

Safety Aspects of Implantable Cardioverter Defibrillators in Patients Participating in Exercise Therapy: A Systematic Review and Meta-Analysis

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Abstract

Background: The safety of exercise therapy (ET) in patients with an implantable cardioverter defibrillator (ICD) remains unclear. We sought to explore the current state of evidence and conduct a systematic review on the safety of ICDs during ET.

Methods: A systematic review was performed using CINAHL, Cochrane Library, EMBASE, Google Scholar, MEDLINE, PubMed (excluding Medline records), and Web of Science databases searched through April 2015. Studies that quantitatively assessed adverse events during ET and after ET in ICD patients compared to one of two control groups (non-ICD ET or non-ET ICD patients) were included. The primary outcome was adverse events during ET. Secondary outcomes were events during ET and follow-up.

Results: Meta-analyses were performed on ten eligible studies. During ET, ICD patients experienced an increased risk of adverse events [relative risk (RR)=2.63, 95% confidence interval (CI) (1.71-4.05), P=0.01] compared to non-ICD controls. There was no significant increase risk of adverse events compared to non-ET ICD controls [RR=0.99, 95% CI (0.11-8.95), P=0.99]. ET-ICD patients had fewer adverse events during follow-up compared to non-ET ICD populations [RR=0.90, 95% CI (0.82- 0.99), P=0.02]. A sensitivity analysis including only randomized trials showed similar findings showed no difference in the primary outcome.

Conclusions: Our analysis showed increased adverse event during exercise in ICD patients as compared with non-ICD patients. Comparative adverse event rates between exercising and sedentary ICD patients were similar during ET and lower after ET, suggesting that exercise can be safe and potentially protective among ICD patients. More rigorous data from larger randomized trials is needed to further quantify the incremental risk of exercise in high-risk ICD populations.

Keywords: Arrhythmias; Clinical electrophysiology; Drugs; Ablation; ICD; Surgery; Exercise; Rehabilitation

Abbreviations

ICD: Implantable cardioverter defibrillator ; ET: Exercise therapy; ATP: Anti-tachycardia pacing; VT: Ventricular tachycardia; EF: Ejection fraction

Introduction

Implantable cardioverter defibrillators (ICDs) result in significant survival benefit in patients with heart failure, high-risk arrhythmias, and survivors of sudden cardiac arrest [1,2]. As such, their use worldwide is increasing for both primary and secondary prevention of sudden cardiac death [3]. Exercise and cardiac rehabilitation also has established benefits in survival, health status, and quality of life in both high and low risk cardiac patients, including those with and without an ICD [4-8]. However, those with an ICD are underrepresented in cardiac rehabilitation, typically report low levels of exercise [9,10] and

are often reluctant to participate in exercise programs due to fear of exercise-induced shocks [11,12]. Rates of appropriate and inappropriate ICD therapy vary during follow-up, regardless of activity levels [13], and are both associated with adverse outcomes [14-16].

Findings from small, single center studies report that rates of ICD shocks during exercise therapy (ET) range from 2.3-12.5% [17] and that adverse cardiac event during ET are higher in ICD patients compared to non-ICD controls [18-20]. Despite the lack of more rigorous data, current exercise and cardiac rehabilitation guidelines make no recommendation for modified activity in ICD patients [21]. Currently, it is unclear whether ICD patients are at an increased risk of adverse events during ET. The primary objective is to explore the state of evidence and conduct a systematic review on the safety of ICDs during ET. To understand the safety of exercise in ICD patients, it is important to first explore what the baseline event rates are during ET among ICD populations. To do so, we compared adverse event rates of ET-ICD patients with ET non-ICD controls. Then, to better explore the incremental extent to which ET was associated with increased adverse

events beyond expected basal rates, we compared ET-ICD to non-ET ICD controls to evaluate the safety of ET among ICD populations.

Materials and Methods

We followed the checklist of MOOSE (Meta-Analysis of Observational Studies in Epidemiology) for background, design, analysis, and interpretation [22]. For purposes of simplicity, we refer to ET as a structured exercise program (i.e. cardiac rehabilitation). Published studies on the safety of ET in ICD patients were identified and cross-checked by two reviewers through a systematic search of the CINAHL, Cochrane Library, EMBASE, Google Scholar, MEDLINE, and Web of Science databases. Searches were restricted to English-language original research articles through April 2015 with no publication date limitations. The following keywords were applied to the search: (exercise OR cardiac rehabilitation) AND (implantable cardioverter defibrillator OR implantable cardioverter defibrillators OR ICD). References from relevant publications and review articles were hand-searched to supplement the electronic searches. A broad and comprehensive search strategy was chosen to encompass the diversity of exercise interventions studied in the ICD population.

The inclusion criteria were primary research studies that assessed the safety of structured exercise in adult ICD participants. Study designs included randomized controlled trials as well as both prospective and retrospective cohort studies. Given the broad range of exercise protocols, exercise had to be at least moderate intensity (defined as >3-6 metabolic equivalents) [23] to be included in our analysis. For purposes of meta-analysis, only studies with a control comparator group were selected. We excluded studies that assessed non-adult populations and those that were descriptive in nature, not directly or quantitatively assessing ICD adverse events in a studied population.

Data were extracted from all articles that met selection criteria and deemed appropriate after detailed review by two authors. If articles of the same study were found, then data were extracted from the most recently published article or the article that presented the outcomes of interest. Details of individual studies were collected and characterized on the basis of authors or year of publication; study design; sample size or characteristics (age, sex, ethnicity, left ventricular ejection fraction (EF), beta-blocker and antiarrhythmic use, primary/secondary ICD indication and duration); data collection methods; study outcomes; and statistical effect sizes. ICD therapy (shocks/ATP) was reported either by direct device interrogation, physician-witnessed events, chart review, or by self-reporting measures. Study quality was assessed within the domains of study population, study attrition, data collection, and data analysis.

The primary outcome included a composite of adverse events that occurred during completion of a structured ET program (i.e. both during and between sessions). The composite primary outcome included ICD shock (both appropriate and inappropriate), ATP therapy (both appropriate and inappropriate), ventricular arrhythmias not receiving ICD or ATP therapy, hospitalizations, and death. The secondary outcome was a similar composite of the primary outcome and adverse events (ICD shock, ATP therapy, ventricular arrhythmias, hospitalizations, and death) that occurred during a pre-specified follow-up period after ET completion. Primary and secondary outcomes were recorded for both ET-ICD and comparator control groups (i.e. non-ICD ET, non-ET ICD). Appropriate ICD therapy occurs when the device correctly identifies life-threatening ventricular rhythms (sustained ventricular tachycardia, ventricular fibrillation);

whereas inappropriate ICD therapy occurs when the device incorrectly interprets a non-life-threatening rhythm (sinus tachycardia, supraventricular tachycardia, etc.), artifact, or lead noise as a life threatening ventricular rhythm [24]. Anti-tachycardia pacing (ATP) attempts to overdrive suppress life-threatening ventricular rhythms in attempt to avoid an ICD shock.

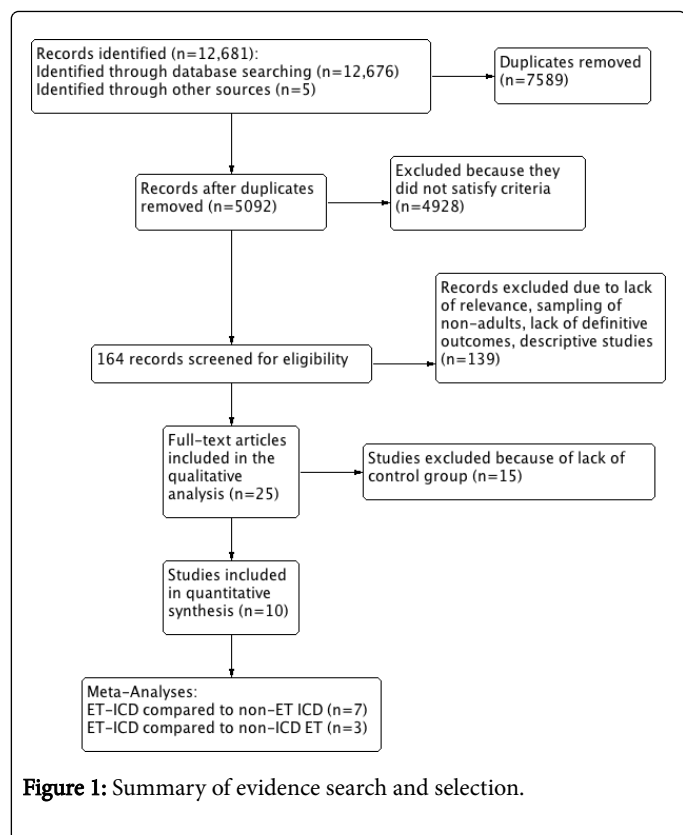
Total number of patients with an occurrence of the primary and secondary outcomes as well as odds ratio (OR), relative risk (RR), and hazard ratio (HR) with associated 95% (confidence intervals) CIs were collected from all studies, if available. The first analysis for our primary outcome of events during exercise included ET-ICD patients compared to non-ET ICD patients. A second analysis for our primary outcome of events was done for ET-ICD patients when compared to non-ICD ET patients. Two comparator groups were examined (exercise non-ICD populations; resting ICD populations) to help contextualize the risk of adverse events associated with ICD populations during exercise as compared with their expected baseline event rate at rest. A third analysis was done for our secondary outcome. A sensitivity analysis was done including only randomized controlled studies comparing ET-ICD patients to non-ET patients (both ICD and non-ICD controls) to account for the heterogeneity among study designs included in the meta-analysis.

Dichotomous variables were analysed using RR with 95% CI to assess the safety of ET in ICD patients for each study population. Statistical heterogeneity was evaluated according to the Higgins I² statistic, derived from Cochran's Q and the degree of freedom [$100(Q-df)/Q$] [25,26]. I² values greater than 25%, 50%, and 75% were considered evidence of low, moderate, and severe statistical heterogeneity, respectively. To account for clinical heterogeneity, we used the random-effects model based on DerSimonian and Laird's method [27]. Potential publication bias was determined by visually inspecting funnel plots. Data analyses were performed using Review Manager Version 5.3 (The Nordic Cochrane Center, Copenhagen, Denmark) and MIX version 2.0 (BiostatXL, Sunnyvale, CA, USA). $P < 0.05$ was considered statistically significant.

Results

Literature search

A total of 12,681 studies were identified through database searching (629 from PubMed, 170 from MEDLINE, 2363 from Web of Knowledge, 467 from EMBASE, 3227 from CINAHL, 5820 from Google Scholar, and 1942 from the Cochrane Library), and five studies were added after hand-searching in-text citations (Figure 1). 15 (3573 participants) [9,18-20,28-38] studies collected data relevant to our outcomes of interest, specifically safety and/or adverse events during and/or after ET. Of these studies, 10 were examined by meta-analyses (3171 participants) [9,19,20,28,30,32,33,36,37,39] as they included a comparator control group: 7 studies (2498 participants) [9,28,30,32,33,36,37] used non-ET ICD controls compared to ET-ICD patients and 3 studies (673 participants) [19,20,38] used ET non-ICD patients compared to ET-ICD patients. Of the 10 studies, 7 had data relevant only to our primary outcome.



Study characteristics

The characteristics of the ten studies assessed by systematic review are summarized in Table 1. Five were randomized controlled trials with one using a crossover design. Of the non-randomized studies, 3 were prospective cohort designs, 2 were retrospective cohort designs, and 1 was a case-controlled study. Only 1 study used self-reporting to quantify details of ET. ICD therapy and adverse events were ascertained either as per study protocol, device interrogation, witnessed events, chart review, or self-reporting. 3 studies did not record adverse events during ET (primary outcome) and 2 did not have any follow-up events after ET (secondary outcome). The majority of subjects were male, Caucasian, had depressed EF (mean EF 24-44%), and were on beta-blocker therapy. The indication for ICD varied among populations; however, the overwhelming etiology was ischemic cardiomyopathy. The time of ICD implant ranged from 7 weeks to 4 years. The majority of exercise interventions were structured, longitudinal cardiac rehabilitation sessions. Exercise strategies varied among studies, however, almost all focused on aerobic activity at a moderate intensity (target heart rate 50-80%) followed by a 5-minute cool down. For ICD patients, the maximum heart rate was set 10-30 beats/minute below ventricular tachycardia detection threshold.

Study Characteristics				Baseline Characteristics						Exercise Details	Primary Outcome Total (Shock/ATP/Death/VA/Hosp)		Secondary Outcome Total (Shock/ATP/Death/VA/Hosp)		
Study	Design	Control Group	Sample Size, Total* (ET-ICD/control)	Mean Age (years)	Female (%)	LVEF (%)	Beta-blocker (%)	Primary / Secondary ICD Indication (%)	Ischemic (%)	ET-ICD	Control	Follow-up	ET-ICD	Control	
Dougherty et al. [32]	Prospective, controlled, randomized	non-ET ICD	160 (84/76)	54.9 (56.1/53.6)	22.5 (20.2/25)	40.6 (38.7/42.6)	100 (100/100)	43/57	43 (44/42)	Aerobic @THR; 5 days/week; 6 weeks	1 (0/1/0/NA/0)	0 (0/0/NA/0)	6 months	22 (22/0/0/NA/0)	27 (27/0/0/NA/0)
Berg et al. [9]	Prospective, controlled, randomized, crossover design	non-ET ICD	196 (99/97)	NA (57.6/56.7)	21 (20/22)	NA (32.2/32.7)	NA	66/34	NA (46/59)	Aerobic @50-80% THR + Resistance @60-80% MHR; 2 days/week; 12 weeks	0 (0/0/NA/0)	0 (0/0/NA/0)	12 months	† NA(0.2/3.7/NA/3.7/NA)	† NA(0.43/9.8/NA/10.7/NA)
Piccini et al. [37]	Retrospective, case-controlled, non-randomized	non-ET ICD	1053 (546/507)	61 (61/60)	21 (21/21)	NA (24/24)	94 (94/94)	NA	61 (61/62)	Aerobic @ 60-70% THR; 3-5 days/week; 6 weeks	NA	NA	2.2 years (mean); 4 years max	284 (108/NA/NA/176 ‡)	290 (113/NA/NA/177 ‡)
Fan et al. [19]	Case-controlled, non-	ET non-ICD	84 (42/42)	NA (61/61)	NA (24/21)	NA (32/36)	(79/79)	22/78	5 (NA)	Aerobic @50-85% of HRR; 3	5 (1/NA/0/NA/4)	1 (0/NA/NA/0)	NA	NA	NA

	randomized									days/week; 8 weeks		0/NA/1)			
Davidson et al. [30]	Retrospective; controlled, non-randomized	non-ET ICD	82 (28/54)	61 (60/62)	13 (18/11)	36 (37/35)	82 (82/81)	NA	100 (NA)	Self-reported METS; 3-4 days/week; NA	0 (0/NA/NA/NA/NA)	9 (9/NA/NA/NA/NA)	NA	7 (7/NA/NA/NA/NA)	36 (36/NA/NA/NA/NA)
Vanhees et al. [20]	Prospective, controlled, non-randomized	ET non-ICD	565 (92/473)	NA (57/56)	10 (14/10)	NA	55/78	NA	NA	Aerobic @50–80% of MHR; 3 days/week; 12 weeks	23 (5/2/0/16/NA)	47 (0/0/0/47/NA)	3 months	NA	NA
Fitchett et al. [33]	Prospective, controlled, randomized, crossover design	non-ET ICD	32 (16/16)	58 (NA)	12 (NA)	38 (NA)	56	NA	NA	Aerobic @ 75% THR; 2 days/week; 12 weeks	7 (2/3/0/2/NA)	3 (0/2/0/1/NA)	4 months	26 (2/2/0/22/NA)	
Vanhees et al. [38]	Prospective, controlled, non-randomized	ET non-ICD	24 (8/16)	NA (54/52)	21 (13/25)	NA (44/43)	(100/69)	NA	NA	Aerobic; 3 days/week; 12 weeks	1 (0/0/1/0/NA)	0 (0/0/0/0/NA)	NA	NA	NA
Belardinelli et al. [28]	Prospective, controlled, randomized	non-ET ICD	53 (30/22)	NA (55/53)	NA	NA (30/33)	(87/82)	63/37	100 (NA)	Aerobic @ 60% peak VO ₂ ; 3 days/week; 8 weeks	NA	NA	18 months	20 (0/NA/0/NA/20)	18 (8/NA/0/NA/10)
O'Connor et al. [36]	Prospective, controlled, randomized	non-ET ICD	1285 (641/644)	NA	NA	NA (24.9/24.6)	NA	NA	NA	Aerobic @ 60-70% THR; 3 days/week; 6 weeks	NA	NA	NA	142 (142/NA/NA/NA)	151 (151/NA/NA/NA)
Implantable cardioverter defibrillator (ICD); Exercise therapy (ET); Ejection fraction (EF); Not available (NA); Target heart rate (THR); Maximal heart rate (MHR); Metabolic equivalents (METS); Ventricular Arrhythmias (VA); Hospitalization (Hosp) *Refers to the entire study population †Reported as mean events/patient ‡Reported as hospitalization or death															

Table 1: Study Characteristics.

Publication bias and heterogeneity

Visual inspection of the funnel plot (Figure 2) for all 7 studies with primary outcomes did not reveal any substantive publication bias. Figures 3 and 4 summarize the degree of heterogeneity across the studies. For ET-ICD patients compared to non-ET ICD controls, there was low statistical heterogeneity between populations ($P=0.72$, $I^2=0\%$).

For ET-ICD patients compared to non-ICD ET controls, there appeared to be moderate statistical heterogeneity between the populations ($P=0.07$, $I^2=63\%$). For the 5 randomized trials included in the sensitivity analysis, there was low heterogeneity among the studies included ($P=0.26$, $I^2=25\%$).

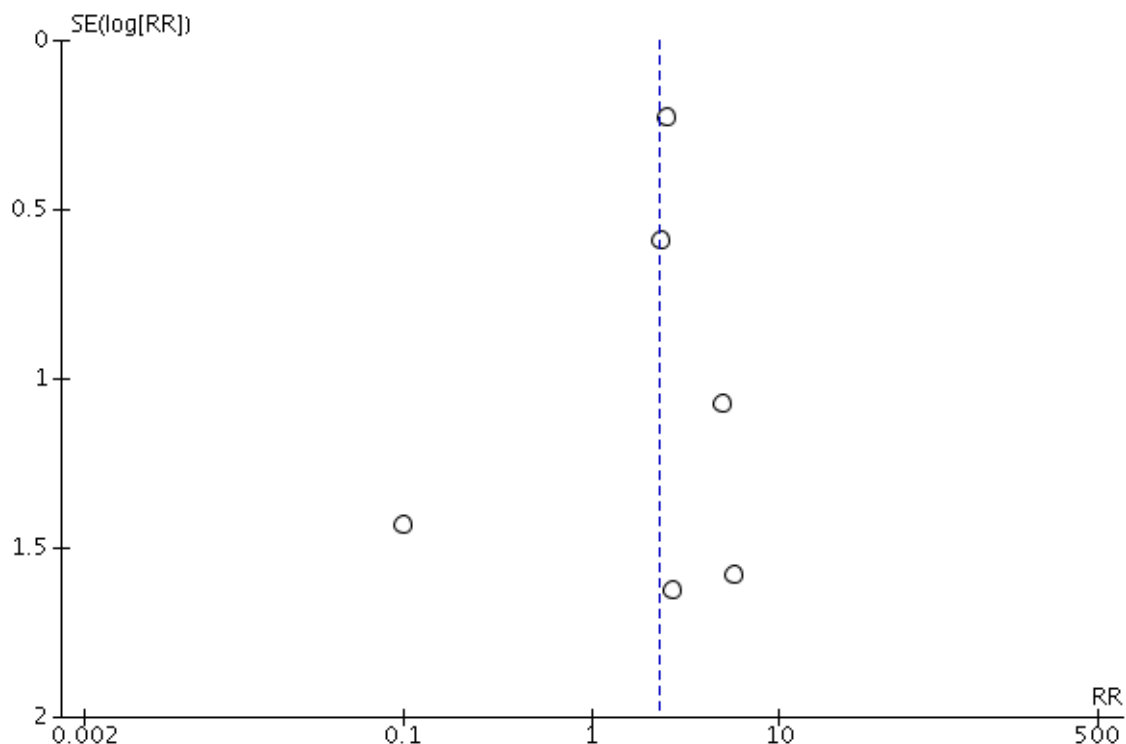


Figure 2: Funnel plot of 7 studies included in the meta-analyses of the primary outcome. Relative risk (RR); Standard error (SE). Of the 7 studies, 1 study had no events. A total of 6 studies with events are displayed.

Meta-analysis of adverse events in ET-ICD patients compared to non-ICD ET patients

674 patients were included in the analysis: 142 (21%) exercise ICD patients were compared to 531 (79%) non-ICD ET controls. Baseline characteristics were similar between groups within each study, including EF. Exercise regimens were similar between ICD and non-ICD groups, with training heart rates at 50-80% of maximum heart rate, 2-5 times per week, for 6-16 weeks. A total of 29 events were seen in the ET-ICD group: 6 ICD shocks, 3 ATP therapies, 16 ventricular

arrhythmias, 4 hospitalizations. A total of 48 events were seen in the non-ICD ET group: 47 ventricular arrhythmias and 1 hospitalization. Compared to non-ICD ET controls, at least moderate intensity exercise was associated with a 2.6-fold increased risk of adverse events during exercise [RR=2.63, 95% CI (1.71-4.05), P=0.01] (Figure 3). Secondary outcomes were available for only 1 study which report six ICD shocks in the ET-ICD group but a higher ventricular arrhythmia burden in the non-ICD ET group 3 months after ET.

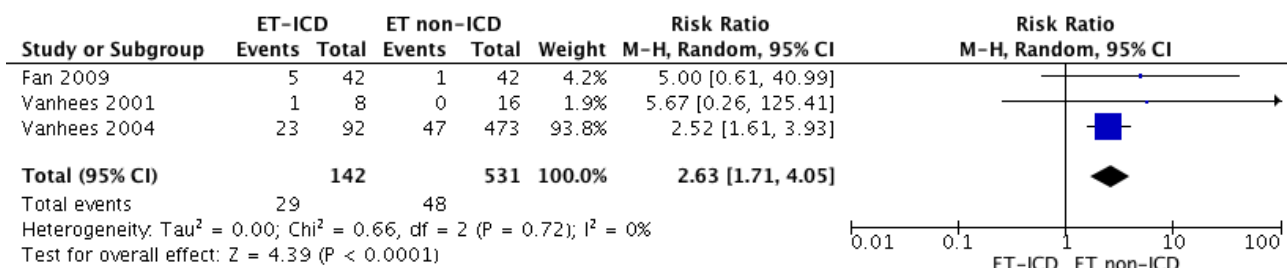


Figure 3: Adverse events during ET in ICD patients compared to non-ICD ET patients (primary outcome). A RR>1 suggests that exercise is harmful. Diamonds indicate pooled RRs with associated 95% CIs. ICD=implantable cardioverter defibrillator; ET=exercise therapy; RR=relative risk. The relative risk was pooled by using random-effects meta-analysis.

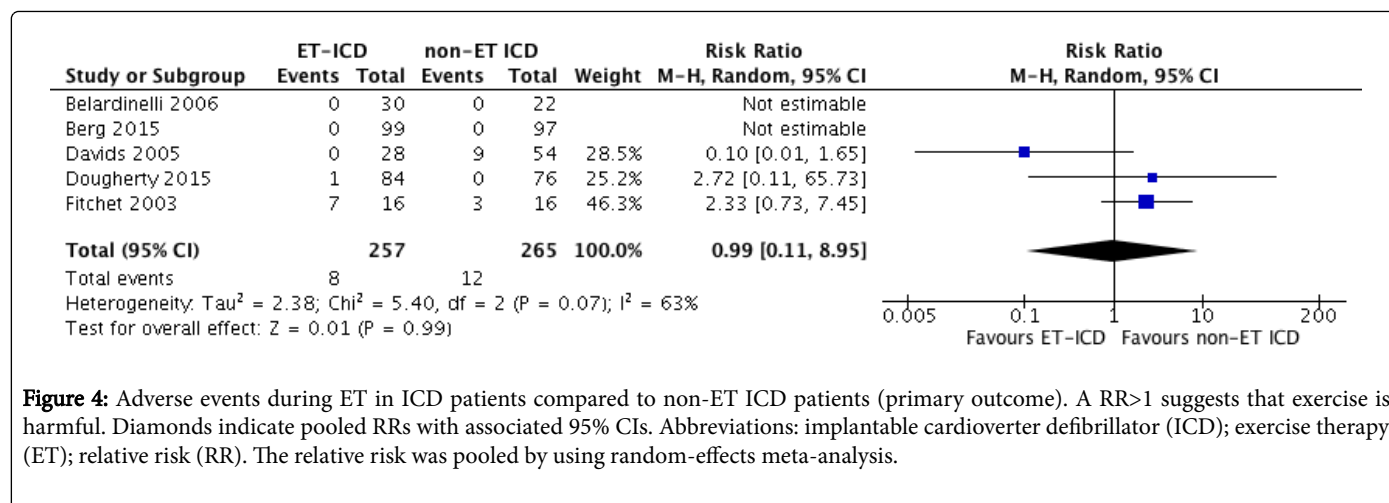


Figure 4: Adverse events during ET in ICD patients compared to non-ET ICD patients (primary outcome). A RR>1 suggests that exercise is harmful. Diamonds indicate pooled RRs with associated 95% CIs. Abbreviations: implantable cardioverter defibrillator (ICD); exercise therapy (ET); relative risk (RR). The relative risk was pooled by using random-effects meta-analysis.

Meta-analysis of adverse events in ET-ICD patients compared to non-ET ICD patients

3154 patients were included in the analysis: 522 had data relevant to our primary outcome of events during ET and 2632 had outcomes relevant to our secondary outcome of events after ET completion. Baseline characteristics within each study were comparable between groups. For the ET subjects, the exercise protocol, frequency, and durations varied among studies, however, all included primarily aerobic exercise multiple times per week for at least 6 weeks. Adherence to exercise was excellent. For our primary outcome, 257 ET-ICD patients were compared to 265 non-ET ICD controls. There

were a total of 8 adverse events in the ET-ICD: 2 ICD shocks, 4 ATP therapies, 2 ventricular arrhythmias. A total of 12 events were seen in the non-ET ICD control group: 9 ICD shocks, 2 ATP therapies 1 ventricular arrhythmia. Among ET-ICD patients, there was no significant increased risk of adverse events among exercising as compared with non-exercising ICD populations, but confidence-intervals were wide [RR= 0.99, 95% CI (0.11-8.95), P=0.99] (Figure 4). Following completion (mean follow-up range 4 months to 2.2 years) of the structured exercise program, compared to non-ET ICD controls, ET-ICD patients had a significantly lower rate of adverse events [RR=0.90, 95% CI (0.82- 0.99), P=0.02] (Figure 5).

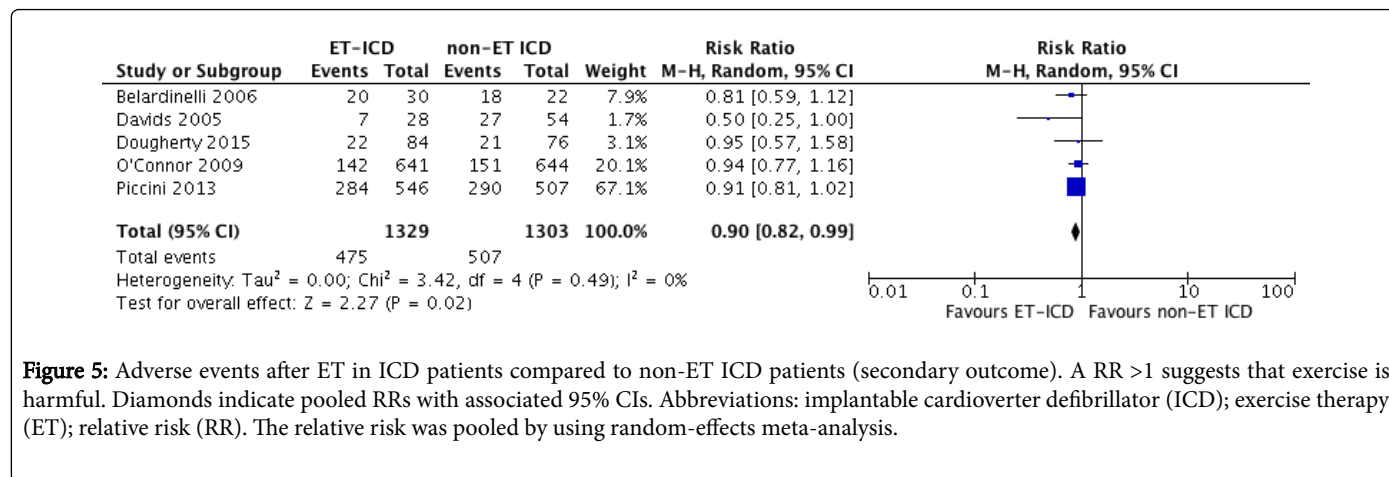


Figure 5: Adverse events after ET in ICD patients compared to non-ET ICD patients (secondary outcome). A RR >1 suggests that exercise is harmful. Diamonds indicate pooled RRs with associated 95% CIs. Abbreviations: implantable cardioverter defibrillator (ICD); exercise therapy (ET); relative risk (RR). The relative risk was pooled by using random-effects meta-analysis.

Sensitivity analysis

1725 patients were included in 5 randomized studies: 870 ET-ICD and 855 non-ET controls (Figure 6). There was no difference in the

primary outcome between the two groups [RR=1.17, 95% CI (0.65-2.10)].

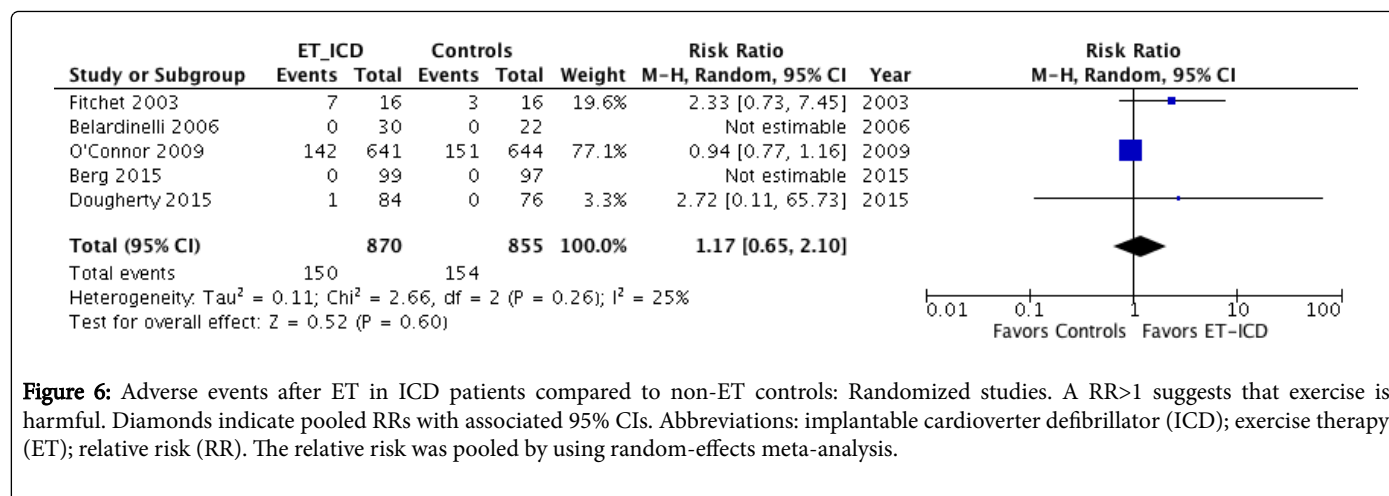


Figure 6: Adverse events after ET in ICD patients compared to non-ET controls: Randomized studies. A RR>1 suggests that exercise is harmful. Diamonds indicate pooled RRs with associated 95% CIs. Abbreviations: implantable cardioverter defibrillator (ICD); exercise therapy (ET); relative risk (RR). The relative risk was pooled by using random-effects meta-analysis.

Discussion

The results of our systematic review have highlighted the gaps in knowledge in the current state of evidence regarding ICD safety during ET. We were able to identify 10 studies, 5 of which were randomized, high quality trials, suggesting that at least moderate intensity exercise was associated with a 2.6 fold higher adverse event rate during exercise in ICD patients as compared with non-ICD patients. Comparative adverse event rates between exercising and sedentary ICD patients were similar, suggesting that exercise can be safe among ICD patients. More rigorous data from larger randomized trials is needed to further quantify the incremental risk of exercise in high-risk ICD populations.

To the best of our knowledge, our systematic review is the first to explore the safety of exercise among ICD patients. Few studies have evaluated ICD safety compared to non-ICD exercise controls and those published suggest that adverse events during exercise are not uncommon, reflecting the higher risk nature of ICD patients [19,20,35,37]. Our study suggests that compared to non-ICD controls, ET can be associated with a 2.6-fold increase in adverse events. This finding must be contextualized with an understanding of the basal event rate in non-exercising, sedentary ICD patients. We included two control comparators to assess the safety of exercise in ICD patients by first establishing a basal event rate or safety profile compared to non-ICD ET patients. Not unexpectedly, events were higher, reflecting an overall higher risk population receiving an ICD. Once established that ICD patients do have higher event rates, our second analysis complements the first analysis by establishing that ET is safe among ICD patients (i.e. no difference in adverse events). Data on exercise within the ICD population seems to support its safety as well as efficacy [9,17,30,32,33,36,37].

Although we did not appreciate a statistically significant increase in adverse events compared to non-ET ICD controls, our results may have been underpowered to do so. We cannot conclude with certainty that event rates were higher than expected rates in non-exercising ICD controls. Nonetheless, our study did suggest that ET was associated with reduced adverse events during longer-term follow-up in ICD populations, which may underscore the beneficial, protective arrhythmogenic properties of exercise conditioning [39]. Moreover, at least one study showed that exercise itself was not associated with ICD shock, but history of atrial fibrillation or prior sustained VT was [37]. Such patients at higher risk for exercise-induced adverse events could theoretically be carefully selected prior to participation in structured

exercise programs for device reprogramming that may mitigate inappropriate therapy during exercise [3]. Stress-testing device interrogation before, during, and after ET may provide greater insight into better establishing these safety margins. Nonetheless, more research is required to understand adverse event rates among exercise and sedentary ICD high-risk populations, and during different modalities of exercise (resistant training, high-intensity interval training, etc.). In this regard, at least one large trial of the high-intensity interval training safety in heart failure patients including ICDs has been completed with pending results [40].

While available evidence has demonstrated cardioprotective benefits associated with exercise among high-risk cardiac populations [4-8], safety research necessitates a search for “rare events” which may require a population surveillance approach to acquire larger numbers of ICD patients. Large international consortiums that enroll ICD patients with primary survey data are likely required to determine how event rates during exercise compare incrementally with what might be expected at resting states. The absence of statistical significance, wide confidence intervals, and underpowered data in our study limit conclusions on safety of ET in ICD populations. For now, an individualized approach is required together with the implementation of broader surveillance and monitoring of ICD populations.

There are several limitations to the results of our study. We did not include free text or Scopus databases in our search strategy. Although not significant, there was heterogeneity in the studies included for meta-analysis. All studies employed various inclusion criteria including the proportion of primary vs. secondary indications as well as cardiomyopathy etiology. Patients with underlying conditions such as arrhythmogenic right ventricular cardiomyopathy, catecholaminergic polymorphic VT, etc., are a much higher risk for exercise-induced arrhythmias compared to other ICD populations. Exercise interventions varied in mode, intensity, duration, and frequency. Exercise level also varied among control groups: some were sedentary while others were compared to “usual care” which may include exercising patients. One study included self-reporting as a measure of exercise, which cannot be validated. Clinical outcomes also varied in reporting and definition. ICD shocks and ATP therapy, although associated with adverse events, may not be surrogate for sudden cardiac death [41]. Significant variation in ICD programming exists and was not acknowledged or discussed in most studies. Programming higher rate cut-offs, longer arrhythmia-detection windows, and parameters for discrimination of supraventricular

tachyarrhythmias reduce appropriate and inappropriate shocks and other adverse outcomes. [42,43]. Without knowledge of such device programming, our results may falsely increase the benefits of ICD.

Not all studies confirmed ICD shock with device interrogation and may have reflected phantom shocks, defined as the sensation of ICD shock without objective evidence of a deployed shock, which can be as high as 10% during exercise [44]. Some studies recorded only ICD therapy without appropriate *vs.* inappropriate discrimination. ATP without hemodynamic significance may not represent an outcome of significance and, similar to ICD shocks, may simply reflect poor ICD programming rather than an exercise induced arrhythmia. Furthermore, ventricular arrhythmias also varied in definition and included ventricular ectopy and non-sustained VT, which itself may not be of prognostic significance. Detailed device-observation reporting can alter management strategies significantly: exercise induced adverse events may not reflect inducible dysrhythmias but rather inappropriate device programming. There was also insufficient data on long-term follow-up in ICD patients compared to non-ICD controls. We were unable to assess if the increased risk seen during exercise dissipated with regular aerobic conditioning and autonomic nervous system adaptation. The clinical diversity and heterogeneity of ICD populations studied, however, enhances the generalizability of our results. Lastly, our search included English-only studies and may result in a language or cultural bias. Despite our exhaustive search strategy, we were only able to include ten studies and cannot therefore exclude publication bias.

Conclusion

In conclusion, our review underscores the limited knowledge regarding the safety of exercise in ICD populations. The uncertainty over the magnitude of adverse events due to exercise among ICD populations justify the need for more research into establishing the safety of exercise among high-risk arrhythmogenic populations. Until then, we advocate that moderate intensity exercise therapy can be safe and effective with an individualized approach, careful patient selection, monitoring of high risks populations in a supervised cardiac rehabilitation setting, and incorporation of routine device-interrogation and reprogramming as needed. Further research around the risk-benefit trade-offs of higher-intensity exercise protocols among arrhythmogenic populations is needed.

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