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Research Article

Device Therapy in Ischemic Heart Disease: Are we there yet?

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Abstract

Background: More than a decade has passed since the publication of landmark randomized controlled trials on primary prevention of sudden cardiac death, which have served until the present as the basis for implantable cardiac defibrillator use in patients with left ventricle systolic dysfunction and heart failure. Recent studies have shown that patients with reduced ejection fraction may improve over time and some of these patients will receive a defibrillator without a clear need. We hypothesized that patients with ischemic heart disease are being better managed, faster and with newer medical therapies and thus, resulting in a reduction of mortality and need for implantable cardiac device therapy.

Methods: Retrospective cohort study of 655 patients with acute coronary syndrome. Primary outcome**:** 1-year mortality rate and unplanned revascularization. Secondary outcome**:** incidence of cardiac device implantation for primary prevention of sudden cardiac death. Follow-up period of 633 days.

Results: Median age 65 years, male 68,7%. 403 (61.3%) with non-ST elevation myocardial infarction and 252 (38.5%) with ST elevation myocardial infarction, underwent invasive coronary angiography. One-year mortality occurred in 3.8%, and unplanned revascularization in 8,2%. 98 patients received device therapy for primary prevention of sudden cardiac death.

Conclusion: There is trend towards reduction in mortality and cardiac device therapy implantation in patients with ischemic cardiomyopathy.

Keywords: *ST Elevation; Myocardial Infarction; Cardiac Device Therapy Implantation*

Introduction

More than a decade has passed since the publication of landmark randomized controlled trials (RCTs) on primary prevention of sudden cardiac death (SCD), which have served until the present as the basis for implantable cardiac defibrillator (ICD) use in patients with left ventricle (LV) systolic dysfunction and heart failure (HF). Patient profiles and medical treatments have changed significantly since then [1]. Early trials showed that, prophylactic use of ICD in ischemic heart disease resulted in a reduction of all-cause mortality [2,3]. Nonetheless, contemporary data has shown that patients with reduced ejection fraction may improve over time and some of these patients will receive a defibrillator without a clear need.

We hypothesized that patients with ischemic heart disease are being better managed, faster and with newer medical therapies and thus, resulting in a reduction of mortality and need for implantable cardiac device therapy. In order to reject the null hypothesis, we conducted a retrospective cohort study of patients with acute coronary syndrome.

Methods

Retrospective-forward cohort study of consecutive patients admitted do emergency department with acute coronary syndrome, between June 2017 and June 2018. They were assigned to 2 groups, ST Elevation Myocardial Infarction (STEMI) and Non-ST Elevation Myocardial Infarction (NSTEMI). We then conduct a subgroup analysis of patients that underwent device implantation for primary sudden cardiac death prevention. Follow-up period was 633 days.

Primary outcome

- Overall mortality 1-year mortality; unplanned readmission with acute coronary syndrome requiring revascularization (PCI) within the first year of primary event.

Secondary outcome

- Overall incidence of implantable cardiac defibrillator (ICD) and cardiac resynchronization therapy defibrillator.

Inclusion criteria:

- Male and female patients 18-year-old or more.
- Acute coronary syndrome (STEMI, NSTEMI, UA) with indication to urgent/emergency coronary angiography.

Statistical analysis

Statistical analysis of descriptive statistics (absolute and relative frequencies, means and their standard deviations) and inferential statistics. To compare the groups, the student t-test was used for independent samples. It accepted the normality of distribution in samples with a dimension greater than 30, according to the central limit theorem. The significance level to reject the null hypothesis was set at $\alpha \leq .05$. The Chi-square independence test and Fisher's test were used. The homogeneity of variances was tested with the Levene test. The statistical analysis was done with the SPSS (Statistical Package for the Social Sciences) version 25 for Windows.

Results

Between June 2017 and June 2018, a total of 655 patients were admitted for acute coronary syndrome. Of these patients, 403 (61.3%) with NSTEMI and 252 (38.5%) with STEMI, underwent invasive coronary angiography. The median age of the patients was 65 years; 72.8% had hypertension; 34.8% diabetes mellitus, and 9.7% were receiving dialysis (Table 1).

Variables	n = 655
Age (y) Mean ± SD	65,2 ± 13.4
Male sex n, (%)	450 (68.7)
Body-Mass Index	
Underweight n, (%)	5 (0,8)
Normal weight n, (%)	193 (32,4)
Overweight n, (%)	268 (45,0)
Obesity class I n, (%)	91(15,3)
Obesity class II n, (%)	22 (3,7)
Obesity class III n, (%)	17 (2,9)
Index event	
NSTEMI n, (%)	403 (61,3)
STEMI n, (%)	252 (38,5)
Medical history	
Diabetes Mellitus n, (%)	228 (34,8)
Dyslipidemia n, (%)	305 (46,6)
Hypertension n, (%)	477 (72,8)
Smoking n, (%)	265 (40,5)
Coronary Artery Disease[1] n, (%)	181 (27,6)
Chronic Kidney Disease n, (%)	63 (9.7)
Left Ventricle Ejection Fraction	
> 50% n, (%)	174 (26,6)
41 - 50% n, (%)	44 (6,7)
31 - 40% n, (%)	40 (6,1)
21 - 30% n, (%)	27 (4,1)
< 21% n, (%)	20 (3,1%)
Missing data n, (%)	350 (53,4%)

Table 1: *Characteristics of the patients at baseline*.

There were significant differences in baseline characteristics between the two groups, as patients with STEMI were younger, when compared do patient with NSTEMI (p = .001). Hypertension and tabaco use were significantly higher in the patients with NSTEMI, (79.5%, p = .001) and (40.5%, p = .001), respectively.

Previous myocardial infarction and coronary angioplasty were higher in the NSTEMI group, 24.2% (p = .001) and 25.3% (p = .002). They also had significantly higher coronary artery bypass grafting, 11,5% vs 1,3% (p = .001).

[1]Percutaneous and CABG (Coronary Artery Bypass Graft)

There was a higher proportion of patients with chronic kidney disease in the NSTEMI group (p = .001).

Overall, 33 patients (8,3%) in the non-ST elevation myocardial infarction group and 26 (10.3%) in the ST elevation myocardial infarction group were lost to follow-up. The mean follow-up period was 1 year.

Characteristic	NSTEMI (n = 403)	STEMI (n = 252)	P value
Age (Y)			.001***
≤ 40	1,5%	6,0%	
41 - 50	10,3%	15,5%	
51 - 60	17,3%	23,8%	
61 - 70	28,7%	27,8%	
71 - 80	25,3%	15,5%	
> 80	17,0%	11,5%	
Body Mass Index			.817
Underweight	0,5%	1,4%	
Normal weight	33,0%	31,6%	
Overweight	45,4%	44,2%	
Obesity class I	15,0%	15,3%	
Obesity class II	3,7%	3,7%	
Obesity class III	2,4%	3,7%	
Diabetes Mellitus			.285
Type II	96,8%	100%	
Type I	3,3%		
Dyslipidaemia			.184
Hypertriglyceridemia	0,5%	2,1%	
Hypercholesterolemia	53,3%	59,6%	
Mixed hyperlipidaemia	46,2%	38,3%	
Arterial Hypertension	79,5%	62,7%	.001***
Tobacco			.003**
Non-smokers	61,3%	56,7%	
Active smokers	21,8%	32,5%	
Former smoker (discontinued > 1 year)	17,0%	10,7%	
History of Cardiovascular Disease			
Previous Myocardial Infarction	24,2%	10,4%	.002**
Previous Percutaneous Intervention	25,3%	14,8%	.002**
Previous CABG	11,5%	1,3%	.001***
Chronic Kidney Disease			.001***
Mildly to moderately decreased	0,5%	0,4%	
Moderately to severely decreased	4,6%	0,9%	
Severely decreased	3,6%	0,4%	
Kidney failure (dialysis)	5,6%	1,3%	

Table 2: *Comparison between ST elevation myocardial infarction (STEMI) and non-ST elevation myocardial infarction (NSTEMI).*

A primary outcome (Table 3) occurred in 3.8% (22 patients), with no significant differences among the two groups, 3.1 vs 4.5, respectively.

Outcome	1 year	P-value
All-Cause Mortality		> .05
Overall	3,8%	
NSTEMI	3,1%	
STEMI	4,5%	
Revascularization		> .05
Overall	8,2%	
NSTEMI	8,2%	
STEMI	7,5%	

Table 3: *Primary outcome.*

Unplanned revascularization due to myocardial infarction during the follow-up period occurred in 8.2% of the patients. There were no significant between-group differences in the incidence of myocardial infarction at one year of follow-up, p = > .05.

Of the total cohort 98 (14,9%) patients received device therapy (Table 4). Seventy-six percent were male. -one-half received ICD (50%) and the other half received CRT-D (50%). At implant date, a quarter of the patients (24.5%) were in atrial fibrillation.

Outcome	N (98)	%
Device Type		
ICD	49	50
CRT-D	49	50
Baseline rhythm at implant date		
Atrioventricular Block	3	3,1
Atrial Fibrillation	24	24,5
Sinus Rhythm	69	70,4
Unknown	2	2,0

Table 4: *Secondary outcome.*

Subanalysis of these group of patients showed that the mean age and BMI of the CRT-D group is significantly higher (p = .008 and p = .006, respectively). Procedure time in minutes of the CRT-D group is significantly higher, 57 vs 163 (p = .001). The mean acute LV threshold and mean LV pulse duration threshold were also significantly higher in the CRT-D group, (p = .030) and (p = .022), respectively.

	ICD		CRT-D		
	M	**SD**	**M**	**SD**	**P-value**
Age	62	12	68	8	,008**
Body Mass Index	25,82	4,05	28,61	4,69	,006**
Procedure time (minutes)	57	21	163	47	,001***
Acute Atrial threshold	,000	,000	,044	,178	,088
Acute RV threshold	,128	,397	,068	,216	,360
Acute LV threshold	,000	,000	,089	,279	,030*
Atrial pulse duration threshold	,000	,000	,027	,107	,082
RV pulse duration threshold	,067	,194	,048	,143	,591
LV pulse duration threshold	,000	,000	,048	,143	,022*
Atrial wave amplitude threshold	,026	,180	,172	,807	,225
RV wave amplitude threshold	1,376	3,714	1,027	3,141	,620
Follow Up (days)	633	217	548	241	,074

Table 5: *Sub-analysis comparison between devices ICD/CRT-D.*

Discussion

Despite major advances in heart failure (HF) therapy over the past decades, mortality rate in these patients remain is still reportedly high [4]. Coronary artery disease accounts for 60 - 75 percent of these patients [5,6].

Coronary artery disease and heart failure with reduced ejection fraction both share many predisposing conditions, such as hypertension, diabetes, tobacco smoking and obesity. Hypertension is reported to be present in about 40 percent of patients that had myocardial infarction and about 20 percent with diabetes [7,8]. In the present cohort, the incidence of hypertension and diabetes were, 72 and 34 percent, respectively.

The link between smoking and atherosclerotic disease is well established, and hence these patients are more likely to have a myocardial infarction [9]. In this study, smoking incidence was 40 percent, which is similar with previous reports.

Our study reports a history of previous coronary artery disease (either percutaneous intervention or coronary bypass graft) of 27 percent, in line with reported in TRITON-TIMI 38 [10].

Chronic kidney disease (CKD) is an independent risk factor for the development of coronary artery disease, accounting for about 15.7 percent of the cases of myocardial infarction [11-13]. In the present study the overall incidence of chronic kidney disease is 9.7 percent, with 6 percent of the patient being on dialysis.

Heart failure (HF) progression accounts for about one-third of sudden cardiac death (SCD), with ventricular tachycardia (VT) and ventricular fibrillation (VF) being the most common cause [14,15]. Non-arrhythmic cardiac death due to progressive HF, may be as high as 50 percent, and noncardiac death, such as pulmonary and renal disease accounts for about 20 - 30 percent of the cases [16]. Our study reports a one-year all cause mortality rate of 3,8 percent, with no significant difference between the groups (NSTEMI 3,1% vs STEMI 4,5%; $p = >.05$). A retrospective cohort study reported a 40 percent mortality rate during a mean follow-up of 3.8 ± 3.1 years, in patients with acute myocardial infarction, despite having coronary revascularization and receiving ICD [17]. Although we did not stratify the mortality as being of cardiac cause or not, arrhythmic or not, the present study shows that there seems to be a trend towards a lower all-cause mortality. Unplanned revascularization rate due to myocardial infarction at one year was 8,2 percent, in the present study. This was also demonstrated by a randomized study with 7,9 percent revascularization rate, though this may vary according to initial strategy adopted (culprit-lesion vs complete revascularization) [18].

Implantable cardioverter-defibrillators (ICDs) with or without cardiac resynchronization therapy (CRT) are known have been proven highly effective in the treatment and prevention of sudden cardiac death (SCD). Indications for implant of these devices are now well established by society guidelines [1,19]. In the present cohort, 98 (14,9%) patients, met the criteria and underwent device implantation, 49 (50%) patients received ICD and 49 (50%) patients received CRT-D. One study of 1798 patients, reported that 64,9 percent (587 patients) with ICD and 68,7 percent (614 patients) with CRT-D, had ischemic heart disease, respectively [20]. Nonetheless, studies have showed no benefit of ICD therapy at the time of revascularization and that implantation should be delayed beyond 40 days post myocardial infarction [21,22].

After a mean device follow-up period of 633 days, all our patients were alive. This cohort showed that there seems also to be a trend towards lower need for device therapy in ischemic heart disease, considering that only about seven percent of the totality of the patients had an ICD implanted (about 14 percent when including CRT devices), which is still lower than previous reports.

Limitations of the Study

First, this is a retrospective observational analysis with an inherent risk of confounding variables that were not taken into account in the analysis. Second, we did not necessarily perform a long-term follow-up. Many patients may have developed criteria to receive device therapy, and were not identified, thus been incompletely treated.

Conclusion

This study showed that there seems to be a trend towards reduction in mortality and cardiac device therapy implantation in patients with ischemic cardiomyopathy. More studies are needed to truly identify and validate the results of this study.

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