CHANGING VIEWS: SAFETY AND EFFICACY OF IMPLANTABLE CARDIOVERTER-DEFIBRILLATOR THERAPY IN ATHLETES

Luděk Pavlů, Martin Hutyra, Miloš Táborský

1st Department of Internal Medicine – Cardiology, University Hospital, Olomouc, Czech Republic

SUMMARY

The implantable cardioverter–defibrillator (ICD) is highly effective in reducing sudden death from ventricular tachyarrhythmia among high-risk cardiac patients. Conventional advice given to patients with ICD is to avoid physical activity more strenuous than playing golf or bowling. This recommendation is given due to a theoretical risk of arrhythmia precipitation, and thus increased risk of death due to failure to defibrillate, injury resulting from loss of control caused by arrhythmia-related syncope or shock, and also due to sport related direct damage to the ICD system. Recent prospective data from an international registry involving 372 athletes with ICDs in situ and actively participating in sports has been published. This indicates that, although physical activity resulted in an increased number of shocks compared to rest, there was no significant difference between intensive physical activity and any other activity (10% vs. 8%, p = 0.34) in frequency of shocks. Furthermore, over a median follow-up period of 31 months (21–46 months), in the period of sports activity and 2 hour rest directly after there were no occurrences of death, resuscitated arrest or arrhythmia, or shock-related injury. This data is likely to start a shift in every-day clinical decision-making leading to revision of the high level of precautions imposed on the rapidly enlarging ICD recipient population.

ICD Therapy Rationale

Implantable cardioverter-defibrillator (ICD) therapy delivers significant mortality reduction in patients at high risk for sudden cardiac death. This cohort should be offered ICD therapy. Primary prevention is preventive ICD therapy prior to any major arrhythmic event (ventricular fibrillation/ventricular tachycardia cardiac arrest, sustained ventricular tachycardia with syncope) in high risk patients. The indication criteria for primary prevention heavily lean on assessment of left ventricular systolic function post myocardial infarction in the majority of ICD recipients and have been confirmed in multiple randomized clinical trials (1–4). The most studied populations reflect the prevalence of different cardiac diagnoses in the population. Ischaemic cardiomyopathy and dilated cardiomyopathy as the most common entity of non-ischaemic cardiomyopathy are the most studied in populations. Importantly, many athletes are given ICDs for conditions not readily covered by these guidelines, for example arrhythmogenic right ventricular cardiomyopathy (ARVC) and hypertrophic cardiomyopathy. Secondary prevention indication for ICD therapy is survival of cardiac arrest. In these patients ICD therapy is also markedly more effective than medical therapy and substantially prolongs survival (5–7).

ICD Therapy Risks

ICD therapy brings multiple risks as well. Procedural risks include infection (0.9%), pocket hematoma (1.6%), pneumothorax (0.3%), and infrequently hemopericardium and cardiac tamponade (8). The long-term complications are also well known – lead infraction, infection (pocket, infective endocarditis) and less commonly generator malfunction. Of importance to this review is the phenomenon of an inappropriate discharge. Recent clinical trials have brought attention to not only the significant negative impact on quality of life in patients with inappropriate ICD therapy but also the significant difference in all cause mortality. The MADIT- RIT trial (8) randomized patients into the three different ICD programming groups: low heart rate cut off for ventricular tachycardia treatment zone (2.5 sec delay at 170–199 bpm or 1.0 sec delay at 200 bpm or more), high rate therapy (2.5 sec delay at 200 bpm or more) or delayed therapy for 60 seconds for 170 to 199 bpm, or 12 sec delay for 200 to 249 bpm or 2.5 sec delay for heart rate of 250 or above. The high rate therapy and delayed therapy settings led to a significantly lowered burden of inappropriate ICD discharges and resulted in significant lower all cause mortality.

Effects of Exercise – Possible Trigger of Arrhythmias

There is evidence of a 2.5 times higher risk of sudden death in adolescent and young adults engaged in competitive sport activity in comparison to their non competitive counterparts (9). Physical activity per se is not the cause of higher risk of death but perhaps more of a trigger of sudden death in individuals with a predisposition for sudden death. On the other hand there is epidemiologic evidence that regular vigorous sport offsets the risk of vigorous exercise – induced sudden death by lowering the risk of sudden death from coronary artery disease in the middle aged and older population (10). There is a variety of suggested

and studied pathophysiologic mechanisms for the exercise serving as a trigger for arrhythmic death. Increased catecholamine levels in association with acidosis, electrolyte disturbances, dehydration and ischaemia probably play a mechanistic role (11).

Effects of Exercise in ICD Recipients

Generally, there are limited clinical data on the effect of vigorous exercise in the heterogeneous ICD recipient population. In patients with ARVC regular and intense exercise can worsen the course of disease (12). In the ischaemic cardiomyopathy cohort of ICD recipients, exercise together with anger can trigger ventricular arrhythmia (13). One of the reasons for limited data are the precautions and limitations on intensive physical activity in ICD recipients as outlined in multiple expert position statements (14–16). The ICD recipient should engage at a competitive level only in low static and low dynamic sports (golf, bowling) and at a recreational level only in low to moderate static and dynamic sports (Fig. 1)

Everyday Clinical Practice and Challenging Evidence

In the 2006 retrospective survey of members of the Heart Rhythm Society, more than 40% of participants reported at least one ICD recipient participating in competitive or high intensity recreational sport (17). This survey provided justification for a prospective international registry to identify and quantify the risks of competitive or high intensity sport in ICD recipients (18). A landmark study published by Lampert et al. enrolled 372 ICD recipients. One hundred and thirty seven patients were involved in competitive sport activities (23 in basketball, 19 in soccer, 19 in running, 11 in volleyball, 65 patients in other sports). Two hundred and thirty five participants were engaged in non-competitive group, some of them participating in more than one sport (running 87 patients, skiing 70 patients, soccer 50 patients, cycling 38 patients, tennis 32 patients, and other sports 176 patients). Participants in the competitive group spent a median of 13 hours per week, in the non-competitive group a median of 5.1 hours per week practicing or competing. The spectrum of cardiac diagnosis involved long-QT syndrome 73 patients (20% of study population), hypertrophic cardiomyopathy 65 patients (17%), arrhythmogenic right ventricular dysfunction 53 patients (14%), coronary artery disease 41 patients (11%), idiopathic ventricular

Fig. 1. Classification of sports.
Source: Adapted from J Am Coll Cardiol 2005;45:1364-7.

tachycardia/ventricular fibrillation 40 patients (11%), and dilated cardiomyopathy 31 patients (8%). One hundred and fifty five patients had ventricular fibrillation/cardiac arrest or sustained ventricular tachycardia prior to the ICD implantation. Sixteen patients out of this group were engaged in sport at competitive level. The median follow up was 30 months for the studied population.

The primary end points were tachyarrhythmic death or externally resuscitated tachyarrhythmia caused by shock failure, incessant ventricular arrhythmia, or postshock pulseless electric activity or severe injury, defined as requiring hospitalization, from shock or syncopal arrhythmia during exercise or 2 hours post exercise. None of the primary end points occurred during the cohort follow up period. Two patients died during the follow up period. None of them died during or up to 2 hours after sport activity. One death occurred during office work in a 52-year-old cyclist with coronary artery disease after multiple ICD therapies, the second death occurred in a 32-year-old volleyball and softball player with familial dilated cardiomyopathy during hospitalization for congestive heart failure.

The secondary end points were the number of appropriate and inappropriate shocks, multiple shocks during one appropriate shock episode (i.e. failure of first maximum delivered shock or recurrent arrhythmia), moderate injury (defined as injury requiring an emergency room visit) associated with shock, ICD lead/system damage. Seventy seven individuals suffered 121 shocks. This represents 21% of participants of the study population. ICD programming was set at the mean lowest cut off value of 200 beats per minute (IQR 188–215 bpm) for the non-competitive subgroup and 217 (IQR 210–222) for the competitive group. This is similar to the percentage of participants at the high rate therapy subgroup of MADIT-RIT trial who had experienced a shock (19%) (8). Though in MADIT there are limitations of rather different patient population with over 50% patients with ischaemic cardiomyopathy and a shorter follow up period of 16.8 months. Focusing on the shocks in Lampert et al. trial, 48 participants (13% of population) received at least 1 appropriate shock and 40 (11%) received at least one inappropriate shock (18).

Focusing on the distribution of shocks among the groups: 36 participants (10%) received a shock during competition or practice or up to two hours after competition or practice (total of 47 shocks), 29 participants (8%) received a shock during other physical activity (total of 39 shocks), 23 participants (6%) received a shock during rest (total of 33 shocks). There was no statistically significant difference between number of shocks received during competition/practice and other physical activity (10% vs 8%, p=0.34), the same applied to subgroup of appropriate shocks (6% vs. 4%, p=0.18). There was a significant difference between the number of appropriate shocks received at rest versus any physical activity (3% vs. 8%, p=0.006), the same applies for total number of shocks at rest versus during any physical activity (6% vs. 16%, p=0.0001).

Lampert et al. (18) in their trial also identified a subgroup of patients requiring multiple shocks focusing on the 7 patients (2% of population) with 8 arrhythmia episodes requiring more than one high energy ICD discharge. 4 episodes were during competition/practice, 3 during other physical activity and 1 during rest. The diagnosis mix of those 7 patients consists of 3 patients with coronary artery disease, 1 patient with catecholaminergic polymorphic ventricular tachycardia (CPVT), 2 patients with idiopathic ventricular
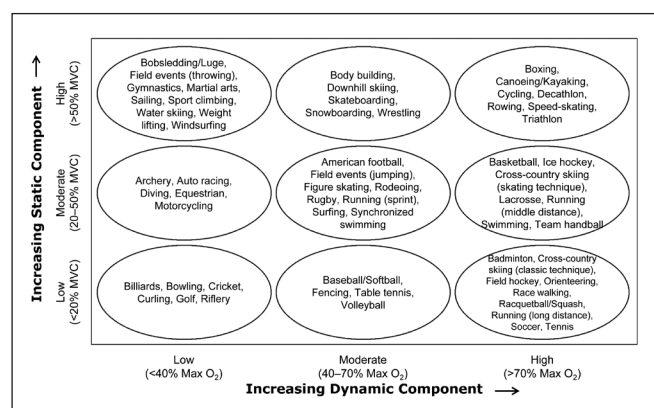
fibrillation, and 1 patient with hypertrophic cardiomyopathy. None of those patients suffered failure of defibrillation as described in several case reports (19–21) but 1 of 10 CPVT participants required multiple ICD shocks on two occasions.

No moderate injury related to shocks or arrhythmia occurred. Generator malfunction did not occur. The rate of definitive lead malfunction (97% at 5 year, 90% at 10 year) was comparable to common ICD recipient population (22).

Lampert et al. (18) study has some very important limitations. The patients were self referred and they may or may not represent the ICD recipient athletic population. The number of shocks was also self-reported with the possibility of underestimation. Most importantly, the role of asymptomatic antitachycardia pacing in abortion of ventricular tachycardia remains unknown. Most subjects had a normal ejection fraction, which limits extrapolation to the majority of ICD recipients with a reduced ejection fraction. Last but not least, the median time in between the ICD implantation to enrollment to the trial was circa two years and there is a possibility of survival and selection bias.

Conclusions for Daily Practice

There is a substantial difference between guidelines and everyday clinical practice in patients wishing to continue in competitive or high intensity recreational sport activities. For the first time, there are sound clinical data by Lampert et al. (18) providing evidence that many previously feared risks and complications in reality have low incidence e.g. technical problems with ICD devices such as generator malfunction and high rate of definitive lead malfunction or the risk of inappropriate ICD shock due to exercise induced sinus tachycardia or T wave oversensing. It should be acknowledged that these favourable outcomes were achieved in centres with high volumes of procedures with expertise in device implantation.

In order to achieve such favourable results one has to pay attention to the basics, e.g. reaching the optimal sensing signals at implantation. Adequate sensing plays a pivotal role in detection of fast heart rhythms therefore possibly limiting the frequency of inadequate shocks. A single lead ICD device brings the durability of a simple system together with less risk if an extraction of single lead instead of two will be required in the future. On the other hand, it limits the discrimination ability in arrhythmia detection. Interestingly the superiority of the dual chamber ICD device in comparison to single lead ICD devices has not been confirmed in clinical trials (23, 24). Whether the ideal solution is single lead device with atrial sensing function remains to be confirmed in a clinical trial. Subcutaneous ICD (S-ICD) could also play an important role in primary prevention patients but there have not been yet sufficient data for such recommendation. Certainly S-ICD should not be used in secondary prevention in patients with pace-terminable arrhythmias.

The standard implantation site in the left subclavicular region has the advantage that the heart located in between the ICD housing and the RV shock coil. It is at the direction of shock vector theoretically resulting in the lowest possible fibrillation threshold. In patients who engage in sports using their left hand, for example racket sports (tennis, squash), the repetitive arm motion might actually result in lead fracture due to costo-clavicular crush. In this case, right sided implantation together with the threshold

testing should be considered. The next generation of smaller sized S-ICD could solve the above problems.

Lampert et al. (18) study with cut off values similar to the MADIT-RIT leads to similar percentage of participant experiencing a shock. But it is mandatory to exercise a great level of caution for application of this concept uniformly without individualization to the heterogeneous ICD recipient athletic population since there is no randomized clinical trial done to support it.

Avoiding physical activity for the first 6 weeks after ICD device implantation is a reasonable demand for any ICD recipient. Stress testing is also a reasonable step prior to engagement in high intensity sport activity especially in patients with coronary artery disease. Stress testing is recommended on a regular basis in the long-term management of patients with ischaemic cardiomyopathy. Patients with idiopathic ventricular fibrillation should be screened for catecholaminergic polymorphic ventricular tachycardia (CPVT). Ischaemia in these patients and perhaps the ICD shock itself through the stress mediated increase in catecholamine levels might contribute in reported cases of defibrillation failure (19–21). Patients diagnosed with CPVT should be treated adequately prior to any exercise testing or sport activity engagement. Full contact sports such as martial arts, rugby, American football, or shooting are still considered contraindications for ICD implantation.

It is important to individualise patient care and take into account the very different social and legal environments of particular countries (25). There is a substantial difference in risk management between Europe and the United States of America (26). This will continue to play a major role in the approach for implantable cardioverter-defibrillator recipients especially in the group of competitive sport and intensive non-competitive sport participants.

CONCLUSION

The majority of current recommendations regarding sports participation in ICD therapy recipients are based on expert opinion rather on the clinical trials. An increasing number of ICD recipients consider sport activity essential for their well-being and will not change their life style. This fuels the need for more clinical research together with a change in current guidelines (14–16).

Conflict of Interest
None declared

REFERENCES

1. Moss AJ, Zareba W, Hall WJ, Klein H, Wilber DJ, Cannom DS, et al.; Multicenter Automatic Defibrillator Implantation Trial II Investigators. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. N Engl J Med. 2002 Mar 21;346(12):877-83.
2. Bardy GH, Lee KL, Mark DB, Poole JE, Packer DL, Boineau R, et al.; Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) Investigators.

Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. N Engl J Med. 2005 Jan 20;352(3):225-37.

3. Buxton AE, Lee KL, DiCarlo L, Gold MR, Greer GS, Prystowsky EN, et al.; Multicenter Unsustained Tachycardia Trial Investigators. Electrophysiologic testing to identify patients with coronary artery disease who are at risk for sudden death. N Engl J Med. 2000 Jun 29;342(26):1937-45.

4. Moss AJ, Hall WJ, Cannom DS, Daubert JP, Higgins SL, Klein H, et al.; Multicenter Automatic Defibrillator Implantation Trial Investigators. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. N Engl J Med. 1996 Dec 26;335(26):1933-40.

5. The Antiarrhythmics versus Implantable Defibrillators (AVID) Investigators. A comparison of antiarrhythmic-drug therapy with implantable defibrillators in patients resuscitated from near-fatal ventricular arrhythmias. N Engl J Med. 1997 Nov 27;337(22):1576-83.

6. Kuck KH, Cappato R, Siebels J, Rüppel R. Randomized comparison of antiarrhythmic drug therapy with implantable defibrillators in patients resuscitated from cardiac arrest : the Cardiac Arrest Study Hamburg (CASH). Circulation. 2000 Aug 15;102(7):748-54.

7. Connolly SJ, Gent M, Roberts RS, Dorian P, Roy D, Sheldon RS, et al. Canadian implantable defibrillator study (CIDS) : a randomized trial of the implantable cardioverter defibrillator against amiodarone. Circulation. 2000 Mar 21;101(11):1297-302.

8. Moss AJ, Schuger C, Beck CA, Brown MW, Cannom DS, Daubert JP, et al.; MADIT-RIT Trial Investigators. Reduction in inappropriate therapy and mortality through ICD programming. N Engl J Med. 2012 Dec 13;367(24):2275-83.

9. Corrado D, Basso C, Rizzoli G, Schiavon M, Thiene G. Does sports activity enhance the risk of sudden death in adolescents and young adults? J Am Coll Cardiol. 2003 Dec 3;42(11):1959-63.

10. Albert CM, Mittleman MA, Chae CU, Lee IM, Hennekens CH, Manson JE. Triggering of sudden death from cardiac causes by vigorous exertion. N Engl J Med. 2000 Nov 9;343(19):1355-61.

11. Lombardi F, Malfatto G, Belloni A, Garimoldi M. Effects of sympathetic activation on ventricular ectopic beats in subjects with and without evidence of organic heart disease. Eur Heart J. 1987 Oct;8(10):1065-74.

12. James CA, Bhonsale A, Tichnell C, Murray B, Russell SD, Tandri H, et al. Exercise increases age-related penetrance and arrhythmic risk in arrhythmogenic right ventricular dysplasia/cardiomyopathy-associated desmosomal mutation carriers. J Am Coll Cardiol. 2013 Oct 1;62(14):1290-7.

13. Lampert R, Joska T, Burg MM, Batsford WP, McPherson CA, Jain D. Emotional and physical precipitants of ventricular arrhythmia. Circulation. 2002 Oct 1;106(14):1800-5.

14. Zipes DP, Ackerman MJ, Estes NA 3rd, Grant AO, Myerburg RJ, Van Hare G. Task Force 7: arrhythmias. J Am Coll Cardiol. 2005 Apr 19;45(8):1354-63.

15. Pelliccia A, Fagard R, Bjørnstad HH, Anastassakis A, Arbustini E, Assanelli D, et al.; Study Group of Sports Cardiology of the Working Group of Cardiac Rehabilitation and Exercise Physiology; Working Group of Myocardial and Pericardial Diseases of the European Society of Cardiology. Recommendations for competitive sports participation in athletes with cardiovascular disease: a consensus document from the Study Group of Sports Cardiology of the Working Group of Cardiac Rehabilitation and Exercise Physiology and the Working Group of Myocardial and Pericardial Diseases of the European Society of Cardiology. Eur Heart J. 2005 Jul;26(14):1422-45.

16. Heidbüchel H, Corrado D, Biffi A, Hoffmann E, Panhuyzen-Goedkoop N, Hoogsteen J, et al.; Study Group on Sports Cardiology of the European Association for Cardiovascular Prevention and Rehabilitation. Recommendations for participation in leisure-time physical activity and competitive sports of patients with arrhythmias and potentially arrhythmogenic conditions. Part II: ventricular arrhythmias, channelopathies and implantable defibrillators. Eur J Cardiovasc Prev Rehabil. 2006 Oct;13(5):676-86.

17. Lampert R, Cannom D, Olshansky B. Safety of sports participation in patients with implantable cardioverter defibrillators: a survey of heart rhythm society members. J Cardiovasc Electrophysiol. 2006 Jan;17(1):11-5.

18. Lampert R, Olshansky B, Heidbuchel H, Lawless C, Saarel E, Ackerman M, et al. Safety of sports for athletes with implantable cardioverter-defibrillators: results of a prospective, multinational registry. Circulation. 2013 May 21;127(20):2021-30.

19. Mohamed U, Gollob MH, Gow RM, Krahn AD. Sudden cardiac death despite an implantable cardioverter-defibrillator in a young female with catecholaminergic ventricular tachycardia. Heart Rhythm. 2006 Dec;3(12):1486-9.

20. Palanca V, Quesada A, Trigo A, Jiménez J. Arrhythmic storm induced by AICD discharge in a patient with catecholaminergic polymorphic ventricular tachycardia. Rev Esp Cardiol. 2006 Oct;59(10):1079-80. (In Spanish.)

21. Pizzale S, Gollob MH, Gow R, Birnie DH. Sudden death in a young man with catecholaminergic polymorphic ventricular tachycardia and paroxysmal atrial fibrillation. J Cardiovasc Electrophysiol. 2008 Dec;19(12):1319-21.

22. Kramer DB, Maisel WH. Guidelines for managing pacemaker and implantable defibrillator advisories. In: Ellenbogen KA, editor. Clinical cardiac pacing, defibrillation, and resynchronization therapy. 4th ed. Philadelphia, PA: Elsevier Saunders; 2011. p. 1028-39.

23. Deisenhofer I, Kolb C, Ndrepepa G, Schreieck J, Karch M, Schmieder S, et al. Do current dual chamber cardioverter defibrillators have advantages over conventional single chamber cardioverter defibrillators in reducing inappropriate therapies? A randomized, prospective study. J Cardiovasc Electrophysiol. 2001 Feb;12(2):134-42.

24. Sinha AM, Stellbrink C, Schuchert A, Mox B, Jordaens L, Lamaison D, et al.; Phylax AV Investigator Group. Clinical experience with a new detection algorithm for differentiation of supraventricular from ventricular tachycardia in a dual-chamber defibrillator. J Cardiovasc Electrophysiol. 2004 Jun;15(6):646-52.

25. Pelliccia A, Zipes DP, Maron BJ. Bethesda Conference #36 and the European Society of Cardiology Consensus Recommendations revisited a comparison of U.S. and European criteria for eligibility and disqualification of competitive athletes with cardiovascular abnormalities. J Am Coll Cardiol. 2008 Dec 9;52(24):1990-6.

26. Knapp v Northwestern University. 101 B3d (7th. Cir. 1996), cert. denied, 117 S. Ct. 2454 (1007).