Original Article

Implantable Cardioverter Defibrillators in Octogenarians: Clinical Outcomes From a Single Center

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Abstract

Aims: Limited data exist on outcomes in very elderly ICD recipients. We describe outcomes in new ICD and Cardiac Resynchronisation Therapy with Defibrillator (CRT-D) implants in octogenarians at our institution.

Methods: Patients aged 80 years and above who underwent de novo ICD or CRT-D implantation from January 2006 to July 2012 were identified. Clinical data were collected from the procedural record, medical and ICD notes. Baseline characteristics were compared using independent sample t test for continuous variables and Fisher's exact test for categorical variables. Kaplan-Meier curves were constructed.

Results: Ten per cent of all new ICD/CRT-D implants were aged 80 years and over. Median age was 83.0 years. Median follow-up was 29 months. Death occurred in 17 (34%). Median time to death was 23 months. Three deaths (6%) occurred within 12 months of ICD implantation. Appropriate therapy (ATP or shock) occurred in 19 (38%). Inappropriate therapy occurred in 6 (12%).

Rates of appropriate shocks and inappropriate therapy (shocks and ATP) and significant valvular incompetence were higher amongst deceased patients (P=0.03 OR 5.9 95% CI 1.3-27) and (P=0.02 OR 12 95% CI 1.3-112). Univariate analysis identified diuretic use (P=0.008 95% C.I. 0.05 to 0.63) and appropriate shock (P= 0.025 95% C.I. 1.25 to 26.3) as predictors of mortality.

Conclusion: Octogenarians make up a small but increasing number of ICD recipients. This study highlights high survival rates at one year with acceptable rates of appropriate and inappropriate device therapy. Ongoing debate regarding the appropriateness of ICD in very elderly patients is warranted.

Key words: sudden cardiac death, implantable defibrillators, octogenarians

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Introduction

Elderly patients were largely excluded from the pivotal studies in implantable cardioverter-defibrillators (ICDs) and therefore evidence of effectiveness in elderly patients is based on single centre studies and registry data. In the United Kingdom, there is an aging population. The Office of National Statistics estimates that in 2035, 5% of the population will be aged 85 years and above, an increase of 250% compared to 2010. (UK Office of National statistics 2014)

Decisions to implant ICDs in the very elderly are more complex due to associated co-morbidity and reduced life expectancy. Current guidelines recommend that ICD implantation should be considered in eligible patients if estimated survival is at least one year. [1] There is a paucity of ICD outcome data in the very elderly and all the data available on the octogenarians and nonagenarians is from North-American populations. [2-5] There is therefore need for UK outcome data in this unique population of patients. We describe the outcomes in all new ICD and Cardiac Resynchronisation Therapy with Defibrillator (CRT-D) implants in octogenarians at our institution.

Materials and Methods

All patients aged 80 years and above who underwent de novo ICD or CRT-D implantation from January 2006 to July 2012 at the Bristol Royal Infirmary (subsequently called Bristol Heart Institute) were identified from the hospital’s ICD and CRT-D database. Clinical data for demographics, comorbidities and device therapy were collected from the procedural record, medical notes and ICD notes. The study was found to conform to the service evaluation standards set out by the hospitals Research and Development department.

Implant and follow up

All devices were implanted under the supervision of one of five supervising consultants working in the cardiac electrophysiology department during the study period. Implant technique varied between physicians according to preference and training. Defibrillation testing was performed at the discretion of the implanting physician. Programming of monitor zone, anti-tachycardia pacing and defibrillation zones was at the discretion of the implanting physician. Follow up was provided at regular intervals of 3-6 months.

Endpoints

Clinical outcome of all-cause mortality, date of first appropriate shock and date of first inappropriate shock were collected from ICD interrogation records. Local referring centres were contacted to ascertain outcomes in cases where patients had been followed up elsewhere. Information about device deactivation was collected. The study data collection date was the 22nd May 2013.

Definitions

Implant indication was defined as secondary prevention if the patient has survived a cardiac arrest or experienced ventricular tachyarrhythmia needing intervention or lasting for more than 30 seconds. Primary prevention was defined as the absence of cardiac arrest or ventricular tachyarrhythmia requiring intervention. An appropriate shock was defined as delivery of a defibrillation or cardioversion shock in the presence of VT/VF. An inappropriate shock was defined as the delivery of therapy in the absence of a ventricular tachyarrhythmia but in response to supraventricular tachycardia, oversensing or lead malfunction.
Statistical analysis

Categorical variables are expressed as absolute numbers and percentages. Continuous variables were presented as mean standard deviation. Baseline characteristics of primary and secondary-prevention patients were compared using independent sample t-test for continuous variables and Fisher's exact test and Chi-squared test for categorical variables. Kaplan-Meier curves were constructed to determine cumulative incidence of mortality. Univariate analysis and multivariate analyses were performed to identify predictors of mortality. A P-value of less than 0.05 was considered statistically significant for all tests. Statistical tests were performed using Prizm for Mac OsX version 5.0c (Graphpad software, Inc.) and IBM SPSS statistics version 21 (IBM corp.)

Results

Seventy-four de novo ICD or CRT-D recipients were aged 80 years and over in the study period (10% of total de novo implants). The proportion of octogenarians receiving an ICD/CRT-d increased over the study period. (Figure 1)

![Figure 1: Graph illustrating in change in proportion of octogenarians receiving de novo ICD / CRT-D over the study period. Percentages indicate percentage octogenarian / total number receiving ICD / CRT-D x 100](image)

Fifty patients met the inclusion criteria. (Table 1)

Twenty-one patients (42%) received ICDs for primary prevention (PP) indications. (Table 2) PP patients had higher rate of CRT-D implant (P=0.02 95% CI 1.4-26).

Secondary prevention (SP) patients had higher rates of β blocker (P=0.01 95% CI 1.5-22), amiodarone (P=0.01 95% CI 1.5-27) and aspirin (P=0.01 95% CI 1.5-45) use. Kaplan-Meier survival curves were constructed for overall mortality (Figure 2) and mortality according to PP or SP indication (Figure 3).

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Table 1: Study participant demographics in primary and secondary prevention categories.

|                        | Primary prevention N | Secondary prevention N | P value |
|------------------------|----------------------|------------------------|---------|
| Number                 | 21       | 58.0                  |         |
| Age (median)           | 83.3     | 83.2                  | 0.89    |
| Age (Max)              | 89.9     | 80.4                  |         |
| Age (min)              | 80.4     | 86.4                  |         |
| Deceased               | 6        | 28.6                  |         |
| Male                   | 21       | 100.0                 |         |
| SSI                    | 3        | 14.3                  |         |
| DDD                    | 9        | 42.9                  |         |
| CRT-D                  | 9        | 42.9                  |         |
| VT stimulation testing | 2        | 9.5                   |         |

Median age at implant was 83.0 (range 80-89.9) years. Median follow-up was 29 months (range 11-68 months). Death occurred in 17 (34%). Median time to death was 23 months (range 1-81 months). Three deaths (6%) occurred within 12 months of ICD implantaion. Cause of death was pneumonia in 5, heart failure in 2, stroke in 1, malignancy in 1, sudden death in 1 and unknown 5.
The survival curves according to indication were not statistically different (P=0.15). There was no significant difference in rates of appropriate or inappropriate shocks between the 2 groups. (Table 3) There was trend towards increased appropriate therapy (ATP and shocks) in the SP group (P=0.14).

Appropriate therapy (ATP or shock) occurred in 19 (38%) and inappropriate therapy occurred in 6 (12%). Kaplan-Meier curves for time to appropriate shock were constructed (Figure 4). Death occurred with no appropriate therapy in 10 (20%) patients.

Figure 3: Kaplan-Meier survival curve of octogenarians according to implant indication. P=0.15

Figure 4: Kaplan-Meier curve of time to appropriate therapy (ATP and shocks) for all patients.
Table 2: Study participant medication and co-morbidity in primary and secondary prevention categories.

|                          | Primary prevention N | %    | Secondary prevention N | %    | P value |
|--------------------------|----------------------|------|-------------------------|------|---------|
| B Blocker                | 11                   | 52.4 | 25                      | 86.2 | 0.012   |
| Ace-i                    | 16                   | 76.2 | 26                      | 89.7 | 0.464   |
| ARB                      | 5                    | 23.8 | 9                       | 31.0 | 0.752   |
| Statin                   | 15                   | 71.4 | 27                      | 93.1 | 0.105   |
| Aspirin                  | 13                   | 61.9 | 27                      | 93.1 | 0.011   |
| Clopidogrel              | 3                    | 14.3 | 12                      | 41.4 | 0.061   |
| Amiodarone               | 3                    | 14.3 | 15                      | 51.7 | 0.006   |
| Warfarin / OAC           | 9                    | 42.9 | 6                       | 20.7 | 0.129   |
| Diuretic                 | 15                   | 71.4 | 17                      | 58.6 | 0.388   |
| EF                       | 31.5 (±10.0)         |      | 33.8 (±10.9)            |      | 0.542   |
| Significant valve stenosis ≥ moderate | 1 | 4.8 | 0 | 0.0 | 0.420   |
| Significant valve regurgitation ≥ mod | 2 | 9.5 | 3 | 10.3 | 1.00    |
| NYHA I                   | 3                    | 14.3 | 4                       | 13.8 | 1.00    |
| NYHA II                  | 3                    | 14.3 | 8                       | 27.6 | 0.319   |
| NYHA III                 | 8                    | 38.1 | 1                       | 3.4  | 0.002   |
| NYHA IV                  | 2                    | 9.5  | 0                       | 0.0  | 0.171   |
| NYHA not recorded        | 5                    | 23.8 | 16                      | 55.2 | 0.042   |
| AF                       | 10                   | 47.6 | 12                      | 41.4 | 0.775   |
| Hb mean                  | 12.4 (±1.0)          |      | 12.5 (±1.7)             |      | 0.830   |
| eGFR mean                | 57.7 (±17.7)         |      | 56.4 (±17.3)            |      | 0.778   |
| QRS duration             | 132.8 (±35.8)        |      | 124.6 (±35.5)           |      | 0.438   |
| LBBB                     | 10                   | 47.6 | 7                       | 24.1 | 0.130   |
| Ischaemic aetiology      | 17                   | 81.0 | 19                      | 65.5 | 0.341   |
| MI                       | 12                   | 57.1 | 21                      | 72.4 | 0.366   |
| Previous PCI             | 8                    | 38.1 | 6                       | 20.7 | 0.213   |
| Previous CABG            | 6                    | 28.6 | 8                       | 27.6 | 1.0     |
| Previous replacement     | 0                    | 0.0  | 0                       | 0.0  | -       |
| CVA                      | 2                    | 9.5  | 7                       | 24.1 | 0.271   |
| COPD                     | 3                    | 14.3 | 2                       | 6.9  | 0.638   |
| PVD                      | 6                    | 28.6 | 3                       | 10.3 | 0.140   |
| >CKD III                 | 1                    | 4.8  | 0                       | 0.0  | 0.420   |
| RRT                      | 0                    | 0.0  | 0                       | 0.0  | -       |
Table 3: Rates of ICD therapy, complication and deactivation amongst study participants in primary and secondary prevention categories.

|                      | Primary prevention N | %   | Secondary prevention N | %   | %   |
|----------------------|----------------------|-----|------------------------|-----|-----|
| Appropriate shock    | 3                    | 14.3| 7                      | 24.1| 0.488|
| Appropriate ATP      | 5                    | 23.8| 12                     | 41.4| 0.238|
| Appropriate therapy  | 5                    | 23.8| 14                     | 48.3| 0.139|
| VT storm             | 1                    | 4.8 | 1                      | 3.4 | 1.0 |
| VT ablation          | 0                    | 0.0 | 0                      | 0.0 | -   |
| Inappropriate therapy| 1                    | 4.8 | 5                      | 17.2| 0.380|
| ICD deactivated      | 1                    | 4.8 | 3                      | 10.3| 0.383|
| Lead complication    | 2                    | 9.5 | 3                      | 10.3| 0.638|
| Death with no        | 4                    | 19.0| 6                      | 20.7| 1.0 |
| appropriate therapy  |                      |     |                        |     |     |

Rates of appropriate shocks and inappropriate therapy (shocks and ATP) were significantly higher amongst deceased patients (P=0.03 OR 5.9 95% CI 1.3-27) and (P=0.02 OR 12 95% CI 1.3-112). Significant valvular incompetence was more common in the deceased group (P=0.05 OR 8.9 CI 0.91-87).

Univariate analysis identified diuretic use (P=0.008 95% C.I. 0.05 to 0.63) and appropriate shock (P= 0.025 95% C.I. 1.25 to 26.3) as predictors of mortality. In a cox regression multivariate analysis using the backward conditional method, only diuretic use was found to be a predictor of mortality (P=0.007 HR 4.0 95% C.I. 1.45 to 11.06).

Discussion

Decisions to implant ICDs in elderly patients can be challenging and controversial. Proponents argue that patients benefit due to an increased incidence of sudden cardiac death (SCD) in this age group and age alone should not be a barrier to treatment. [6] Conversely, critics argue that the diminished life expectancy of elderly patients limit the potential benefit of ICDs, the high costs of implantation and follow up of patients are not offset by the potential gains and lastly SCD may seem an attractive proposition for some elderly patients with other significant co-morbidities. Nevertheless, current international guidelines do not have an age cut off for ICD implantation. Guidelines state that potential candidates need to meet recommended criteria for implantation and have an estimated life expectancy of at least one year. [1]

The elderly demonstrate an increased incidence of SCD. The annual incidence of SCD in an 80-year-old male is approximately seven times greater than in a 40-year-old male. [2] In women, this trend is more marked; the incidence of SCD in women aged over 70 years is more than 40 times greater than in women aged less than 45 years. [7,8] This phenomenon is attributable to the increased incidence of coronary heart disease and heart failure in the elderly population. However, despite this, the proportion of SCD to non-SCD diminishes in the elderly, a phenomenon referred to as the SCD paradox. This is due to an even greater overall number of deaths in this age group. Moreover, the proportion of deaths attributable to pulseless electrical activity (PEA), a condition not treatable by ICDs, increases with advancing age. [10]
Evidence of effectiveness of ICDs in the elderly from clinical trials

Elderly patients are under-represented in ICD trials and analyses of their results have revealed mixed results. The MADIT II trial, a primary prevention ICD trial, included the greatest number of elderly patients, with approximately 20% aged over 75 years. In a sub-study analysis of this study evaluating 204 elderly patients (aged more than 75 years) with ischaemic cardiomyopathy, an equivalent reduction in mortality in elderly and younger patients was found (hazard ratio hazard ratio, 0.56; 95% confidence interval, 0.29-1.08 vs 0.56; 95% confidence interval 0.29-1.08). [11] However, it is important to note that follow up in over 75-year-old group was relatively short at 17.2 months. Thus the effect of subsequent non-SCD deaths affecting that population will not be accounted for and as a consequence, the overall benefit derived from the ICD may be over-estimated. In a meta-analysis involving three primary prevention trials, DEFINITE, MADIT II and SCD-Heft, a significant reduction in mortality was seen in elderly patients randomised to ICD therapy (HR 0.75, 95% CI 0.61-0.91, \( P = 0.004 \)). However, elderly patients were defined as over 60-65 years and most of the effect was driven by the MADIT II cohort, though the results are consistent with a previous meta-analysis of primary prevention ICD trials. [12] A meta-analysis of secondary prevention trials also failed to demonstrate the benefit of an ICD in the over 75 year old population. [13]

Mortality

Knowledge of outcomes in very elderly ICD recipients can help inform clinicians in future implanting decisions. Overall annual mortality in this study was 14%. This is higher than the clinical trials described above where reported annual mortality in those who received ICDs ranged from approximately 5.8% to 8.5% per annum. [14-17] However, our mortality data is in line with registry data from Canada in which octogenarian patients receiving ICDs for primary and secondary prevention indication had 10.2 and 15.5 deaths per 100 person-years respectively. [2] Conversely, the 2-year mortality in a US registry of over 4,500 patients in which 12% of patients were aged over 80 years demonstrated more favourable mortality rates (17.8%) compared to ours (28%). [4] In healthcare systems with restrictive policies on ICD implantation, a 5% annual mortality is reported in their ICD recipients. [18]

In this study, rates of appropriate shock, inappropriate therapy and at least moderate valvular incompetence were statistically more common in the deceased patients. However, only diuretic use and appropriate shock were found to be statistically significant predictors of mortality in multivariate analysis (hazard ratio 4.0). Similarly, other studies identified NYHA class, diuretic use, and peripheral vascular disease to be predictors of mortality in elderly patients with primary and secondary prevention indications for ICDs. Appropriate shock has been found to be a predictor of death in some clinical trials. [19] The use of CRT is associated with improved survival compared to ICD alone in appropriately selected patients. In this study, we did not find that CRT conferred reduced mortality, and this may be a reflection of the relatively small numbers included in the study.

Appropriate and inappropriate therapy

In this study, rate of appropriate and inappropriate therapy occurred in 38% and 12% over the 2.5 year follow up period. These are consistent with those reported in large European and Canadian ICD registries that in addition also reported no significant differences between rates of appropriate and inappropriate therapy between age groups. [2,20] Furthermore, older patients have been found to have lower rates of inappropriate therapy compared to younger patients, presumably due to lower incidence of sinus tachycardia as a cause of inappropriate shock and similarly impaired AV nodal conduction reducing ventricular rates during atrial arrhythmia. [2]
Increasing numbers of elderly patients referred

The proportion of octogenarians receiving ICDs in this study increased year on year until 2010, from 2.9% in 2006 to 12.7% of total implants in 2010. This trend is also seen in a large European ICD registry. In another large US ICD registry, 10% of ICD recipients were aged 80 years and above. [4] US ICD data has been criticised in the past for having a large proportion of ICD implanted outside evidenced-based criteria. [21] However, potentially inappropriate rates of ICD use appear significantly lower in older than in younger Americans suggesting that even in very liberal ICD prescribing environment, physicians appear to be more conservative when referring older adults and deferring those with high co-morbidity. [3]

Selecting ICD recipients appropriately

When considering ICD patient selection there is a 'sweetspot' of effectiveness, where risk of SCD is elevated enough for the risks of ICD implantation to be outweighed by the benefits and for patient survival to be sufficiently long to maximise cost effectiveness. The MADIT II investigators identified a number of predictors of increased mortality (age more than 70 years, NYHA class more than II, impaired renal function, broad QRS and atrial fibrillation) and found a U shaped relationship between these predictors and ICD benefit. Those at the extremes (very low and high risk of death) appeared to derive the least benefit from the ICD, whereas an intermediate score predicted the greatest benefit. In our study, 12 patients had non-resynchronised ICDs for primary prevention and 11/12 (92%) had intermediate MADIT II risk scores suggesting they had been well selected on the basis of relatively few co-morbidities. Age is an important variable in this equation, and is an independent predictor of death in ICD recipients. [20] So every decision to implant must be individualised and based on fully informed consent.

End of life and deactivation

ICDs were deactivated in 4 (8%) of the study participants. Often this was prior to death occurring in hospital. One patient had requested deactivation of the ICD within one year of implantation and continues to be followed up and has not suffered any syncope or cardiac arrest. Data from analysis of the ICD patients who died the MADIT II trial identified 3 groups of patients: Group 1 consisting of individuals who underwent ICD, deactivation, 15 (15%); Group 2 patients without ICD deactivation who were in hospice or with "do not resuscitate" (DNR) orders, 36 (37%); and Group 3 patients without ICD deactivation who were not in hospice care and did not have DNR orders, 47 (48%). [23] End of life discussions prior to ICD implantation occurred on a patient-by-patient basis rather than a systematic fashion. Good practice suggests that fully informed consent should involve discussions regarding end of life issues and deactivation of ICDs. [24]

Limitations

This study suffers form a number of limitations. It is a retrospective analysis of a relatively small number of patients. No comparator group was used as the principle aim of the study was to describe the outcomes of a unique ICD population rather than compare with a group who were almost by definition going to have improved outcomes. Approximately one third of patients were not analysed due to incomplete data that limits the power of the analysis. Complications of ICDs were not specifically analysed although there is evidence to suggest that complications associated with ICD implantation are no greater in an elderly population. [2,5,20]

In conclusion, this is the first report from the UK on outcomes in octogenarian ICD recipients. As with other series, the number of octogenarians referred for and receiving ICDs
is increasing. Mortality rates and rates of appropriate and inappropriate therapy are similar to North American and European series. This study highlights high survival rates at one year with acceptable rates of appropriate and inappropriate device therapy during follow up. Importantly however, the cost effectiveness of ICD implantation in octogenarians has not been examined. Ongoing debate regarding the appropriateness of ICD in very elderly patients is warranted.

**Contributorship**

Wilson DG contributed to the conception, design, data collection and interpretation and manuscript preparation.

Ahmed N, Nolan R and Frontera A contributed to the data collection, interpretation.

Thomas G and Duncan E contributed to the intellectual design and critical appraisal of the manuscript.

**Competing interests**

Wilson DG has received funding from Medtronic Inc. for a research fellowship
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