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Do octogenarians benefit from primary prevention implantable cardiac defibrillators?

Introduction
The benefit of implantable cardioverter-defibrillator (ICD) therapy in the primary prevention of sudden cardiac death in patients with a left ventricular ejection fraction (LVEF) <35% has been proven in randomised controlled trials. In primary prevention ICD trials the mean age of patients enrolled was <65yrs (MADIT-I, MADIT-II and DEFINITE had a combined mean age of 61years, and MUSTT and SCD-HeFT had a combined median age of 62years.) The elderly are poorly represented in these trials with most studies only having a small minority or a total absence of octogenarians. The elderly included in these trials were also a highly selected group as shown in MADIT-II where few differences in sub-group characteristics were observed between <75 and >75years age groups. Guidelines have been developed from these randomised controlled trials with a lack of reference to age. Registry data shows that increasing numbers of octogenarians are having ICDs implanted for primary prevention. However, a survey in the USA of over 1400 physicians noted that one quarter of physicians frequently withheld ICD referral because of age.

The benefit of ICDs is controversial in elderly patients. Some studies suggested that it is effective treatment for life threatening arrhythmias irrespective of age however this has to be balanced with studies showing that mortality is higher in the elderly with an increase in non-arrhythmic death which may negate the benefit of ICD therapy.

The guidelines
In June 2014 NICE guidelines expanded the indication for defibrillator therapy without any reference to specific age limits (Table 1).

<table>
<thead>
<tr>
<th>QRS Duration</th>
<th>NYHA</th>
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<td></td>
<td>I</td>
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<td>&lt;120 milliseconds</td>
<td>ICD if there is a high risk of sudden cardiac death</td>
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<tr>
<td>120–149 milliseconds without LBBB</td>
<td>ICD</td>
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<tr>
<td>120–149 milliseconds with LBBB</td>
<td>ICD</td>
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<tr>
<td>≥150 milliseconds with or without LBBB</td>
<td>CRT-D</td>
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LBBB, left bundle branch block; NYHA, New York Heart Association

Table 1. NICE guidelines. Treatment options with implantable cardioverter-defibrillator (ICD) or cardiac resynchronisation therapy (CRT) for people with heart failure who have left ventricular function.
The 2013 Appropriate Use Criteria for Implantable Cardioverter-Defibrillators and Cardiac Resynchronization Therapy guidelines state that primary ICD implantation in patients \( \geq 90 \text{ years old} \) is rarely appropriate if they are in NYHA Class I but may be appropriate if they are in NYHA class II-III or if they are 80-89 years old. They state that it is rarely appropriate in patients with life expectancy less than 1 year from cardiac or non-cardiac conditions but may be appropriate if they have a non-cardiac disease with life expectancy 1 to 2 years.

The current situation

Real world data from 2 registries\(^8,9\) of primary and secondary prevention ICD implantation rates in the USA show that \( \sim 12\% \) of patients are \( \geq 80 \) years. The rates were lower in Canadian\(^10\) and UK based registries\(^18\) at 8% and 5%, respectively. The majority of defibrillators were implanted for primary prevention in those \( \geq 80 \) years, with registry data showing that this accounts for approximately 77% of defibrillators\(^19\).

As the population ages the number of elderly patients meeting the criteria for primary ICD implantation is increasing. Ruskin et al found that octogenarians fulfilled 28% of the population eligible for implantation\(^19\) (those with a diagnosis of ventricular tachycardia (VT), ventricular fibrillation (VF), ventricular flutter, or cardiac arrest, with previous myocardial infarction or congestive cardiac failure.)

Elderly patients have a higher prevalence of coexisting conditions/comorbidities such as AF, hypertension, coronary artery disease, chronic lung disease, liver disease and cancer compared to their younger counterparts\(^20,21\).

Arrhythmias in the elderly - do the elderly die of sudden cardiac death/ventricular arrhythmias and will an ICD potentially be of benefit?

It is difficult to obtain data solely for octogenarians as many trials use a different age range for ‘elderly’. Both Fauchier et al\(^1\) (\( \geq 75 \) yrs) and Yung et al\(^10\) (\( \geq 80 \) yrs) found that rates of appropriate therapy were similar in the older age groups compared to rates found in younger patients in primary prevention ICD implantation. Fauchier et al also showed the rates of inappropriate therapy were reduced in the elderly.

Mortality in the elderly

When discussing mortality it is important to consider that an appropriate shock does not equal a life saved. For example, in SCD-HeFT \( 21\% \) of patients had shocks appropriate for fast VT/VF yet the absolute mortality reduction at 5 years was only 7.2%.\(^5\) Also in the DEFINITE trial patients in the ICD group had double the shocks than were fatal events in the control group, yet there was no survival benefit\(^22\).

As to be expected age is an independent risk factor for mortality irrespective of baseline co-morbidity data\(^23\). Fauchier et al\(^1\) reported that the annual mortality rate increased with age for primary prevention ICD recipients in France, with older age associated with a greater risk of death. As patients with cardiomyopathy age they have an increased rate of both sudden and non-sudden death, although proportionally are more likely to die from a non-sudden death than a sudden arrhythmic death. One study analysed over 6000 patients with structural heart disease and showed that only 26% of deaths are sudden above the age of 80 yrs\(^24\). Another study showed that there was an increased mortality with age, mostly due to heart failure deaths\(^25\). However, a study by Epstein et al\(^8\) found that overall mortality was increased in patients \( > 75 \) years compared to those \( < 75 \) years and this was mainly due to non-cardiac death, yet found a similar rate of sudden and non-sudden cardiac death rate in the different age groups. Fauchier et al\(^21\) had similar findings to Epstein et al in that the proportion of cardiac deaths including ICD-unresponsive sudden death was similar across different age ranges. Masoudi et al\(^23\) found that mortality and hospitalisations for heart failure was significantly higher in patients \( > 65 \) years compared to \( < 65 \) years, but not for all cause hospitalisations. Most studies are consistent in the finding that there is a greater risk of non-arrhythmic death. This increased relative contribution to non-arrhythmic mortality may negate the survival benefits of ICD therapy\(^19,24,26\).
A systematic literature review and meta-analysis of primary prevention ICDs assessed 579 patients above 75 years from 4 RCTs (MADIT-II, SCD-HeFT, DEFINITE, MUSTT) found that primary ICD therapy remains efficacious in reducing all-cause mortality (HR 0.73, 95% CI 0.51-0.97; p = 0.03). They recommend that ICD should not be withheld on the basis of age alone.

However, the median survival of elderly patients with an ICD has been shown to be <5 years in most studies and yet the benefit of ICD in primary prevention of sudden cardiac death was only seen over 2-5 years in MADIT-II. One study reported that just under 50% of patients >75 years died within 5 years of primary prevention ICD implantation versus 15% of those <65 years. If they have an appropriate shock 22% died within 1 year if >75 years, versus 5% if less than 65 years. Another study found the death rate in primary prevention octogenarians is 10.2 deaths per 100 person-years.

Goonewardene et al. in a retrospective study of 42 patients with ICD implantation ≥80 years old found that 65% died within 3 years of the procedure. In patients who had devices implanted for primary prevention the risk of mortality was higher compared to secondary prevention and most episodes of VT were in those with ICDs for secondary prevention. There were no ventricular fibrillation triggered ICD therapies. They found that the median additional years of life after ICD implantation in patients who died before data retrieval was 2.5.

Chan et al. in a prospective cohort study of 494 patients, with ≥269 patients above 75 years showed comparable absolute and relative mortality risk reductions with ICD use amongst older patients despite higher annual mortality rates.

The evidence suggests that ICD therapy should be considered in the elderly for the prevention of sudden cardiac death as suggested by focused studies/subgroup analysis/observation and registry data. Barra et al. have reviewed the data for implantable cardioverter-defibrillators in the elderly and looked at the rationale and specific age-related considerations. They conclude that although octogenarians have a higher annual all-cause mortality rates, ICD therapy may remain effective in highly selected patients at high risk of arrhythmic death and with minimum comorbidities despite advanced age.

Disadvantages of an ICD
The disadvantages include complications which are increased at the time of generator change, lead displacement, cost, anxiety/psychological distress including inappropriate shocks. Many studies have reported on the complications of ICD implantation in the elderly. Most recently Fauchier et al. showed a higher risk of early device-related complications requiring surgical intervention with older age. Masoudi et al. also found that older patients had higher risk of haematoma requiring evacuation or transfusion compared with younger patients but other complications were not statistically significant. These studies conflict with some other studies which show complication rates are not significantly different to the younger age groups.

Generator change
I have not reviewed the data for generator replacement in elderly in this editorial, however, one recent study has looked at this and concluded that in patients who need an elective generator replacement above the age of 80 yrs who have had no previous ICD therapies there is hardly any clinical benefit.

Summary
Elderly patients have a similar chance of receiving appropriate ICD therapies and therefore can gain as much benefit as those in the younger age groups. On the other hand, mortality (total, cardiac and non-cardiac) is strongly associated with increasing age, even after controlling for potential confounders and comorbidities. There is a significantly larger proportion increase in non-sudden death, which is unlikely to be prevented by ICD therapy.

Age is a predictor of mortality but it does not identify which patients will benefit from an ICD. Additional information must be reviewed to guide who will benefit. I believe that we should use risk scores developed for the prediction of mortality in potential ICD recipients to guide implantation. An example is Goldenberg et al. risk stratification for primary implantation of a cardioverter-defibrillator in in patients with ischaemic left ventricular dysfunction. This has been validation in long-term follow up and in the elderly. No benefit was seen in patient with zero risk factors (HR 0.96) or in very high risk individuals (HR >1.0) whereas in patients with at least one risk factor (age >70 years, NYHA >II,
Urea >9.3mmol/L, QRS >0.12, AF) ICD therapy was associated with a 49% reduction in risk of death (most had 1-2 risk factors). Among patients with at least 3 risk factors mortality was only slightly lower in the ICD group than in the conventional therapy group (29% vs 32%). The 2 year-mortality rate was almost 50% in very high-risk patients irrespective of having an ICD. There are other scoring systems that also are likely to be useful in guiding the clinician as to whether their patient is likely to benefit from an ICD.

In summary, I believe that octogenarians who meet the guidelines for primary prevention ICD warrant consideration on an individual basis taking into account comorbidities, quality of life and patient choice. It is essential to discuss the options with the patient and to emphasize that ICDs may prolong life but usually do not improve quality of life. Risk scoring should help in the decision making process of this complex issue.

References:


