International Journal of Cardiology 163 (2013) 309–315

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Cost-effectiveness of cardiac resynchronization therapy in patients with heart failure: The perspective of a middle-income country's public health system ☆,☆☆

Eduardo G. Bertoldi [a,1], Luis E. Rohde [b,d,1], Leandro I. Zimerman [c,1], Maurício Pimentel [c,1], Carisi A. Polanczyk [d,*,1]

[a] Postgraduate Program in Cardiology and Cardiovascular Sciences, Federal University of Rio Grande do Sul, Porto Alegre, Brazil
[b] Heart Failure and Cardiac Transplantation Unit, Cardiovascular Division of Hospital de Clínicas de Porto Alegre, Brazil
[c] Cardiovascular Division of Hospital de Clínicas de Porto Alegre, Brazil
[d] Postgraduate Program in Cardiology and Cardiovascular Sciences, Medical School of the Federal University of Rio Grande do Sul, Porto Alegre, Brazil

ARTICLE INFO

Article history:
Received 10 April 2011
Accepted 6 June 2011
Available online 24 June 2011

Keywords:
Heart failure
Cardiac resynchronization therapy
Implantable cardioverter–defibrillator
Cost-effectiveness

ABSTRACT

Background: Cardiac resynchronization therapy (CRT) improves symptoms and survival in patients with heart failure (HF). However, the devices used to deliver it are costly and can impose a significant burden to the relatively constrained health budgets of middle-income countries such as Brazil.
Methods: A Markov model was constructed, representing the follow-up of a hypothetical cohort of HF patients, with a 20-year time horizon. Input data were based on information from a Brazilian cohort of 316 HF patients, as well as meta-analyses of data on devices' effectiveness and risks. Stochastic and probabilistic sensitivity analyses were performed for all important variables in the model. Costs were expressed as International Dollars (Int$), by application of current purchasing power parity conversion rate.
Results: In the base-case analysis, the incremental cost-effectiveness ratio (ICER) of CRT over medical therapy was Int$ 15,723 per quality-adjusted life years (QALYs) gained. For CRT combined with an implantable cardioverter–defibrillator (ICD), ICER was Int$ 36,940/QALY over ICD alone, and Int$ 84,345/QALY over CRT alone. Sensitivity analyses showed that the model was generally robust, though susceptible to the cost of the devices, their impact on HF mortality, and battery longevity.
Conclusions: CRT is cost-effective for HF patients in the Brazilian public health system scenario. In patients eligible for CRT, upgrade to CRT + ICD has an ICER above the World Health Organization willingness-to-pay threshold of three times the nation's Gross Domestic Product per Capita (Int$ 31,689 for Brazil). However, for ICD eligible patients, upgrade to CRT + ICD is marginally cost-effective.

1. Introduction

Heart failure (HF) is a leading cause of cardiovascular morbidity and mortality worldwide, with increasing prevalence in the last decade, and generating high costs for healthcare systems [1,2]. Brazilian epidemiological data indicates that HF is the most common cause of hospital admission in the elderly population and a major cause of expenditure for the public system in this country [3].

Multisite (biventricular) pacemakers, capable of delivering Cardiac Resynchronization Therapy (CRT), can reduce HF morbidity and mortality [4]. Different devices can deliver resynchronization pacing alone (CRT-P) or in combination with cardiac defibrillation therapy (CRT-D). The recently published RAFT trial [5], showing that CRT-D devices reduce mortality in New York Heart Association (NYHA) class II HF patients, when compared to ICD alone, has the potential to expand the indication of multisite pacemakers to a very large number of patients.

However, HF device therapies are costly, and widespread implementation of CRT can put a significant burden on healthcare budgets, particularly in the case of low- and middle-income countries with great populations, such as Brazil, India, China and Russia. The decision of whether the countries' Public Health System should reimburse these treatment modalities to all patients that could derive clinical benefit should be based on proper economical evaluations.

Abbreviations: CRT, cardiac resynchronization therapy; CRT-D, combined cardiac resynchronization therapy and implantable cardioverter–defibrillator; CRT-P, cardiac resynchronization therapy alone; HF, heart failure; ICD, implantable cardioverter–defibrillator; Int$, International Dollars; LY, life years; OMT, optimal medical therapy; QALY, quality-adjusted life years; NYHA, New York Heart Association; WTP, willingness-to-pay.

☆ Funding: National Institute of Science and Technology for Health Technology Assessment (IATS), Brazil.
☆☆ Corporate affiliations: The authors have no affiliation to manufacturers of medical supply or equipment, and have no potential conflicts of interest to declare.
* Corresponding author at: Serviço de Cardiologia, Hospital de Clínicas de Porto Alegre. Rua Ramiro Barcelos 2350, Sala 2061, Porto Alegre, RS, Brazil. Tel.: +55 90035 3.
E-mail address: carisi@terra.com.br (C.A. Polanczyk).
[1] From the Cardiovascular Division of Hospital de Clínicas de Porto Alegre, Postgraduate Program in Cardiology and Cardiovascular Sciences, Federal University of Rio Grande do Sul, Porto Alegre, Brazil.

0167-5273/$ – see front matter © 2011 Published by Elsevier Ireland Ltd.
doi:10.1016/j.ijcard.2011.06.046

We performed a cost-effectiveness study of CRT in HF patients in Brazil, using a Markov process decision-analytic model to address the incremental cost-effectiveness ratio of adding CRT to the standard of care in HF patients.

2. Methods

2.1. Target population

The target population was patients with HF due to systolic dysfunction (ejection fraction under 35%), in NYHA class II, III or IV, and with prolonged QRS on electrocardiogram. This profile represents the population in which CRT has showed significant reduction in mortality and hospitalization in the published clinical trials [4]. All patients in the hypothetical cohort enter the model with 60 years of age. Relevant input parameters for the model are summarized in Table 1.

2.2. Model structure

We used TreeAge Pro Suite 2009 (TreeAge Software, Inc., Williamstown, Massachusetts) to build a model with two components. The short-term component is a simple decision tree, representing the costs and consequences of initial device implantation. Afterwards, a state-transition Markov Model represents the long-term follow-up of the hypothetical cohort until the time horizon of 20 years.

The model evaluates four different scenarios: optimal medical therapy (OMT), addition of a cardioverter–defibrillator device (ICD) to OMT, addition of a multisite pacing device with capability of CRT only (CRT-P) to OMT, or addition of a multisite pacing device with capability of both CRT and cardioversion–defibrillation (CRT-D) to OMT.

The short-term portion of the model accounts for the possibilities of failure to implant the device, successful implantation with no major complications, successful implantation with major nonfatal complications, and implant-related death, all within one month of the procedure.

In the long-term Markov model, patients on OMT may remain stable, change NYHA class, have an unplanned hospitalization (with possible change in NYHA class after discharge), or die. Patients on device therapy have all these possibilities and, additionally, can experience device related complications, namely infection and lead failure. Additionally, the devices need periodical battery replacements, and this brings an additional risk of procedure-related complications. Figs. 1, 2-a and b schematically display the model structure.

Table 1
Input data.

Variable	Base-case	Lowest estimate	Highest estimate	References
Short term				
Implant failure—CRT	8.0%	6.0%	11%	Pooled data [5,6,8,10–17]
Implant failure—ICD	1.1%	0.9%	1.3%	[40]
Major implant complication—CRT	13.2%	7.3%	23.9%	Pooled data [5,6,12–14,17]
Major implant complication—ICD	9.8%	5.5%	16.8%	Own assumption, based on [6,12–14,16,17]
Peri-implant death—CRT	0.6%	0.02%	2.2%	Pooled data [5,6,10,11,14]
Peri-implant death—ICD	1.3%	1.2%	1.4%	[40]
Long term				
CRT-P mortality, RR	0.76	0.64	0.9	Pooled data [6,9,10,14,15]
ICD mortality, RR	0.74	0.67	0.83	[18]
CRT-D mortality, RR (compared to ICD)	0.83	0.72	0.96	Poled data [5,11–13,16,17]
CRT hospitalization, RR	0.6	0.48	0.75	Pooled data [5,6,8,9,14]
ICD hospitalization, RR	1	0.8	1.2	Own assumption
Battery longevity	5	3	7	[26] and expert opinion
Utilities				
NYHA class I	0.9	0.71	0.94	[27,28,41]
NYHA class II	0.83	0.61	0.94	[27,28,41]
NYHA class III	0.74	0.52	0.84	[27,28,41]
NYHA class IV	0.6	0.421	0.74	[27,28,41]
Unplanned hospitalization (disutility)	0.1	0.05	0.2	Assumption based on [41]
Costs (Int$)				
CRT-D device	32,051.28	16,025.64	48,076.92	[3]
CRT-P device	10,077.03	5,038.51	15,115.54	[3]
ICD device	23,134.22	11,567.11	34,701.33	[3]
CRT replacement lead	3,833.41	1,916.71	5,750.12	[3]
ICD replacement lead	4,534.79	2,267.39	6,802.18	[3]
Device implantation	1,062.76	531.38	1,594.13	[3]
HF hospitalization	448.37	224.19	672.56	[3]
Stable HF—yearly cost	1,345.51	672.76	2,018.27	[3,29]

CRT = cardiac resynchronization therapy; ICD = implantable cardioverter–defibrillator; RR = relative risk; NYHA = New York Heart Association; CRT-P = cardiac resynchronization therapy (without ICD); CRT-D = cardiac resynchronization therapy combined with ICD; Int$ = international dollars (purchasing power parity); HF = heart failure.

2.3. Clinical data

Rates of hospitalization and mortality for patients in OMT were based in a cohort of patients followed at a HF outpatient clinic in a teaching hospital in Porto Alegre, Brazil [unpublished data]. The cohort follows 316 HF patients, 69% are males, with median age of 61 years (inter-quartile range [IQR] 50–69). HF etiology is ischemic in 37% of the cases, and the median follow-up time is 36 months (IQR 16–62).

The survival data from this cohort were used to create a Weibull function that represents the probability of survival for patients in OMT in any given cycle (Fig. 3). The gamma and lambda parameters for the Weibull function were 1.0715 and 0.1000325, respectively, and the resulting curve is similar to the one observed in the conventional therapy group in the CARE-HF trial [6], which is the CRT study with the longest follow-up time [7]. The model starts with patients evenly distributed among NYHA classes II, III and IV. Annual rates of hospitalization for each NYHA class were also obtained from this cohort, and were 13% for class I, 25% for class II, 29.7% for class III and 40% for class IV.

2.4. Effectiveness data

We performed a systematic review of the published clinical trials involving CRT in HF patients, with a final selection of twelve studies [5,6,8–17]. Pooled data from these trials using inverse variance random-effects models was used to obtain the effectiveness parameters for CRT devices. In this analysis, we found a relative risk (RR) for all-cause mortality of 0.76 (95% confidence interval [CI] 0.64–0.9) for CRT-P versus OMT and 0.83 (95% CI 0.72–0.96) for CRT-D versus ICD. Tests for heterogeneity were negative. For impact of CRT in the yearly risk of hospitalization for HF, we pooled the results from the trials that had published this endpoint [6,8,9,14], and found a RR of 0.6 (95% CI 0.48–0.75) [data submitted for publication].

For the effectiveness of ICDs, we used data from a published meta-analysis by Nanthakumar et al. [18], as previously done in a cost-effectiveness study performed by our group [19]. In this meta-analysis, the RR for all-cause mortality was 0.74 (95% CI 0.67–0.83) for ICD versus OMT.

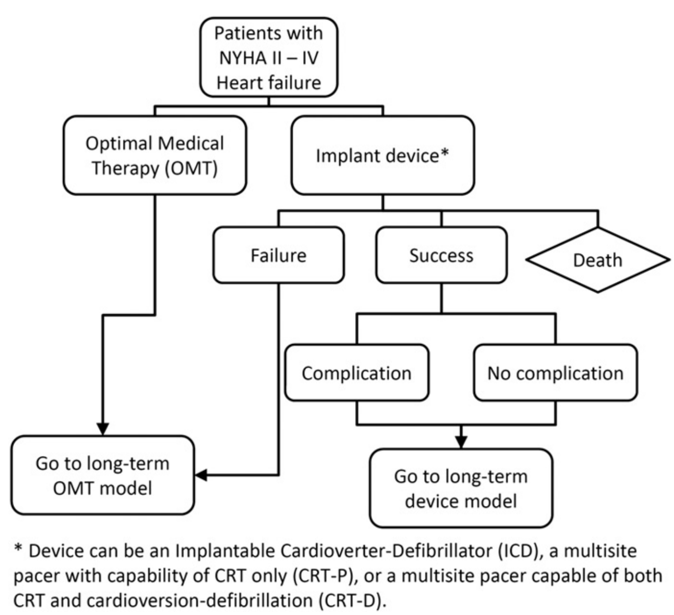

Fig. 1. Short-term model.