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Clinical Perspective

Cost-effectiveness of implantable cardioverter-defibrillator in today's world

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ABSTRACT

The implantable cardioverter-defibrillator (ICD) is an example of an effective intervention with high up-front costs and delayed benefits. It has become a proven and well-accepted therapy not only for secondary but also for primary prevention of sudden cardiac death in patients with ischemic and non-ischemic heart disease. In recent years, the international guidelines have extended the indications to the prophylactic ICD, increasing the number of eligible patients and, together, the financial challenges of a widespread implementation. In this article, we review the available economic tools that can help address the ICD cost issue. We think that the awareness of such knowledge may facilitate dialogues between physicians, administrators and policy-makers, and help foster rational decision making.

1. Introduction

New opportunities in the field of preventive and curative medicine are now available thanks to rapid technological advances. However, since many effective new interventions entail considerable financial cost, affordability issues are rising, mostly because of limited financial resources. Primary prevention is a particularly challenging area, since often the benefits of an intervention could be perceived only many years later[1,2]; therefore, expensive primary prevention initiatives may cause diffidence, or even active resistance, due to the financial burdens which inevitably accompany their widespread adoption.[3]

The implantable cardioverter-defibrillator (ICD) is an example of an effective intervention with high up-front costs and delayed benefits.[4–9] It has become a proven and well-accepted therapy not only for secondary but also for primary prevention of sudden cardiac death in patients with ischemic and non-ischemic heart disease. In recent years, the international guidelines have extended the indications to the prophylactic ICD, increasing the number of eligible patients[7–9] and, together, the financial challenges of a widespread implementation.[2,3,10]

In this article, we will discuss how the available economic tools can help address the ICD cost issue, and, according to the available estimates, how it's desirable a cultural change in the

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way many physicians, administrators and policy-makers view and approach this sort of issue.

2. The ICD cost issue

Despite the decline in overall mortality from cardiovascular diseases observed over the last decade, the proportion of deaths due to sudden cardiac death has been increasing: in Western countries, sudden cardiac death is responsible for more victims each year than AIDS, lung cancer, breast cancer, or stroke.[11,12] In economically developed countries, use of ICDs for primary prevention of sudden cardiac death can be seen as a relevant public health consideration: indeed, evidence from a series of large randomized trials now provides very strong evidence that use of ICDs improves overall survival at 2–5 years in appropriately selected patients with left ventricular dysfunction.[5,7,9] The ICD is commonly perceived as a rather expensive therapy with high up-front costs due to the device itself and the implant followed over time by maintenance costs for device replacement and possible complications.[2] Despite marked price reductions in the last decade, the main limit to a full acceptance and adoption of ICD therapy, especially regarding primary prevention, is still the cost issue[2,13]; this matter concerns all the organizations involved in the care of patients with heart failure, not only electrophysiologists.

The role of ICD therapy has expanded hugely since the device was first conceived by Dr. Michel Mirowski over 25 years ago for secondary sudden cardiac death prevention in selected patients with documented ventricular tachyarrhythmias.[14,15] Demonstrated efficacy of ICDs in primary prevention was initially established in patients with ischemic heart disease (MADIT I, MUSTT, MADIT II trials),[4–9] and was then extended to patients with heart failure (NYHA class II and III) of either ischemic or non-ischemic etiology (SCD-HeFT trial).[4–9] These findings were progressively translated into the recommendations for ICD implantation provided by consensus guideline: the widening of evidence-based indications to implantation is expected to lead to an impressive rise in the potential number of implants. In response to concerns that increased use of ICDs may cause a dramatic financial burden on healthcare systems, a debate is emerging on how to find a balance between the weight of evidence and spending on ICD therapy.[2]

Whereas there is broad scientific consensus regarding the efficacy of using ICDs in appropriately selected patients, a search to reach a similar consensus on the cost issue appears more problematic: the affordability of relatively expensive treatments of clearly proven efficacy is a delicate issue, that should be kept separate from clinical guidelines based on scientific evidence of efficacy.[16,17]

Despite the mounting costs that healthcare systems have had to face in recent years, in many high-income countries the balancing of benefits against costs has yet to become a primary criterion for deciding whether a medical treatment should be covered by public services (the U.K. National Institute of Clinical Excellence is a prominent exception in this respect).

In many European countries, consideration of the effects of adopting a new treatment has mainly been based on strictly financial concerns rather than on in-depth economic analysis, with a consequent tendency to limit or even reject costly new treatments, despite proven clinical efficacy.[18]

Affordability considerations will inevitably vary between countries with very different healthcare systems and economies: nevertheless, analytical tools do exist to help address specific questions of affordability within national, regional or even local contexts.

3. Available tools for economic analysis

A range of economic tools allows us to weigh up the benefits and the costs of given medical treatments, providing a formal economic basis for implementation decisions. In order to go beyond the assessment of financial burden of competing candidate treatments, a genuine economic approach should include cost-effectiveness and cost-utility estimates, expressed in terms of 'years of life saved' (YLS) and 'quality-adjusted life years' (QALY) gained, respectively, and cost-benefit analysis, which assigns a monetary value to therapeutic benefits.[18] These tools address questions such as "which treatment is most likely to provide maximum health benefits for a given level of financial resources?" or "which treatment provides a given level of health benefits at the lowest cost?"; the different approaches generate different measures.[18]

Cost-effectiveness analysis aims to assess the cost of any therapeutic intervention with respect to its predictable outcome benefits.[18] "Incremental cost-effectiveness" analysis compares alternative therapeutic strategies and generate a cost-effectiveness ratio, often expressed in dollars per year of life saved ($/YLS). In the literature,[13,18,19] treatments are sometimes referred to vary from "very attractive" to "absolutely unfavorable" depending on the cost-effectiveness ratio. As shown in Table 1, cost-effectiveness ratios can vary considerably depending on the subset of treated population: identification of high-risk patients[13] seems to be the single most important factor in order to reach a favorable figure.[13] Notably, long-term use of relatively "cheap" medications which do not exert major long-term survival benefits can generate unfavorable cost-effectiveness ratios (examples include lipid lowering treatments or antiplatelet drugs in patients at relatively low risk); conversely, when high initial treatment costs are offset by long-term survival benefits (as can be the case with ICDs) the cost-effectiveness ratio may turn out to be surprisingly favorable. Improved risk stratification may allow identification of patients for whom the option of ICD implantation appears more favorable or attractive, and thus, it might help optimize health outcomes within the context of financial restrictions.[20,21]

4. Available economic estimates for use of ICDs

Various economic models generated a broad range of cost-effectiveness estimates for ICDs, ranging from unfavorable to economically attractive values.

The most authoritative cost-effectiveness analysis of ICD therapy in the primary prevention of SCD was provided by Sanders et al. Eight landmark ICD trials were considered, and

Table 1 – League table on the cost-effectiveness profile of various medical interventions according to €/QALY ratio (modified from Leyva et al and Thjissen et al).[22,23] Estimates are reported in € per quality-adjusted life year saved, or in some cases, as reported, in € per life year saved.

Treatment	€/QALY
Enalapril for heart failure	83
Intensive insulin therapy for a 25-years-old	6907
Liver transplantation	18,678*
Heart transplantation	20,115*
Primary prevention ICD in MUSTT	28,500
Primary prevention ICD in MADIT I	29,254
Primary prevention ICD in COMPANION	42,163
Primary prevention ICD in DEFINITE	43,001
Primary prevention ICD in MADIT II	45,348
Lung transplantation	55,317*
Primary prevention ICD in SCD-HeFT	58,842
ACEI for hypertension in echo-LVH	143,680
Screening at 50 years for proteinuria, then ACEI	203,177
ACEI for hypertension in unselected patients	502,880
Statin for primary prevention	38,793–1,005,760
Intensive insulin therapy for an 85-years-old	1,508,640

Legend: * = € per life year saved; QALY, quality-adjusted life year saved; ACEI, angiotensin-converting enzyme inhibitors; echo-LVH, left ventricular hypertrophy according to echocardiography.

a Markov model of costs, quality of life, survival, and incremental cost-effectiveness was used to compare ICD therapy to control therapy over a lifetime horizon. Whilst in two of those trials the lack of clinical efficacy of ICD therapy led to a lack of cost-effectiveness over control therapy, in the six other trial populations, primary prevention single-chamber ICD implantation was projected to add between 1.01 and 2.99 QALYs and the incremental cost-effectiveness (discounted at 3%) ranged from €28.500 to €58.842 per QALY gained.[22] Importantly, the cost-effectiveness ratio was below $100.000 in all the trial populations, as long as the effectiveness of the ICD was assumed to continue for at least 7 years.[23]

Concerning the European healthcare systems, a meta-analysis by Cowie et al examined the lifetime benefits, costs and cost-effectiveness of prophylactic implantation of an ICD adopting the perspective of the Belgian healthcare system: in this analysis, primary prevention single-chamber ICD implantation was associated with an estimated mean LY and QALY gain of 1.88 and 1.57, respectively, and an estimated mean lifetime cost per QALY gained of €31.717 according to the probabilistic sensitivity analysis.[24] These results are comparable with those reported by Thijssen et al based on clinical data and costs derived from routine clinical practice.[22] In the latter analysis it was shown that single and dual-chamber ICDs are cost-effective as primary prevention therapy also in the real world.

An important source of variability is the horizon within which cost-effectiveness is estimated.[25,26] In this respect, a review of eight trials has shown that the benefit from ICD therapy increases non-linearly with the square of time.[27] This implies that at 3 years the LYS per ICD implanted in MADIT was 4.6 times that observed at 1 year. The increase in benefit from ICD therapy with time from implantation has important implications for its cost-effectiveness, particularly as the therapy involves high up-front costs. For instance, in the SCD-HeFT study, the base-case lifetime ICER was €27.579 per QALY: model projections revealed that the ICER per LYS was reduced from €150.526 at 5 years, and to €35.920 at 14 years.[23]

An extension of device longevity can be achieved in most recent devices reducing long-term costs of ICD therapy; this may further improve its cost-effectiveness, as well as the cost per day of ICD therapy.[28,29]

The most comprehensive available analysis on cost-effectiveness was commissioned by NICE specifically for the UK national context.[30,31] This study included a decision analytic model based on evidence critically extracted from 8 randomized controlled trials, 2 systematic reviews and a meta-analysis. Taking into account both secondary and primary prevention, the results indicated that ICD use can lead to variable survival improvements, with incremental cost-effectiveness values ranging from 98,000 to over 379,000 $/QALY depending on mortality risk and the assumptions adopted.[31] This commissioned work exemplifies how cost-effectiveness analysis can be applied to a specific national context to guide rational health care decision making.

As regards cost-benefit analysis, to our knowledge there is only one currently available study of ICDs in primary prevention of sudden cardiac death.[32] This study challenges the widespread assumption that ICDs should be viewed as a worrying financial burden for society. The researchers used the results of SCD-HeFT to compare cost-benefit values estimated for ICDs in comparison with amiodarone (the most widely used prophylactic antiarrhythmic drug). The conclusion was that in countries where society values a life more than €2 million, ICDs can be considered a more worthwhile long-term investment than amiodarone for primary prevention of sudden cardiac death.[32] This cost-benefit evaluation may radically change the perspective of ICD use in high-risk patients, supporting the view that this option can be seen as a worthwhile investment not only for individual patients, but also for society as a whole.[33]

5. Conclusions

Despite continuing price reductions, ICD cost will probably remain a major issue in implementation of current guidelines.[34–36] In the light of broadened indications to implantation and locally available resources, physicians might face societal limitations (limited economical funding) which compete with individual imperatives (offering the best to each patient).

In this article, we have tried to illustrate how economic analysis can provide a key tool to weigh ICD costs against projected long-term outcome benefits. Considering the relatively high up-front ICD costs, this approach seems appropriate for assessing whether implantation in specific subsets of patients will eventually be more or less economically valid in comparison with alternative treatments involving more “continuous” costs. Most studies indicate that use of ICDs in appropriately selected patients at high risk of sudden cardiac death is cost-effective, and thus it can be considered a worthwhile long-term investment.

Improved awareness of this concept among physicians, administrators and policy-makers may help foster rational decision making for the allocation of available resources.

Conflicts of interest

All authors have none to declare.

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