A 45-year-old man with end-stage cardiomyopathy died while waiting for a heart transplant after living almost 1 year in a coronary care unit supported by intravenous medications. Around the time of his death, an off-duty police officer in a neighboring town watching a high school football game saw one of the player’s fathers slump forward unconscious. The officer ran to his patrol car, grabbed the automated external defibrillator he had recently been assigned, and defibrillated the father’s ventricular fibrillation. The man immediately regained consciousness and protested being taken to the hospital because he wanted to watch his son finish the game! These extremes provide dramatic bookends to the spectrum of how we spend money to save a life. Some therapies are inexpensive and others are not, and society has to make difficult choices about how to use our limited resources.

The opinions expressed in this editorial are not necessarily those of the editors or of the American Heart Association.

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Implantable Cardioverter-Defibrillator: A Volkswagen or a Rolls Royce

How Much Will We Pay To Save A Life?

Douglas P. Zipes, MD

The implantable cardioverter-defibrillator (ICD) represents one of the most important advances in the past 50 years in the treatment of patients with life-threatening ventricular tachyarrhythmias. Five pivotal prospective, randomized, clinical trials have helped define its use. In 3 secondary prevention trials, Antiarrhythmics Versus Implantable Defibrillators (AVID), Canadian Implantable Defibrillator Study (CIDS), and Cardiac Arrest Survival Hamburg (CASH), secondary prevention trials established that the ICD did not confer added benefit compared with amiodarone in patients with life-threatening ventricular tachyarrhythmias. Further analysis of data from the 3 primary prevention trials, Multicenter Automatic Defibrillator Implantation Trial (MADIT) and Multicenter Unsustained Tachycardia Trial (MUSTT), the ICD was superior to antiarrhythmic drugs (mostly or exclusively amiodarone) in reducing mortality in patients with life-threatening ventricular tachyarrhythmias. Further analysis of data from the 3 secondary prevention trials established that the ICD did not confer added benefit compared with amiodarone in patients who had ejection fractions (EF) >35%. Additional examination of data from CIDS showed that patients who were in the highest risk quartile enjoyed a 50% relative risk reduction in mortality from the ICD that was not found in the lower 3 quartiles. Higher risk patients had ≥2 of the following risk factors: age ≥70; EF ≤35%, or New York Heart Association (NYHA) class III or IV. Consistent with these observations, a preliminary review of MADIT data revealed that the major benefit of the ICD was found in those with an EF ≤26%.

In this issue of Circulation, O’Brien et al present relative use data from an economic substudy conducted on the first 430 patients (of 659 total) enrolled in CIDS. In the original trial, CIDS investigators found an annual risk of death from any cause with the ICD of 8.3%, compared with 10.2% with amiodarone ($P=0.14$), whereas arrhythmic death risks were 3.0% per year with the ICD and 4.5% with amiodarone ($P=0.09$). In the present study, they show that life expectancy, discounted to present value at 3% per year for use in cost-effectiveness analysis, is 4.5 years with amiodarone and 4.58 years with the ICD, for a difference of 0.23 years in favor of the ICD. Including costs over the 6-year period of follow-up (and, for purposes of this analysis, converting costs of the early thoracotomy implants to that of transvenous implants), the cumulative expected cost per patient (all costs expressed in Canadian dollars; CDN $1=US $0.68) was CDN $87 715 for the ICD and CDN $87 600 for amiodarone, a difference of CDN $115. That value, divided by the gain in life expectancy of 0.23 years, equals an incremental cost-effectiveness of ICD therapy of CDN $213 543 per additional life-year gained, which is rather expensive when compared with other acceptable therapies, even after conversion to US dollars.

The authors provide further helpful analyses. If the cost of the hardware was CDN $16 000 rather than CDN $22 000, cost-effectiveness would fall to CDN $22 614 per life-year gained. If hospitalization had been 1 day instead of a lengthy 4.7 days in intensive care plus 12 days in the ward, cost-effectiveness would have been reduced to CDN $170 284. In patients with a left ventricular EF $<35$, the cost-effectiveness was CDN $108 484 per life-year gained.

The authors also provide 3 extrapolations for cost-effectiveness that are based on the following assumptions: (1) that benefit continues over a 12-year follow-up (CDN $99 420), (2) that benefit becomes equivalent between years 6 and 12 (CDN $118 668), and (3) that benefit declines so that survival curves converge at 12 years (CDN $149 710). Because the reduction of mortality by the ICD did not reach statistical significance in CIDS, the authors could have provided another analysis by calculating the cost-effectiveness from the combined results of AVID, CASH, and CIDS. That analysis
indicates that those costs at 6 years would be $132,743 for an undiscounted cost (additional survival, 0.37 years) and $148,833 for a cost discounted at 3% (additional survival, 0.33 years).

Certain criticisms can be levied at this well-done study that may not affect the conclusions materially but, nevertheless, still need to be recounted. The analysis was performed on the first 430 patients in the study. Therefore, the conclusions might be incorrect if treatment or the type of patient changed in the remaining 229 patients; for example, if the latter had higher ejection fractions than the former. This is not likely to occur in a randomized trial. Also, the calculations came from cost data collected at only 1 hospital and from an underpowered study that did not reach a statistically significant outcome. Despite the fact that those point estimates may have been imperfect, they were used to model life expectancy, making generalizations potentially risky. However, as noted above, even if the combined survival data from CIDS, CASH, and AVID are substituted, cost-effectiveness was still relatively high. Another criticism is that although treatment category was appropriately based on an intention-to-treat classification, such a methodology may not yield an accurate appraisal of costs. For example, 2 ICDs were initially implanted in patients in the amiodarone treatment arm; this group also received 36 new ICD implants (crossovers) subsequent to the initial hospitalization. The ICD, by providing improved survival in amiodarone-treated patients, could have narrowed the difference in survival between both treatment groups, thus exaggerating the cost of the device per life-year gained. Finally, the cost per quality-adjusted life-year gained might have been somewhat lower, but the authors used the Nottingham Health Profile, which cannot be used to make that calculation.

The cost-effectiveness ratios from CIDS are considerably greater than those found in MADIT and can be explained in large part by the attributable difference in survival between the 2 trials. As the authors note, over a 4-year period, MADIT investigators found a 0.8-year gain in life-years with the ICD compared with amiodarone, which reduced the cost of the ICD to a very acceptable $39,764 per life-year gained. This certainly places the ICD into a more affordable range. The increased benefit compared with the present study and with the meta-analysis may reflect the difference in randomized patients. In MADIT, the mean age was 63 years, the median ejection fraction was 26%, and 51% of patients had a history of heart failure. For CIDS, the mean age was also 63 years, but 40% of patients were in NYHA class 1 or 2, only 11% were in NYHA class 3 or 4, and the mean left ventricular EF was 33%. In the pooled CIDS, CASH, and AVID database, the mean age of the ICD patients was the same (63 years); however, the mean left ventricular EF was 34%, 9% had a NYHA class ≥3, and 4% had no structural heart disease. Thus, as several studies have now documented, if the benefits of the ICD compared with amiodarone are greater in patients with more advanced heart disease, MADIT could have been more cost-effective on that basis. One could postulate that patients with advanced heart disease die from episodes of ventricular tachycardia that are otherwise transient and tolerated in patients with better cardiac function. Of course, one could also raise the argument that, because there was no placebo group with which to compare outcome, amiodarone increased the mortality in the sicker group, making the ICD treatment seem more effective. However, data from other controlled trials do not indicate an increased mortality due to amiodarone.

If the ICD is really more effective in patients with more advanced heart disease, this should probably become evident in MADIT II (entry criterion, EF ≤30%) and the Sudden Cardiac Death–Heart Failure (SCD-HeFT; entry criterion, EF ≤35%) trials, which are testing the ICD versus amiodarone in patients with heart failure. Indeed, if those studies show a benefit for the ICD, the number of patients who would qualify for device implantation becomes quite large. One cautionary note is that there are probably some patients with such advanced forms of heart failure that the ICD may not provide benefit.

What can we recommend at the present time? I think that the retrospective observation that the ICD does not benefit patients with normal or minimally reduced cardiac function when compared with amiodarone first needs to be tested and established prospectively. If the outcome supports ICD implantation only in arrhythmia patients with reduced EFs, then that would focus device implantation on a more selected arrhythmia population. Of course, it is possible that within the high-EF group, certain patients will still benefit from the ICD compared with amiodarone, but that needs to be established. In addition to the arrhythmia patients, those who have heart failure may qualify for ICD implantation on the basis of the results from MADIT II and SCD-HeFT. This would raise the number of potential ICD implants significantly.

Therefore, I think the most logical approach is for device manufacturers to create a selection of ICDs from which to choose. For some patients, a sophisticated ICD that could be used to treat comorbidities and monitor a variety of physiological functions may be indicated, whereas in others, an inexpensive ICD in the $10,000 to $15,000 range might be preferable. The latter could be achieved if the manufacturers made an ICD with limited function capabilities—a Volkswagen instead of a Rolls Royce. It could have restricted but adequate detection and storage capabilities and a battery capacity to deliver only 8 or 10 shocks. If the patient used up that number of shocks, the device could be replaced with a more advanced unit. Certainly, the large number of implants in heart failure patients could make that approach profitable for industry and acceptable to society. We cannot have the “one size fits all” ICD anymore because of the costs involved, as this study shows. Physicians should be able to choose the type of ICD most applicable for the needs of a given patient. Implanting the ICD in the outpatient setting with minimal preimplant evaluation can also reduce costs.

In the final analysis, many medical decisions are based on how much money society is willing to spend to save a life. Making automated external defibrillators as common as fire extinguishers is a “no brainer” and offers an incredible return on the investment, as the opening example illustrates. However, the potential expense of implanting large numbers of ICDs calls for more judgment. Careful patient selection, a less expensive device, and benefits extending...
over a 10- to 12-year period will make it an acceptable treatment option for many more patients.

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