium. The prognostic value of EF in these patients may need augmentation with additive variables in both a qualitative and quantitative manner [16].

The response to CRT modulates the risk of SCD and as such any study evaluating the efficacy of ICD should be correcting for the improvement in EF secondary to it. The quantum of increase may carry greater weight in patients with NICM. Those with larger increases in EF post CRT may perhaps be indicative of a less advanced form of myocardial disease.

4. Novel therapies aiding survival

CRT therapy improves survival and decreases heart failure hospitalization. However, the co-existent presence of severe MR, despite the improvement in EF or in patients who are non-responders to therapy, increases the all-cause mortality. This may therefore confound studies which do not evaluate the cause of death. Recent trials have begun to evaluate the effect of reversing co-existent MR in these patients and as such addition of this therapy may influence outcomes in the future particularly in the absence of occluded coronary vessels [17].

5. Decision making in elderly patients

In patients with structural heart disease, although both SCD and non-SCD rates increase with age, the increase of non-sudden death is out of proportion to the increase in SCD. This reduces the SCD/all-cause mortality ratio progressively (0.51 at <50 years - 0.26 at 80 years) This change in risk is predicted only by age [18]. Overall survival(OS) is therefore a flawed metric for evaluating the role of ICDs in this population, given that ICDs prevent SCD only. The decision therefore, should be based on the likelihood of risk of death due other causes and the risk of SCD, particularly given that the benefit of primary prevention is evident between 2 and 5 years [19]. There may be need to therefore revisit the guidelines in this cohort to determine an appropriate duration of estimated OS to allow for benefit after the implantation of the ICD. In addition, the choice between OS versus quality of life(QoL) assumes great importance in this group and hence the patient's decision needs to carry heavy weightage particularly given the paucity of RCT based data [20,21]. SCD has a profound impact on the family members left behind and its' impact on them, should also feature in the

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discussions with the patient. In those agreeing to the implantation of the ICD, it is critical to chart an end of life decision tree prior to implantation, to avoid anguish later. Similar thought needs to be given when recommendations for device pulse generator change are made on follow-up, where the entire decision making should be revisited as anew with the patient, rather than it being an automatic choice [22–24].

Risk scores defining the susceptibility to complications have been created and greater use may perhaps aid in delivering optimum benefit in this population [25–27]. A critical additional cog in the wheel of decision making is the economic impact of the device implant on the family. In resource-limited situations, this remains an important component of the conversation with the patient [28–30].

6. Why did the study not show any benefit?

It is in this light that the study by Saba et al. needs to be interpreted [31]. There is a significantly higher QRS width, incidence of congestive heart failure, lower EF, lower Charlson co-morbidity score and higher use of angiotensin converting enzyme inhibitors in the group with ICDs. While acknowledging the limitations of the study design, this study concludes that in older patients with CRT devices, the addition of ICD therapy does not improve survival.

In addition to the varied causes of death in patients within this age group contributing to overall mortality, hypothetically it is possible that given the sicker population, (as suggested by a wider QRS) the CRT benefit is so large that additional mortality benefit is not seen. Thus, at both ends of the spectrum, incremental value for an ICD may not be appreciated although standalone value might be present in a different population, with lesser morbidity.

7. ICD in elderly: are they that different?

The rates of appropriate shocks for primary events, when ICDs are implanted under current guidelines, remain the same as younger patients (4.2 event/100 person years) and their 30-day survival rates too, remain near complete [32–34]. Predisposition to electromechanical dissociation or unsuccessful shocks is not higher in them, indicating thereby that, there is no age-related factor undermining the termination of the tachyarrhythmia in these patients. Appropriate programming should prevent inappropriate shocks in much the same manner as in younger patients [35,36]. These benefits were reflected even in the DANISH trial where the incidence of SCD in the study group patients with ICDs was significantly reduced($p < 0.005$) and in keeping with the available RCT evidence, younger patients were protected from SCD(15). Data on the incidence of ICD-related operative in-hospital or long-term complications is conflicting and needs to be assessed considering the co-morbidities [25,32–34,37,38].

In conclusion, therefore, the use of ICDs in elderly patients with NICM remains a query without any RCT based data with sufficient power to answer it. This manuscript by Saba et al. adds to the list of recent literature seeking to throw light on this real-world conundrum showcasing the need for RCTs to answer it. In the interim, the clinicians need to individualize their decision making utilizing both OS and disease status to offer a tailored solution.

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