Implantable Cardioverter Defibrillators for Primary Prevention of Sudden Cardiac Death: Too Little and Too Late?

Running title: Albert et al.; ICD for Primary Prevention of SCD

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The implantable cardioverter defibrillator (ICD) has been one of the most significant advances made in sudden cardiac death (SCD) prevention. Landmark randomized clinical trials convincingly demonstrated survival benefits of ICD therapy in patients 40 days after myocardial infarction (MI) with left ventricular ejection fraction (LVEF) of less than 30%\(^1\) and in patients with stable New York Heart Association Class II-III CHF and LVEF of less than 35%\(^2\), and subsequent observational studies have confirmed these mortality benefits\(^3\). Results from clinical trials were rapidly incorporated into guidelines\(^4,5\), and the centers for Medicaid and Medicare services (CMS) approved both indications for primary prevention ICDs by 2005. At the same time, CMS mandated that data on all patients receiving ICDs be entered into a national registry to track utilization. Approximately 10 years later, what progress have we made with respect to allocating and disseminating this life-saving technology and what further impact can be made with this technology on mortality due to SCD? The article by Chugh et al in this issue of Circulation highlights these questions\(^6\).

The authors examined the proportion of sudden cardiac arrest (SCA) victims in the Portland Oregon Metropolitan Area who had an ICD implanted for primary prevention prior to their cardiac arrest from 2003-2012. Among individuals where echocardiogram results were available, only a minority (13%) of victims who met contemporary guidelines for prophylactic ICD implantation had received an ICD. This rate of ICD use is much lower than that for patients enrolled in heart failure registries, where utilization rates range from 35% in the inpatient\(^7\) to 51% in the outpatient setting\(^8\). Since these registries were specifically designed to evaluate and improve the use of medical therapies among heart failure patients, these utilization rates probably represent a best-case scenario. Does the present population based study provide us with a more "real-world" assessment of underutilization of ICDs in the community? A couple of issues need
to be considered when attempting to place these data into context relevant to the general population and prior registry data.

First, the present study only includes those who died or required resuscitation from SCA. We don’t know the prevalence of ICDs among the much larger pool of patients with systolic dysfunction in the Portland Metropolitan area who did not suffer a SCA during the study period. Based upon the effectiveness of the ICD in preventing arrhythmic death, patients with an ICD would be expected to be less likely to suffer a SCA and end up in the study case group. If one extrapolates hazard ratios for arrhythmic death from the ICD arms in randomized trials (hazard ratios of 0.33-0.44) \(^9,10\), the percentage of patients with ICDs would be approximately 2.5 to 3 times higher in the general population with systolic dysfunction, bringing the utilization numbers closer to the 50% found in the registry studies. Second, guidelines specify that ICDs are not warranted for subjects who have comorbidities or psychiatric illnesses which are likely to limit survival with an acceptable functional status to less than one year and/or prevent compliance with device follow-up\(^4\). It is difficult to assess the presence of these factors from retrospective review of medical records. Indeed, sudden death victims without ICDs in this study were older and thus more at risk for comorbidities. There was also a significant burden of psychiatric illness among those without ICDs. Retrospective determination of NHYA Class, a critical component of eligibility criteria, is also difficult and subject to error. Therefore, there are likely some patients who were considered eligible based upon the limited data available to the study investigators, but who in reality should not have received an ICD. Despite these limitations, the present study suggests that an important number of eligible patients are not receiving ICDs and some go on to suffer a SCA, which might have been prevented by an ICD. So in response to the first question posed, there appears to be room for significant improvement in disseminating ICD therapy to
those who will benefit in the population.

What can be done to improve the use of ICD therapy in appropriate patients? To date, efforts to improve appropriate ICD utilization have centered on quality and performance improvement interventions in heart failure populations. In the Registry to Improve the Use of Evidence-Based Heart Failure Therapies in the Outpatient Setting (IMPROVE HF), a multidimensional practice specific performance improvement intervention resulted in a 27% increase in ICD use over 24 months from 50.1% to 77.5%. ICD use has also significantly increased in hospitalized patients participating in the Get With the Guidelines Heart Failure Program (GWTG-HF). Recognizing the success of performance improvement initiatives, a new metric regarding counseling about the potential benefits of ICD therapy has been added to the ACCF/AHA/AMA-PCPI 2011 Performance Measures for Adults With Heart Failure. The writing committee chose to develop a measure that addresses counseling instead of the actual implantation in recognition that the decision to implant an ICD is complex and there are a multitude of reasons why an individual decision might be made to not implant an ICD. Such initiatives need to be accompanied by appropriate balanced education of physicians, patients, and the public regarding the benefits and risks of ICD placement so that effective counseling can be provided. Even with proper access, counseling and education; there will always be a certain fraction of the “at-risk” population who will elect not to undergo ICD therapy for reasons of personal preference.

Although addressing the underuse of ICDs is undoubtedly important, the analysis from the Oregon-SUDs population demonstrates that these patients represent "a drop in the bucket" with respect to the total SCA problem. Even if all of the additional SCA victims who had an echocardiogram and met low LVEF criteria for an ICD had received an ICD only a very small
portion of the SCA victims in the Oregon-SUDs population (4.4%) would have been impacted. The overwhelming majority of patients who suffered a SCA in the study did not have a depressed LVEF documented prior to SCD, and therefore would not have been candidates for ICD therapy. Only 23.3% had an assessment of LVEF, and although there were undoubtedly some low EFs that were missed in this population-based study, this is unlikely to account for a large fraction of the population. Rather, as has been documented in other populations\textsuperscript{14}, it is more likely that a majority of these individuals simply did not fall into one of the high-risk subsets where echocardiographic screening would be indicated. For the majority of SCA victims, there is no preceding history of clinically recognized heart disease and SCA is the first manifestation of heart disease\textsuperscript{14-16}, most often coronary heart disease (CHD)\textsuperscript{17, 18}. Even among the smaller subgroup of SCA victims who had clinically recognized heart disease prior to death, most do not have a prior diagnosis of heart failure\textsuperscript{10} or an LVEF below 30%. In the present study, over two thirds of the 448 sudden death victims who did undergo echocardiograms would not have qualified for ICD therapy because their left ventricular ejection fraction was greater than 35%.

So in response to the second question, while initiatives that increase ICD use in patients who meet present guidelines have the potential to save lives, the data by Chugh et al. illustrate the potential ceiling to the absolute number of lives which can be saved with this approach. In order to further impact mortality from SCA, we need to focus effort, research, and resources on multiple strategies aimed at SCA prevention at earlier stages and in populations at all levels of risk. Currently, there are a number of lifestyle and dietary habits that have been associated with coronary artery disease and SCA incidence, and interventions involving risk factor modification could be applied to the population at large without further risk stratification\textsuperscript{19, 20}. However, if we are to achieve a more targeted approach, where advanced therapies such as the ICD could be
applied to benefit larger populations, substantially better markers of arrhythmic risk beyond LVEF are required, and this is a current active area of research. These novel markers should be relatively accessible and have adequate discriminatory power for arrhythmic death such that they could be applied to broader populations such as patients with CHD without severe systolic dysfunction or more broadly to patients with multiple CHD risk factors. It is unlikely that one marker will be sufficient, and combinations of markers will likely be needed as risk stratification tools. This search for improved risk stratification tools along with continued basic arrhythmia research may lead to a better understanding of the biological pathways and mechanisms underlying the predisposition to arrhythmias, which might eventually lead to new targeted approaches for SCD prevention beyond the ICD.

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