TrialResults-center.org

www.trialresultscenter.org

Resynchronization (CRT) - defibrillators (ICD) for heart failure in patients with non ichaemic cardiomyopathy

A systematic review and meta-analysis of randomized clinical trials

2017 - 6 - 14

Browse interactively these data at http://www.trialresultscenter.org/go-Q15

This report should be referenced as follows:
TrialResults-center.org; Results of all major randomized clinical trials about Resynchronization (CRT) - defibrillators (ICD) for heart failure in patients with non ichaemic cardiomyopathy.

Contents

0.1 Synthesis of the meta-analysis results

In all 3 randomised controlled trials (RCTs) were included. These included 1 studie of **combined CRT + ICD** involving 103 patients and 2 studies of **implantable cardioverter defibrillator therapy** involving 562 patients. Results obtained by the meta-analysis are reported in the following tables, with the endpoints categorized according their results. Three classes are considered: endpoints for wich a benefit effect was detected, endpoints revealing a harmful effect and the other for wich no statistically significant difference was obtained (no evidence).

0.1.1 Combined CRT + ICD

Only one trials including 103 patients was found.
Among these comparisons, one trial are about Combined CRT + ICD.
No trial was excluded on grounds of potentially flawed methodology or incomplete presentation of results. No ongoing trial was found.
Results obtained with combined CRT + ICD for all the endpoints with data in at least one trial are summarized table 1.

Table 1: *Results summary - Combined CRT + ICD*

Benefit	Harmful	No evidence
	Combined CRT + ICD versus no CRT no ICD	
		→ all cause death RR=0.87^{NS} [0.32;2.42] k=1

* $p < 0.05$; † $p < 0.01$; ¶ $p < 0.001$ RR: relative risk

H: heterogeneity with fixed effect model detected (heterogeneity test $p < 0.05$)

0.1.2 Implantable cardioverter defibrillator therapy

Reports of 2 trials (including 562 patients) were identified .
Among these comparisons, two trials are about ICD.
No trial was excluded on grounds of potentially flawed methodology or incomplete presentation of results. No ongoing trial was found.
Results obtained with ICD for all the endpoints with data in at least one trial are summarized table 2.

Table 2: *Results summary - ICD*

Benefit	Harmful	No evidence
	ICD versus no ICD	
		→ all cause death RR=0.74^{NS} [0.52;1.06] k=2

* $p < 0.05$; † $p < 0.01$; ¶ $p < 0.001$ RR: relative risk

H: heterogeneity with fixed effect model detected (heterogeneity test $p < 0.05$)

1 Introduction

1.1 Aim of the report

This report review all the randomized clinical trials of resynchronization (CRT) - defibrillators (ICD) for the treatment of heart failure in patients with non ichaemic cardiomyopathy. The following classes of treatment are considered:

1. Combined CRT + ICD
2. Implantable cardioverter defibrillator therapy

1.2 Search strategy

The search aimed to identify all randomized clinical trials relating to the clinical effectiveness of resynchronization (CRT) - defibrillators (ICD) for the treatment of heart failure in patients with non ichaemic cardiomyopathy.

1.2.1 Sources searched

The following electronic databases were searched for relevant published literature for the period up to 2017 - 6 - 14:

- MEDLINE,
- EMBASE,
- Cochrane Database of Systematic Reviews (CDSR),
- Cochrane Central Register of Controlled Trials (CCTR),
- Health Technology Assessment (HTA) database,
- ISI Web of Science Proceedings (Index to Scientific and Technical Proceedings),
- ISI Web of Science Science Citation Index Expanded,

Each database was searched as far back as possible, with no language restrictions.
Search strategies of relevant clinical keywords were developed through reference to published strategies, and by iterative searching, whereby keywords identified in references retrieved by initial scoping searches were used to extend the search strategy and so increase the sensitivity of retrieval.
In addition, the reference lists of relevant articles were handsearched.
Attempts to identify further studies were made by consulting health technology assessment and guideline producing agencies, and research and trials registers via the Internet.
Titles and, when available, abstracts of all studies identified in the searches were assessed by a single researcher for relevance to the review. In cases of doubt, the full article was obtained.

1.2.2 Search restrictions

No language, study/publication or date restrictions were applied to the main searches.

1.3 Inclusion criteria

Participants only those studies were included in which the participants had been diagnosed as having established heart failure.

Interventions studies in which resynchronization (CRT) - defibrillators (ICD) was used. Studies using other interventions in addition to resynchronization (CRT) - defibrillators (ICD) therapy were included only if the treatment received by the intervention and control groups was identical in all respects other than the use of resynchronization (CRT) - defibrillators (ICD).

Methodology randomised controlled trials (RCTs). Trials were accepted as RCTs if the allocation of subjects to treatment groups was described by the authors as either randomised or double-blind.

1.4 Exclusion criteria

Studies considered methodologically unsound. The list of excluded studies with reason of their exclusion are given in a separate section for each treatment categories considered.

1.5 Meta-analysis strategy

Studies that met the reviews entry criteria were eligible for inclusion in the meta-analyses provided that they reported outcomes in terms of the number of subjects suffering clinical outcomes, as only this would allow calculation of the relative risk of subjects in the intervention group developing each outcome, compared with subjects in the control group.
Studies that only presented results in the form of relative risks, relative hazards or odds ratios, without the underlying numbers were also include in the meta-analyses.
Binary outcomes were analysed using the fixed-effect model. For continuous outcomes, weighted mean differences (WMDs) were analysed, using a fixed-effect model.
Heterogeneity was tested by the chi-2 test and the I2 statistic was obtained to describe the proportion of the variability.
Where quantitative heterogeneity was indicated, analysis using a random-effects model was conducted for comparison with results of fixed effect-based analysis. Results of the meta-analysis should be considered as being based on fixed-effect model unless stated otherwise.
Meta-analyses were conducted for data on All cause death, .

1.6 Structure of the report

Each of the eligible studies is summarised in part **??**. A summary of the studies together with an evaluation of their quality is given in part I to **??**, listed by therapeutic class. The therapeutic classes included Combined CRT + ICD, Implantable cardioverter defibrillator therapy,
In these sections, studies in which an active intervention was compared with placebo or no treatment are discussed first, by intervention, followed by a discussion of those studies in which two or more active interventions were compared.

Part I

Combined CRT + ICD

2 Overview of combined CRT + ICD

2.1 Included trials

Only one trial which randomized 103 patients was identified. In all, 1 randomized comparison concerned Combined CRT + ICD.
The detailed descriptions of trials and meta-analysis results is given in section 3 (page 16) for Combined CRT + ICD.

This trial included 103 patients and was published in 2003.
This trial was open-label in design.
It was reported in English language.
The table 2.1 (page 14) summmarizes the main characteristics of all the included trials. More detailed description is given in the following section.

2.2 Summary of meta-analysis results

The meta-analysis of the available trials about combined CRT + ICD provide the results listed in tables 2.2 to 2.2 (page 15) and in the following graphs.

2.2.1 Combined CRT + ICD

No significant difference was found between **Combined CRT + ICD** and **no CRT no ICD** in terms of all cause death (RR=0.87, 95% CI 0.32 to 2.42, p=0.7957, 1 trial).

Table 2.1: *Main study characteristics - Combined CRT + ICD*

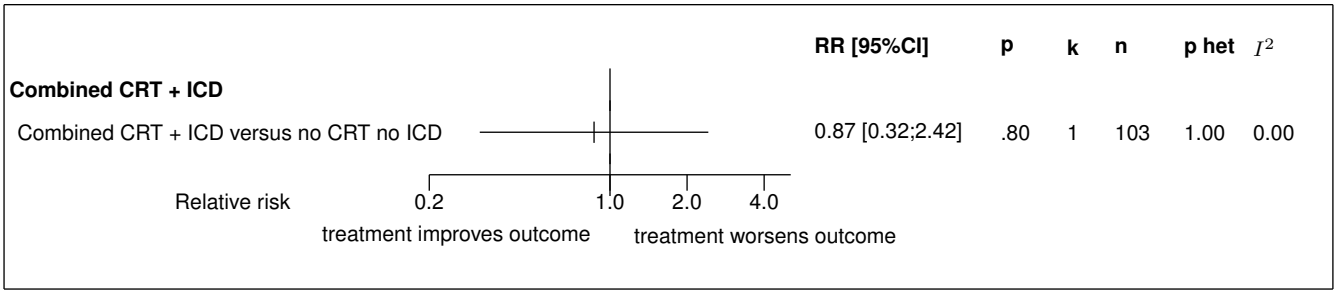
Trial	Patients	Treatments	Trial design and method
Combined CRT + ICD			
Combined CRT + ICD versus no CRT no ICD			
AMIOVIRT, 2003 [1] n = 51 vs. 52	patients with non ischemic cardiomyopathy with EF <=0.35 and Nonsustained ventricular tachycardia	ICD **versus** amiodarone as medical therapy	open parallel groups Primary endpoint: total mortality

Table 2.2: *Summary of all results for Combined CRT + ICD*

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
Combined CRT + ICD versus no CRT no ICD						
all cause death	RR=0.87	0.32;2.42	0.7957	1.0000 (0.00)	1	103

CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients

Figure 2.1: *Forest's plot for all cause death*



Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity test; ʳ: random effect model used

3 Details

3.1 Available trials

Only one trial which randomized 103 patients was identified: it compared Combined CRT + ICD with no CRT no ICD.
This trial included 103 patients and was published in 2003.
This trial was open-label in design.
It was reported in English language.
All cause death data was reported in 1 trials;
Following tables 3.1 (page 16), 3.2 (page 16), 3.4 (page 17), and 3.3 (page 16) summarized the main characteristics of the trial including in this systematic review of randomized trials of Combined CRT + ICD.

Table 3.1: *Treatment description - Combined CRT + ICD - Combined CRT + ICD*

Trial	Studied treatment	Control treatment
Combined CRT + ICD versus no CRT no ICD		
AMIOVIRT (2003) [1]	ICD	amiodarone as medical therapy

Table 3.2: *Descriptions of participants - Combined CRT + ICD - Combined CRT + ICD*

Trial	Patients
Combined CRT + ICD versus no CRT no ICD	
AMIOVIRT (2003) [1]	Patients with non ischemic cardiomyopathy with EF <=0.35 and Nonsustained ventricular tachycardia

Table 3.3: *Design and methodological quality of trials - Combined CRT + ICD - Combined CRT + ICD*

Trial	Design	Duration	Centre	Primary endpoint
Combined CRT + ICD versus no CRT no ICD				
AMIOVIRT, 2003 [1] n=103	Parallel groups open	24 months inclusion period: 1996-2000		Total mortality

Table 3.4: *Trial characteristics - Combined CRT + ICD - Combined CRT + ICD*

Trial
Combined CRT + ICD versus no CRT no ICD
AMIOVIRT, 2003 [1]

3.2 Meta-analysis results

The results are detailed in table 3.5 (page 18). This table is followed by the Forest's plot corresponding to each endpoint.

Combined CRT + ICD versus no CRT no ICD

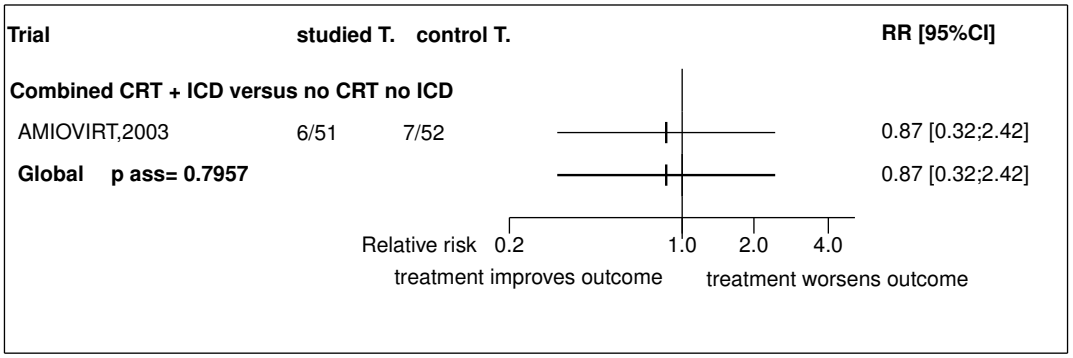
The single study eligible for this comparison provided data on **all cause death**. No statistically significant difference between the groups was found in all cause death, with a RR of 0.87 (95% CI 0.32 to 2.42, p=0.7957).

Table 3.5: *Results details - Combined CRT + ICD - Combined CRT + ICD*

Comparison Endpoint	Effect	95% CI	p ass	p het	k	n
Combined CRT + ICD versus no CRT no ICD						
all cause death	RR=0.87	[0.32;2.42]	0.7957	1.0000 (I^2=0.00)	1	103

CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients; ES: effect size; I^2: inconsistance degree

Figure 3.1: *Forest's plot for all cause death*



References

[1] Strickberger SA, Hummel JD, Bartlett TG, Frumin HI, Schuger CD, Beau SL, Bitar C, Morady F. Amiodarone versus implantable cardioverter-defibrillator:randomized trial in patients with nonischemic dilated cardiomyopathy and asymptomatic nonsustained ventricular tachycardia–AMIOVIRT. J Am Coll Cardiol 2003;41:1707-12. [PMID=12767651]

3.3 Individual trial summaries

Table 3.6: *AMIOVIRT, 2003 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=103 (51 vs. 52) **Follow-up duration:** 24 months **Study design:** Randomized controlled trial Parallel groups Open **Inclusion period:** 1996-2000	Patients with non ischemic cardiomyopathy with EF <=0.35 and Nonsustained ventricular tachycardia	**Studied treatment:** ICD **Control treatment:** amiodarone as medical therapy	All cause death RR=0.87 [0.32;2.42]

Reference

Strickberger SA, Hummel JD, Bartlett TG, Frumin HI, Schuger CD, Beau SL, Bitar C, Morady F. Amiodarone versus implantable cardioverter-defibrillator:randomized trial in patients with nonischemic dilated cardiomyopathy and asymptomatic nonsustained ventricular tachycardia–AMIOVIRT. J Am Coll Cardiol 2003;41:1707-12 [PMID=12767651]

4 Global meta-analysis: all Combined CRT + ICD

4.1 Global meta-analysis: all Combined CRT + ICD versus no CRT no ICD

Table 4.1: *All Combined CRT + ICDversus no CRT no ICD*

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
all cause death	RR=0.87	0.32;2.42	0.7957	1.0000 (0.00)	1	103

CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients; ES: effect size; I^2: inconsistance degree

5 Ongoing studies of Combined CRT + ICD

No ongoing trial was identified.

6 Excluded studies for Combined CRT + ICD

No trial was excluded.

References

Part II

Implantable cardioverter defibrillator therapy

7 Overview of implantable cardioverter defibrillator therapy

7.1 Included trials

A total of 2 randomized comparisons which enrolled 562 patients were identified. In all, 2 randomized comparisons concerned ICD.
The detailed descriptions of trials and meta-analysis results is given in section 8 (page 28) for ICD.

The average study size was 281 patients (range 104 to 458). The first study was published in 2002, and the last study was published in 2004.
All trials were open-label in design. All included studies were reported in English language. We did not found any unpublished trial.
The table 7.1 (page 26) summmarizes the main characteristics of all the included trials. More detailed description is given in the following section.

7.2 Summary of meta-analysis results

The meta-analysis of the available trials about implantable cardioverter defibrillator therapy provide the results listed in tables 7.2 to 7.2 (page 27) and in the following graphs.

7.2.1 ICD

No significant difference was found between **ICD** and **no ICD** in terms of all cause death (RR=0.74, 95% CI 0.52 to 1.06, p=0.1042, 2 trials).

Table 7.1: *Main study characteristics - Implantable cardioverter defibrillator therapy*

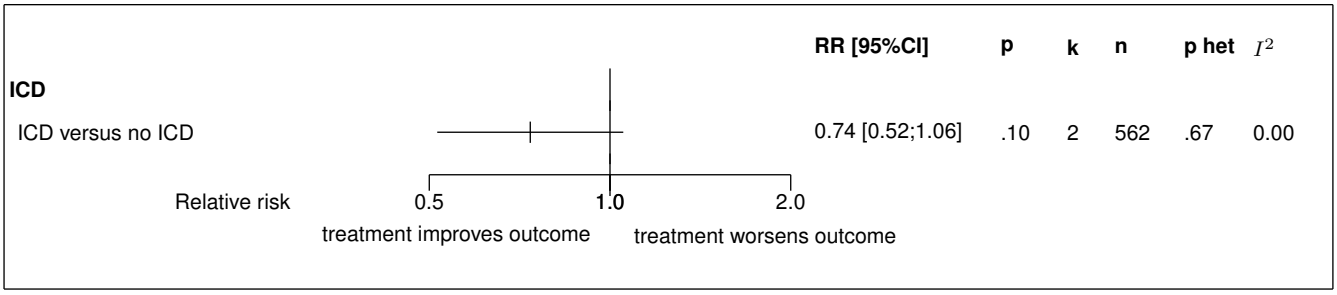
Trial	Patients	Treatments	Trial design and method
ICD			
ICD versus no ICD			
CAT, 2002 [1] n = 50 vs. 54	patients with recent onset nonischemic cardiomyopathy withEF <=0.30	ICD **versus** no iCD, conventional therapy	open parallel groups Primary endpoint: total mortality
DEFINITE, 2004 [2, 3] n = 229 vs. 229	patients with non ischemic cardiomyopathy with EF <0.36 and Nonsustained ventricular tachycardia or frequent premature ventricular complexes	ICD **versus** no ICD, standard medical therapy	open parallel groups Primary endpoint: total mortality

Table 7.2: *Summary of all results for ICD*

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
ICD versus no ICD						
all cause death	RR=0.74	0.52;1.06	0.1042	0.6686 (0.00)	2	562

CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients

Figure 7.1: *Forest's plot for all cause death*



Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity test; ʳ: random effect model used

8 Details

8.1 Available trials

A total of 2 RCTs which randomized 562 patients were identified: all compared ICD with no ICD.
The average study size was 281 patients (range 104 to 458). The first study was published in 2002, and the last study was published in 2004.
All trials were open-label in design. All included studies were reported in English language. We did not found any unpublished trial.
All cause death data was reported in 2 trials;
Following tables 8.1 (page 28), 8.2 (page 28), 8.4 (page 30), and 8.3 (page 29) summarized the main characteristics of the trials including in this systematic review of randomized trials of ICD.

Table 8.1: *Treatment description - Implantable cardioverter defibrillator therapy - ICD*

Trial	Studied treatment	Control treatment
ICD versus no ICD		
CAT (2002) [1]	ICD	no iCD, conventional therapy
DEFINITE (2004) [2, 3]	ICD	no ICD, standard medical therapy

Table 8.2: *Descriptions of participants - Implantable cardioverter defibrillator therapy - ICD*

Trial	Patients
ICD versus no ICD	
CAT (2002) [1]	Patients with recent onset nonischemic cardiomyopathy withEF <=0.30
DEFINITE (2004) [2, 3]	Patients with non ischemic cardiomyopathy with EF <0.36 and Nonsustained ventricular tachycardia or frequent premature ventricular complexes

Table 8.3: *Design and methodological quality of trials - Implantable cardioverter defibrillator therapy - ICD*

Trial	Design	Duration	Centre	Primary endpoint
ICD versus no ICD				
CAT, 2002 [1] n=104	Parallel groups open	66 months inclusion period: 1991-1997		Total mortality
DEFINITE, 2004 [2, 3] n=458	Parallel groups open	29 months inclusion period: 1998-2000		Total mortality

Table 8.4: *Trial characteristics - Implantable cardioverter defibrillator therapy - ICD*

Trial
ICD versus no ICD
CAT, 2002 [1]
DEFINITE, 2004 [2, 3]

8.2 Meta-analysis results

The results are detailed in table 8.5 (page 31). This table is followed by the Forest's plot corresponding to each endpoint.

ICD versus no ICD

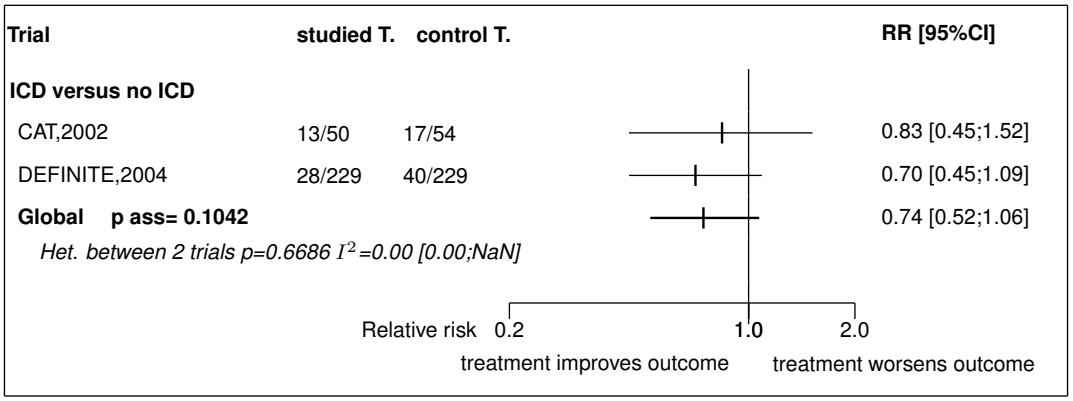
All the 2 studies had extractable data about the number of participants with **all cause death**. When pooled together, there was no statistically significant difference between the groups in all cause death, with a RR of 0.74 (95% CI 0.52 to 1.06, p=0.1042). No heterogeneity was detected (p = 0.6686, I^2 = 0.00%).

Table 8.5: *Results details - Implantable cardioverter defibrillator therapy - ICD*

Comparison Endpoint	Effect	95% CI	p ass	p het	k	n
ICD versus no ICD						
all cause death	RR=0.74	[0.52;1.06]	0.1042	0.6686 (I^2=0.00)	2	562

CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients; ES: effect size; I^2: inconsistance degree

Figure 8.1: *Forest's plot for all cause death*



References

[1] Bnsch D, Antz M, Boczor S, Volkmer M, Tebbenjohanns J, Seidl K, Block M, Gietzen F, Berger J, Kuck KH. Primary prevention of sudden cardiac death in idiopathic dilated cardiomyopathy: the Cardiomyopathy Trial (CAT). Circulation 2002;105:1453-8. [PMID=11914254]

[2] Kadish A, Dyer A, Daubert JP, Quigg R, Estes NA, Anderson KP, Calkins H, Hoch D, Goldberger J, Shalaby A, Sanders WE, Schaechter A, Levine JH. Prophylactic defibrillator implantation in patients with nonischemic dilated cardiomyopathy. N Engl J Med 2004;350:2151-8. [PMID=15152060]

[3] Albert CM, Quigg R, Saba S, Estes NA 3rd, Shaechter A, Subacius H, Howard A, Levine J, Kadish A. Sex differences in outcome after implantable cardioverter defibrillator implantation in nonischemic cardiomyopathy. Am Heart J 2008;156:367-72. [PMID=18657670]

8.3 Individual trial summaries

Table 8.6: *CAT, 2002 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=104 (50 vs. 54) **Follow-up duration:** 66 months **Study design:** Randomized controlled trial Parallel groups Open **Inclusion period:** 1991-1997	Patients with recent onset nonischemic cardiomyopathy withEF <=0.30	**Studied treatment:** ICD **Control treatment:** no iCD, conventional therapy	All cause death RR=0.83 [0.45;1.52]

Reference

Bnsch D, Antz M, Boczor S, Volkmer M, Tebbenjohanns J, Seidl K, Block M, Gietzen F, Berger J, Kuck KH. Primary prevention of sudden cardiac death in idiopathic dilated cardiomyopathy: the Cardiomyopathy Trial (CAT). Circulation 2002;105:1453-8 [PMID=11914254]

Table 8.7: *DEFINITE, 2004 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=458 (229 vs. 229) **Follow-up duration:** 29 months **Study design:** Randomized controlled trial Parallel groups Open **Inclusion period:** 1998-2000	Patients with non ischemic cardiomyopathy with EF <0.36 and Nonsustained ventricular tachycardia or frequent premature ventricular complexes	**Studied treatment:** ICD **Control treatment:** no ICD, standard medical therapy	All cause death RR=0.70 [0.45;1.09]

References

Kadish A, Dyer A, Daubert JP, Quigg R, Estes NA, Anderson KP, Calkins H, Hoch D, Goldberger J, Shalaby A, Sanders WE, Schaechter A, Levine JH. Prophylactic defibrillator implantation in patients with nonischemic dilated cardiomyopathy. N Engl J Med 2004;350:2151-8 [PMID=15152060]
Albert CM, Quigg R, Saba S, Estes NA 3rd, Shaechter A, Subacius H, Howard A, Levine J, Kadish A. Sex differences in outcome after implantable cardioverter defibrillator implantation in nonischemic cardiomyopathy. Am Heart J 2008;156:367-72 [PMID=18657670]

9 Global meta-analysis: all Implantable cardioverter defibrillator therapy

9.1 Global meta-analysis: all Implantable cardioverter defibrillator therapy versus no ICD

Table 9.1: *All Implantable cardioverter defibrillator therapyversus no ICD*

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
all cause death	RR=0.74	0.52;1.06	0.1042	0.6686 (0.00)	2	562

CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients; ES: effect size; I^2: inconsistance degree

10 Ongoing studies of Implantable cardioverter defibrillator therapy

No ongoing trial was identified.

11 Excluded studies for Implantable cardioverter defibrillator therapy

No trial was excluded.

References