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Implantable cardioverter defibrillator therapy for primary prevention of sudden cardiac death in the real world: Main findings from the French multicentre DAI-PP programme (pilot phase)

Abbreviated title: ICDs for primary prevention of sudden cardiac death

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Summary

This review summarizes the main findings of the French multicentre DAI-PP pilot programme, and discusses the related clinical and research perspectives. This project included retrospectively more than 5000 subjects with structural heart disease who received an implantable cardioverter defibrillator (ICD) for primary prevention of sudden cardiac death, and were followed for a mean period of 3 years. This collaborative research programme led to 20 publications. Several useful and clinically relevant findings emerged from this cohort, which are summarized in this review. Firstly, our registry revealed the changing trends in primary prevention ICD implantation over the past decade, with increases in age at implantation and the proportions of cardiac resynchronization therapy and female recipients. The occurrence of early complications after implantation remained significantly associated with global mortality (odds ratio 1.70; $P = 0.003$). Female recipients of resynchronization therapy had a lower incidence of appropriate therapies (hazard ratio 0.62; $P < 0.001$ versus males). Overall mortality was higher among patients with ischaemic compared with non-ischaemic cardiomyopathy (hazard ratio 1.31; $P = 0.01$); incidences of appropriate therapies were similar. During follow-up, 3.2% of ICD recipients had a heart transplantation. Looking at utility of ICD implantation after 80 years of age, 19.4% received at least one appropriate therapy before death. Compared with single-chamber ICDs, dual-chamber ICDs did not reduce rates of inappropriate therapies, and were associated with a higher rate of complications. Finally, this pilot phase has led to a prospective evaluation since May 2018, assessing ICD therapy in primary and secondary prevention in patients with structural and electrical heart diseases followed up with a remote monitoring dedicated platform.

Résumé

Cet article résume les principaux résultats de la phase pilote du programme DAI-PP et discute ses perspectives scientifiques. Ce projet a inclus plus de 5000 sujets ayant une cardiopathie et implantés d'un défibrillateur automatique implantable (DAI) en prévention primaire de la mort subite avec un suivi moyen de 3 ans. Ce programme de recherche collaboratif a abouti à 20 publications dont les principaux résultats sont résumés dans cette revue. Premièrement, ce registre a évalué l'évolution des implantations de DAI sur la dernière décennie, décrivant une augmentation de l'âge à l'implantation, de la proportion de resynchronisation cardiaque, et de femmes implantées. La survenue d'une complication précoce était significativement associée à la mortalité globale (OR 1,70 ; $P = 0,003$).

L'incidence des thérapies appropriées était plus faible chez les femmes implantées d'une resynchronisation (HR 0,62 ; $P < 0,001$ versus hommes). La mortalité globale était plus élevée chez les porteurs d'une cardiopathie ischémique comparé aux non-ischémiques alors que l'incidence des thérapies appropriées était similaire. Durant le suivi, 3,2 % des patients ont bénéficié d'une transplantation cardiaque. Chez les patients ≥ 80 ans à l'implantation, 19,4 % ont reçu au moins une thérapie appropriée avant leur décès. Enfin, comparé aux appareils mono-chambre, les DAI double-chambre ne réduisaient pas le taux de thérapies inappropriées et étaient associés avec un risque plus élevé de complications. Après cette évaluation pilote, un programme prospectif a été initié en France (mai 2018) visant à évaluer les DAI en prévention primaire et secondaire, chez des patients porteurs de cardiopathie structurelle et électrique, suivis en télécardiologie via une plateforme dédiée.

KEYWORDS

Implantable cardioverter defibrillator;

Primary prevention;

Sudden cardiac death;

Complications;

Epidemiology

MOTS CLÉS :

Défibrillateur automatique implantable ;

Prévention primaire ;

Mort subite cardiaque ;

Complications ;

Épidémiologie

Abbreviations: CI, confidence interval; CRT, cardiac resynchronization therapy; HR, hazard ratio; ICD, implantable cardioverter defibrillator; ICM, ischaemic cardiomyopathy; NICM, non-ischaemic cardiomyopathy; NYHA, New York Heart Association; OR, odds ratio.

Background

Sudden cardiac death is a major mode of death in the Western world [1, 2]. Implantable cardioverter defibrillators (ICDs) for primary prevention of sudden cardiac death have been demonstrated to be associated with a significant reduction in overall mortality among selected patients with dilated and ischaemic cardiomyopathies [3, 4]. Nevertheless, the implantation of such devices has the potential for numerous complications [5, 6]. Moreover, accurate prediction of sudden cardiac death is still a considerable challenge, and the number of patients implanted with a primary prevention ICD who will never experience ventricular arrhythmia represents both wasted effort and unnecessary risk, underlining the need for continuous improvements in the selection process for ICD candidates [7].

Although randomized controlled trials have given us a wealth of evidence, long-term data from the real-world setting are valuable and complementary. With this in mind, the pilot phase of the DAI-PP programme was conceived as a retrospective French multicentre registry aiming to assess the characteristics and outcomes of all patients implanted with an ICD for the primary prevention of sudden cardiac death between 2002 and 2012 (ClinicalTrials.gov Identifier: NCT#01992458), across 12 academic and private electrophysiology centres. All data were recorded retrospectively according to a specific protocol. Overall, 5539 consecutive patients were included, and the mean follow-up was 3 years. This registry led to 20 publications, and gave insights into several practical aspects of ICD use in primary prevention. This paper summarizes the main findings from the different DAI-PP analyses, and puts these into perspective, to help to eventually optimize primary prevention of sudden cardiac death using ICD therapy.

Main findings (Table 1)

Trends in primary prevention ICD implantation over a decade

As technology and clinical practice surrounding the use of primary prevention ICD implantation are in a state of constant evolution, the temporal trends in characteristics and outcomes of ICD therapy were assessed between 2002 and 2012 [8]. In addition to a shift in the type of device implanted, significant increases were observed in mean age (from 61.5 ± 11.6 to 63.2 ± 10.9 years; $P = 0.0016$) and the proportions of cardiac resynchronization therapy (CRT) with an ICD (from 43.6% to 60.4%; $P = 0.0001$), non-ischaemic cardiomyopathy (NICM) (from 31.0% to 44.7%; $P < 0.0001$) and female recipients (from 11.4% to 15.8%; $P = 0.004$). Reductions in annual mortality incidence (from 5.4% to

4.3%; $P = 0.05$) and appropriate therapy incidence (from 10.4% to 7.1%; $P = 0.0004$) were seen over the decade. By contrast, the incidence of ICD-related late complications (> 30 days after implantation) increased significantly (from 4.6% to 7.6%; $P = 0.003$). This analysis highlighted significant changes in the patterns of use and outcomes in primary prevention ICD implantation, with reductions in mortality and appropriate therapies, counterbalanced by an increase in complications. While the former is likely to be a reflection of advances in and better adherence to guideline-directed medical therapies, the latter is concerning, and may be the result of increased numbers of implantations in older patients with more co-morbidities. Of note, in this large cohort of primary prevention ICD recipients, more than one quarter were implanted without fulfilling proper guideline criteria, similar to rates reported in other large registries [9]. Despite a less severe clinical profile at implantation and lower mortality rates, off-guideline patients had, rather surprisingly, similar rates of appropriate therapies. These patients were also likely to benefit from their ICDs, underlying the need for better risk stratification in the future.

Special focus on specific groups: Women, advanced functional heart failure class and the elderly

Through the DAI-PP project we were able to assess outcomes according to specific variables, such as sex, New York Heart Association (NYHA) class and age. In most ICD trials, women were markedly under-represented. In our registry also, women constituted a minority of the recipients of an ICD (15.1%), 53.8% of whom received CRT [10]. Compared with men, women presented a different clinical profile, with a significantly higher proportion of NICM (60.2% vs 36.2%; $P < 0.001$), a wider QRS complex (QRS > 120 ms: 74.6% vs 68.5%; $P = 0.003$) a higher NYHA functional class and a lower prevalence of atrial fibrillation. During follow-up, female recipients of an ICD had a lower incidence of appropriate ICD therapies (hazard ratio [HR] 0.59, 95% confidence interval [CI] 0.45–0.76; $P < 0.001$) and all-cause death (HR 0.87, 95% CI 0.66–1.15; $P = 0.324$) than their male counterparts, whereas the rates of inappropriate shocks and early complications were similar in both groups. Scientific data on sex-specific outcomes is still growing, and pooled data might allow sufficient power to eventually lead to sex-specific ICD guidelines in the future [11, 12].

Although guidelines use NYHA class in the decision process for ICD implantation, mortality benefit in NYHA class III patients (especially compared with NYHA class II) is a matter of debate [3, 4]. Analysis of outcomes by NYHA class in the DAI-PP database demonstrated that although patients in

NYHA class III have higher overall mortality (HR per NYHA class 1.63, 95% CI 1.11–2.41; $P = 0.014$), driven by an increase in cardiovascular death, they experienced a similar incidence of appropriate ICD therapies [13]. Incidence of ICD-unresponsive sudden death remained very low, and was also similar across NYHA classes, supporting the efficacy of ICD in relatively advanced heart failure.

The benefit of primary prevention ICD implantation is also controversial in elderly patients, because of the greater competing risk of non-arrhythmic death. For this purpose, patients' characteristics and outcomes were analysed in three age groups: 18–59 years; 60–74 years; and ≥ 75 years [14]. As expected, older patients exhibited higher global mortality after ICD implantation. However, rates of sudden death and appropriate device therapies were similar across age groups. Older age was independently associated with a higher rate of early postimplantation complications (odds ratio [OR] 1.28 for age 60–74 years; OR 1.49 for age ≥ 75 years; $P = 0.03$) and a lower rate of inappropriate therapies. Among patients aged ≥ 80 years, 19.4% received at least one appropriate therapy before death [15]. Our results might suggest that among well-selected older subjects with relatively few co-morbidities, as reflected in our study population, primary prevention ICD implantation may be of relevance. Nevertheless, the inherent limitations in interpreting observational data in this particular competing-risk situation call for randomized controlled trials to provide definitive answers. Meanwhile, a careful multidisciplinary evaluation is needed to guide patient selection for ICD implantation in the elderly population.

Significant impact of early periprocedural complications

To date, the extent to which early complications after ICD implantation are associated with morbidity and mortality longer term, in daily practice, has only been addressed in limited populations. The DAI-PP project assessed the incidence and consequences of early complications (≤ 30 days) after ICD implantation [16]. Overall, early complications occurred in 13.5% of patients, with the most frequent complications being bleeding related (haematoma, 35.9%) and lead dislodgment (20.7%).

Independent factors associated with occurrence of early complications were severe renal impairment (OR 1.66; $P = 0.02$), age ≥ 75 years (OR 1.01; $P = 0.03$), CRT (OR 1.58; $P = 0.01$) and anticoagulant therapy (OR 1.28; $P = 0.03$). After adjustment, early complications remained associated with mortality (OR 1.70; $P = 0.003$) (Fig. 1). These results reinforce the impact of early complications, and particularly avoidance of pocket haematoma, which was the most frequent early complication.

Whereas recent guidelines have demonstrated a high level of evidence regarding vitamin K antagonist management, scientific data are still limited regarding non-vitamin K antagonist oral anticoagulant management in the periprocedural period of implantable cardiac electronic devices [17].

Perioperative defibrillation testing

Recent literature suggests that routine defibrillation testing does not improve defibrillation efficacy or reduce arrhythmic death [18]. Nevertheless, the impact of defibrillation testing had not been specifically evaluated in recipients of CRT with an ICD implanted for primary prevention of sudden cardiac death. Therefore, we compared outcomes between patients who underwent defibrillation testing and those who did not, immediately after the implantation of a CRT ICD [19]. Out of the 1516 patients, defibrillation testing was performed in 958 (63%) patients. All of the three perioperative deaths occurred in the group that had defibrillation testing, and were related to defibrillation testing itself. The adjusted incidence of overall mortality was lower in the group that had defibrillation testing (HR 0.6; $P < 0.0001$), mainly reflecting the less severe cardiac disease in this group (making patients more likely to be selected for defibrillation testing), rather than a lower rate of ICD-unresponsive sudden death during follow-up. Taken overall, our results do not encourage systematic defibrillation testing in recipients of CRT with an ICD.

Outcomes comparison between NICM and ischaemic cardiomyopathy (ICM)

The benefit of primary prevention ICD implantation in NICM has been debated recently, and the evidence level for ICD implantation in NICM is considered to be lower than for ICM in the European Society of Cardiology guidelines [20, 21]. Consequently, the DAI-PP study group compared outcomes between recipients of an ICD implanted for primary prevention with NICM (40% of patients) and with ICM (60% of patients) [22]. Overall mortality was higher in the ICM group than the NICM group (adjusted HR 1.31; $P = 0.01$), and the increase in cardiac mortality in the ICM group was mainly the result of non-cardiovascular causes ($P = 0.0002$). The incidence of appropriate ICD therapy was similar in the two groups. These observational data appear to support the efficacy of ICDs in NICM, similar to other recent registry data and meta-analyses [23].

CRT: Is an additional ICD always required?

The DAI-PP project also collaborated with a large multicentre European cohort, assessing the added value of an ICD over CRT in ICM and NICM [24]. Overall, 5307 consecutive patients with NICM or ICM underwent CRT implantation with ($n = 4037$) or without ($n = 1270$) an ICD. After a mean follow-up period of 41.4 ± 29.0 months, patients with ICM had better survival when receiving CRT with an ICD compared with those who received CRT without an ICD (HR 0.76; $P = 0.005$), whereas in patients with NICM, no such difference was observed (HR 0.92; $P = 0.49$) (Fig. 2). Outcome differences according to sex category were also assessed, and benefit from CRT with an ICD was seen in male patients (HR 0.78; $P = 0.012$), but not in female patients (HR 0.87; $P = 0.43$). These findings were confirmed in another collaborative work assessing sex-specific outcomes with the addition of an ICD to CRT [25]. These results reinforce the importance of careful patient selection, especially among women, to optimize the benefit and cost-effectiveness of an added ICD in patients with an indication for CRT.

In addition, further analyses were carried out from a large European CRT consortium comprising French, UK, Czech and Swedish patients who received CRT implantation or upgrade between 2002 and 2012, in order to provide long-term outcomes, especially with regard to the occurrence of sudden cardiac death, in patients who received CRT with and without an ICD. Progressive heart failure was found to be the most frequent cause of death in patients surviving the first 5 years after CRT implantation. By contrast, sudden cardiac death accounted for a very low proportion of late mortality, irrespective of the presence of an ICD [26].

Reducing the ICD shock burden

The benefits of ICD implantation in the primary prevention of sudden cardiac death are offset to some extent because of the morbidity conferred by both appropriate and, more importantly, inappropriate shocks. The MADIT-RIT trial suggested very-high-rate cut-off and long detection time strategies to reduce inappropriate shocks [27]. We assessed the real-world efficacy of a very-high-rate cut-off programming strategy in our registry, by comparing 500 patients programmed with a very-high-rate cut-off (VH-RATE group: monitor zone 170–219 beats/min; ventricular fibrillation zone ≥ 220 beats/min with 13 ± 4 detection intervals) with 1500 matched control patients programmed with standard one therapy or two therapy zones [28]. VH-RATE programming was associated with reductions in appropriate therapy (HR 0.40; $P < 0.0001$) and inappropriate shock risk (HR 0.42; $P < 0.0001$) (Fig. 3). Nevertheless, there was no significant difference in overall survival between the groups. Optimal ICD

programming, which focuses on the reduction of therapies, could be a safe and effective strategy in preventing subsequent morbidity and/or mortality from ICD shocks.

Efficacy of single-chamber versus dual-chamber ICDs

Another putative way to reduce inappropriate shocks could be the implantation of an atrial lead, to enhance reliability of supraventricular arrhythmia discrimination. However, the benefit of dual-chamber versus single-chamber ICDs could be counterbalanced by a higher rate of complications related to dual-chamber ICD implantation. Using the DAI-PP dataset, we compared 1258 recipients of single-chamber ICDs with 1280 recipients of dual-chamber ICDs [29]. While the rates of periprocedural complications were higher in the dual-chamber ICD group (12.1%) compared with the single-chamber ICD group (8.8%; $P = 0.008$), the proportions of appropriate therapies (24.7% vs 23.8%), inappropriate shocks (8.4% vs 7.8%) and all-cause mortality (12.4% vs 13.2%) were similar between groups (Fig. 4). Thus, our DAI-PP experience does not support the routine implantation of dual-chamber ICDs to reduce inappropriate therapies.

Improving the benefit of ICD therapy by improving selection accuracy

Better patient selection, particularly with regard to identifying those at high risk of non-arrhythmic death, may improve the cost-effectiveness of primary prevention ICD implantation [30]. In this context, a cause-of-death analysis was carried out in 2485 patients, to investigate the extent to which a prognostic score derived from a randomized controlled trial in patients with coronary artery disease was of potential interest in the real-world setting for patients with ICM and NICM [31]. The risk score included points for NYHA functional class III or greater, age > 70 years, QRS duration > 120 ms, atrial fibrillation and glomerular filtration rate < 60 mL/min. After a mean follow-up of 3.0 years, the overall mortality rate was 5.9 per 100 patient-years, which increased progressively with the number of risk factors. The higher mortality rate among patients with the highest scores resulted from an increase in non-arrhythmic mortality (from 2.1 to 14.8 per 100 patient-years; $P < 0.001$), whereas the occurrence of appropriate ICD therapies did not change significantly across the categories. The C-statistic testing of the score was observed to be highly similar for patients with ICM (0.685) and NICM (0.658) and those receiving CRT (0.678). These findings underline the feasibility in the real-world setting of identifying patients who are at significant risk of non-arrhythmic death among those eligible for primary

prevention ICD implantation. A careful analysis of the risk-benefit ratio and additional discussion with the patient would be warranted in such identified cases.

Electrical storm in primary prevention recipients of an ICD

The characteristics and risk of death in patients who developed electrical storm during follow-up were evaluated [32]. Occurrence of electrical storm was associated with poor prognosis, as the probability of death was higher after electrical storm (HR 3.77; $P < 0.001$). In the multivariable survival analysis, renal failure (HR 1.8; $P = 0.007$), left ventricular ejection fraction $< 30\%$ (HR 1.7; $P = 0.03$) and male sex (HR 2.3; $P = 0.05$) were associated with the occurrence of electrical storm. These data underline the prognostic implications of electrical storm, which may be mitigated nowadays by advances in catheter ablation techniques and by neural modulation, and prevented to some extent by the optimization of pharmacological therapies.

CRT response, survival and heart transplantation in recipients of an ICD

Almost a third of patients with heart failure fail to respond to CRT. To help identify such patients, a simple clinical risk score called ScREEN was developed using the DAI-PP cohort, and then validated in an external cohort [33]. This score used the following variables: sex category; renal function; electrocardiogram/QRS width; ejection fraction; and NYHA class. External validation showed good calibration, accuracy and discrimination (C-statistic 0.67), with CRT response increasing progressively from 37.5% in patients with a score of 0 to 91.9% in those with a score of 5 ($P < 0.001$). Finally, our real-world data support findings from other groups. As expected, there were differences in the risk of death and probability of CRT response among co-morbidity groups, but the burden of co-morbidity did not appear to significantly influence the probability of response to CRT, despite a potentially smaller survival benefit in patients with three or more co-morbidities. Although ICD implantation should be carefully considered in patients with multiple co-morbidities, CRT should not be withheld in the context of a patient with heart failure with an enlarged QRS [34].

While ICDs are not recommended for patients with an expected survival of < 1 year, the factors in real life associated with such an outcome have not been well studied. We assessed the prevalence and factors associated with survival of ≤ 1 year among patients implanted with an ICD (unpublished data): 230 of 5457 (4.2%) patients survived for ≤ 1 year. Causes of death were similar in those who

survived ≤ 1 year versus > 1 year, and patients who survived for ≤ 1 year had fewer appropriate and inappropriate ICD therapies than patients who survived for > 1 year (respectively, 14% vs 23% [$P = 0.004$] and 2% vs 7% [$P = 0.009$]). In the multivariable analysis, older age, higher NYHA class (\geq III), atrial fibrillation and lower left ventricular ejection fraction were significantly associated with survival for ≤ 1 year.

Finally, the frequency, characteristics and outcomes of primary prevention recipients of an ICD who undergo heart transplantation during follow-up were described in the DAI-PP study [35]: 176 (3.2%) patients underwent heart transplantation. The median duration between ICD implantation and heart transplantation was 484 days (interquartile range 169–1117 days). The incidence of appropriate ICD therapies was relatively high in patients who had a heart transplantation compared with those who did not (92.7 vs 76.1 per 1000 person-years; $P = 0.64$), reinforcing the importance of specific cardiac rhythm management for these patients, while they await heart transplantation.

Conclusions

The pilot phase of the DAI-PP programme has provided valuable information on several practical and clinically-relevant aspects of primary prevention ICD implantation in the real-world population of patients with ischaemic and non-ischaemic cardiomyopathy. This pilot led to a prospective evaluation that started in May 2018, assessing ICD therapy in primary and secondary prevention in patients with structural and electrical heart diseases, with remote monitoring follow-up using a dedicated platform. This should further enhance our understanding of sudden cardiac death, to eventually optimize the field of preventative actions.

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Figure legends

Figure 1. Survival curves for mortality according to early complication occurrence.

Figure 2. Survival curves comparing cardiac resynchronization therapy with an implantable cardioverter defibrillator (CRT-D) versus cardiac resynchronization therapy with a pacemaker (CRT-P), using Cox regression with adjustment on the propensity score and all mortality predictors. CI: confidence interval; HR: hazard ratio; N: number.

Figure 3. Survival probability of inappropriate shock occurrence according to implantable cardioverter defibrillator settings. VH-RATE: very-high-rate group; 1-zone: one therapy zone; 2-zone: two therapy zone.

Figure 4. Proportions of appropriate and inappropriate therapies during follow-up, according to the type of device: single-chamber (SC-ICD) versus dual-chamber (DC-ICD) implantable cardioverter defibrillator.

Table 1 Main findings.

DAI-PP main findings	<p>Over a decade, age at implantation and the proportions of CRT implantations, NICM and female recipients have increased [8].</p> <p>Compared with males, female recipients of an ICD have a 0.59-fold lower incidence of appropriate ICD therapies [10].</p> <p>Although patients in NYHA class III have a higher overall mortality, driven by an increase in cardiovascular death, they experience a similar incidence of appropriate ICD therapies [13].</p> <p>More than a quarter were implanted without fulfilling proper guideline criteria; despite a less severe clinical profile at implantation and lower mortality rates, off-guideline patients had, rather surprisingly, similar rates of appropriate therapies [9].</p> <p>After ICD implantation, older patients exhibit higher global mortality, but 19.4% experience at least one appropriate therapy before death, and rates of appropriate therapies are similar overall across age groups [14].</p> <p>Overall, long-term mortality was lower among recipients of CRT with an ICD who had undergone perioperative defibrillation testing (HR 0.6); however, this mainly reflected their less severe cardiac disease [19].</p> <p>Early complication after ICD implantation is associated with a 1.7-fold higher risk of mortality; factors associated with early complications are severe renal impairment, age ≥ 75 years, CRT and anticoagulant therapy [16].</p> <p>Programming a very high ventricular tachycardia and fibrillation cut-off rate is associated with a reduction in appropriate therapies and inappropriate shock [28].</p> <p>Compared with single-chamber ICDs, dual-chamber ICDs do not reduce rates of inappropriate therapies, and are associated with a higher rate of complications [29].</p> <p>A risk score including NYHA class $\geq III$, age > 70 years, QRS duration > 120 ms, atrial fibrillation and GFR < 60 mL/min allows identification of patients at risk of non-arrhythmic death, who might not benefit from ICD therapy [31].</p>
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Electrical storm among patients with an ICD is associated with a 3.77-fold higher risk of death [32].

DAI-PP collaborations
main findings Patients with ICM had better survival when receiving CRT with an ICD compared with those who received CRT alone; no such difference was observed in patients with NICM [24].

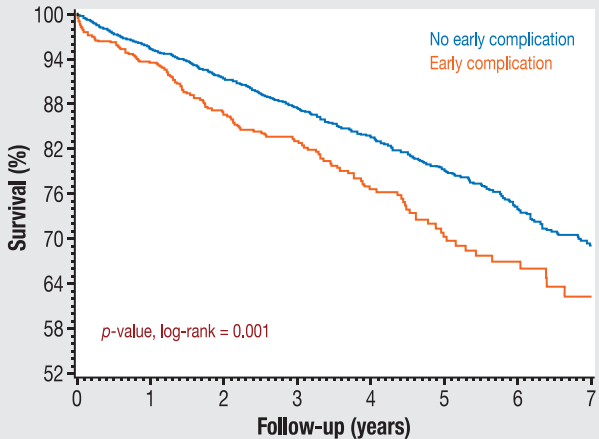
A simple clinical risk score called ScREEN, using sex category, renal function, electrocardiogram/QRS width, ejection fraction and NYHA class variables, is able to identify patients who will not respond to CRT [33].

In patients with an indication for CRT, the addition of an ICD conveys additional benefit in well-selected male patients, but possibly not in female patients [25].

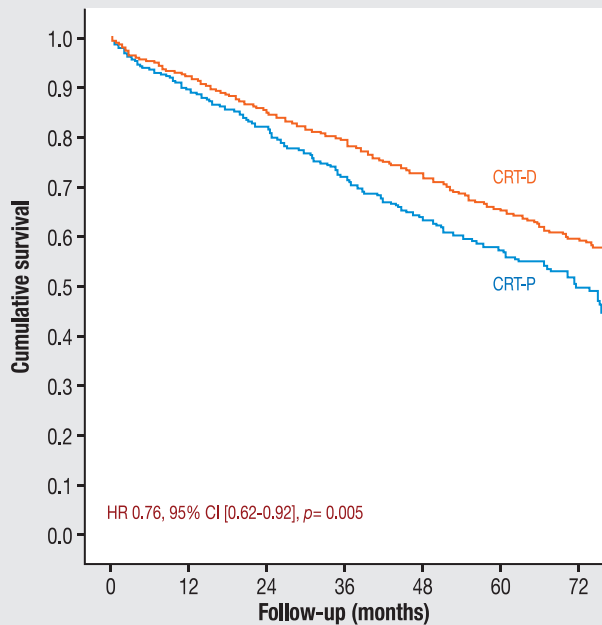
The burden of co-morbidity did not appear to significantly influence the probability of response to CRT, despite a potentially smaller survival benefit in patients with three or more co-morbidities; although ICD implantation should be carefully considered in patients with multiple co-morbidities, CRT should not be withheld in the context of a patient with heart failure with an enlarged QRS [34].

Progressive heart failure was found to be the most frequent cause of death in patients surviving the first 5 years after CRT implantation; by contrast, sudden cardiac death accounted for a very low proportion of late mortality, irrespective of the presence of an ICD [26].

CRT: cardiac resynchronization therapy; GFR: glomerular filtration rate; HR: hazard ratio; ICD: implantable cardioverter defibrillator; ICM: ischaemic cardiomyopathy; NICM: non-ischaemic cardiomyopathy; NYHA: New York Heart Association.

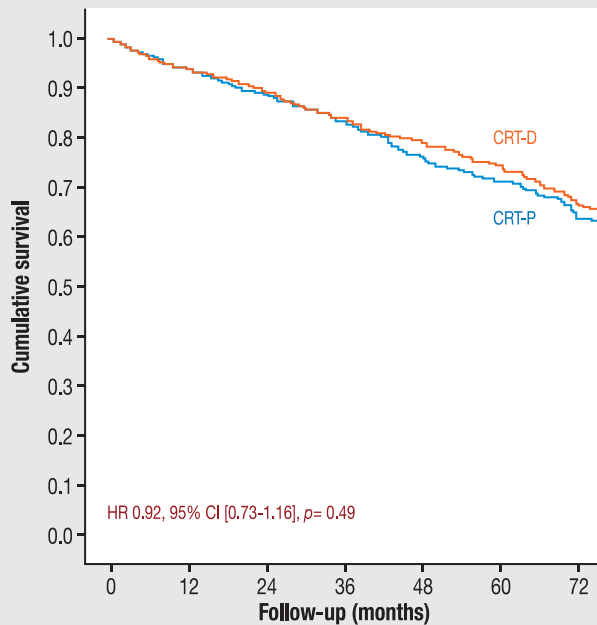


Ischemic cardiomyopathy



N at risk	0	12	24	36	48	60
CRT-D	2,094	1,685	1,295	970	677	476
CRT-P	588	492	420	195	143	96

Non-ischemic dilated cardiomyopathy



N at risk	0	12	24	36	48	60
CRT-D	1,943	1,570	1,239	902	632	458
CRT-P	682	601	535	270	187	132

