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Primary prevention implantable cardioverter-defibrillator implantation in elderly patients: is it a justified consideration to withhold treatment?

ABSTRACT

Implementation of primary prevention implantable cardioverter-defibrillator (ICD) treatment in the current clinical guidelines led to a significant increase in patients that may benefit from implantation of an ICD. Currently non-guideline-guided patient selection takes place by physicians whereby patients at higher age are more frequently excluded for ICD implantation. This editorial focuses on ICD treatment in the elderly and aims to clarify whether it is justified to withhold ICD treatment in these patients.
INTRODUCTION

Sudden cardiac death (SCD) remains a leading cause of death worldwide. It is most frequently caused by ventricular tachycardia, degenerating into ventricular fibrillation. In the western population, the survival rate of such a sudden cardiac arrest is barely 10%. Patients with structural heart disease of either ischaemic or non-ischaemic cause resulting in impaired left ventricular ejection fraction (LVEF) are at high risk for SCD.

Large randomized controlled trials have demonstrated that the implantation of an implantable cardioverter-defibrillator (ICD) reduces all-cause mortality, at first in patients resuscitated from an episode of ventricular tachycardia or fibrillation (secondary prevention), and thereafter also in patients with depressed LVEF (<35%) at high risk for sudden cardiac arrest (primary prevention).

The implementation of primary prevention ICD treatment in the current clinical guidelines led to a significant increase in patients who may benefit from an ICD. However, provision of ICD treatment to all patients eligible for primary prevention ICD treatment might strain financial resources and the pool of trained personnel. Given the under-utilization of ICD treatment, non-guideline guided patient selection is already done by physicians, whereby patients at a higher age (>79 years) and patients with comorbidities are more frequently excluded for ICD treatment. This may have derived from the fact that patients enrolled in the large trials were relatively young and had little comorbidities. Furthermore, additional research focused on ICD benefit in elderly patients remains scarce and results are controversial.

But is it really justified to withhold ICD treatment in elderly patients?

Age & effectiveness of ICD treatment

In current routine clinical practice, more than 40% of the ICD recipients are at least 70 years old, and due to the aging of the population, the number of elderly patients qualifying for ICD is increasing rapidly. Although ICD treatment is clearly beneficial for the reduction of mortality in patients with depressed systolic function, it remains questionable if this is also the case in patients with shorter life expectancy, such as the elderly. Since the risk of sudden cardiac events increases with age, ICD treatment may be even more beneficial in older patients. On the other hand, elderly patients also have a higher burden of comorbidities, and therefore, may be at disproportionally higher risk of non-SCD, which may diminish the beneficial effect of ICD treatment. Even though elderly patients were not excluded from the pivotal trials, they were largely underrepresented. The mean age of patients included in these trials did not exceed 65 years. By including 204 (17%) patients aged ≥75 years, the elderly were best represented in the second Multicentre Automatic Defibrillator Implantation Trial (MADIT-II), which enrolled patients with prior myocardial infarction and LVEF <30%. In a subanalysis performed by Huang et al. ICD treatment in patients aged ≥75 years was associated with a 44% relative reduction of all-cause mortality, which was comparable with their younger peers.

However, in a meta-analysis by Santangeli et al., which included five primary prevention trials (5783 patients of which 44% were ≥65 years) a smaller survival benefit was observed in patients older than 65 years (HR: 0.75; 95%CI: 0.61–0.91; p=0.004).

Kong et al. performed a meta-analysis on the benefit of ICD treatment in patients aged ≥75 years by including 597 (11.6%) elderly patients from four of the large randomized controlled trials for
prophylactic ICD implantation. They observed little but significant benefit of ICD treatment (HR: 0.73; 95% CI: 0.51–0.97; p=0.03).\textsuperscript{16} Thus, although the effect is less in elderly patients, their survival is improved by ICD treatment. Furthermore, recently published national registries demonstrated that although the rate of appropriate ICD intervention is not significantly different between different age categories, the mortality rate is higher in elderly patients receiving a primary prevention ICD.\textsuperscript{17,18} However, since the mean life-expectancy of patients receiving an ICD when ≥80 years is still 4.2 years, the current international guideline states that ‘age itself should not be a predominant consideration in the use of device based treatment among the elderly’.\textsuperscript{19}

**Old age combined with comorbidities; a reason to withhold ICD treatment?**

Probably one of the major differences between the elderly enrolled in the primary prevention trials and the elderly receiving ICD treatment in routine clinical practice is the burden of comorbidities. Due to the aging of the population, people have improved life-expectancy, which is accompanied by a higher burden of comorbidities.\textsuperscript{12} Furthermore, the burden of comorbidities is associated with non-SCD. The presence of chronic kidney disease for example, will increase the risk of mortality with more than three times.\textsuperscript{20} Additionally, Lee et al. described the importance of age, peripheral vascular disease, diabetes (accompanied by microvascular complications), chronic pulmonary disease, and cancer (including non-metastatic) as predictors of mortality.\textsuperscript{21} They observed in a large cohort (N=2467; N ≥75 years=425) of primary and secondary prevention patients that the presence of non-cardiac comorbidities was associated with an increased risk of mortality in ICD recipients. Similar results were observed by Bhavnani et al. When they analysed the effectiveness of ICD treatment by Charlson Comorbidity Index, a pre-existing mortality assessment model considering chronic conditions of primary and secondary prevention ICD patients (N=1067).\textsuperscript{22} A comorbidity index ≥5 corresponded to a more than five times increased risk of early mortality. Finally, different prediction models have been developed using combined age and (non-) cardiac comorbidities to assess the effectiveness of ICD treatment.\textsuperscript{23} The MADIT-II model developed in the MADIT-II study population includes age >70 years, NYHA functional class > II, QRS duration >120 ms, history of atrial fibrillation and blood urea nitrogen >26 mg/dL. The risk of mortality in the 200 (16.8%) patients with three or more risk factors was five times higher, and more importantly ICD treatment did not improve the survival since the mortality in both study-arms (ICD vs non-ICD) was similar. This emphasizes the importance of considering age and the burden of comorbidities before ICD implantation.

**Future of device treatment in frail elderly**

Although data on the effect of ICD treatment in the elderly, especially with comorbidities, are scarce, current literature suggests that this population has less or even no benefit from ICD treatment as compared to their younger peers. Age itself should not be the sole criterion for withholding treatment but to optimize allocation of ICD treatment, one should realize that in a population with high age and concomitant comorbidities, the small potential benefits of ICD treatment might not outweigh the costs and burden of device-related complications.
REFERENCES
