HEART FAILURE AND TRANSPLANTATION

Journal Watch

September 2017

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REVIEW:

Declining Risk of Sudden Death in Heart Failure

Shen L, Jhund PS, Petrie MC, Claggett BL, Barlera S, Cleland JGF, Dargie HJ, Granger CB, Kjekshus J, Køber L, Latini R, Maggioni AP, Packer M, Pitt B, Solomon SD, Swedberg K, Tavazzi L, Wikstrand J, Zannad F, Zile MR, McMurray JJV. N Engl J Med 2017; 377:41-51

Sudden death is a common finding in patients with heart failure with reduced ejection fraction, because of the life threatening ventricular arrhythmias. Therefore, patients with heart failure and left ventricular ejection fraction of less than 35% and on optimal medical treatment, are eligible for implantable cardioverter defibrillators implantation in primary prevention. The current guidelines recommended the following medications for the treatment of heart failure with reduced ejection fraction: angiotensin-converting-enzyme inhibitors/angiotensin receptor blockers, beta blockers and mineralocorticoid-receptor antagonists, and these treatments were shown to reduce the risk of sudden death in heart failure population. Therefore, with the increased use of recommended medications, the risk of sudden death may have changed over time in the heart failure patients with reduced ejection fraction. The study recently published in NEJM aimed to investigate this trend in detail.
The authors analysed data from 40195 patients with symptomatic heart failure with reduced ejection fraction and who were enrolled in any of 12 randomized, controlled trials, in the time span between 1995 and 2014. Patients who had a cardioverter defibrillator at the moment of the inclusion into trials were excluded from the analysis. The authors used weighted multivariable regression to analyse trends in rates of sudden death over time. Cox regression models were applied to calculate adjusted hazard ratios for death in each trial. The cumulative incidence rates of sudden death were assessed at different time points after randomization and according to the length of time between the diagnosis of heart failure and randomization. The confounding effect of a number of baseline variables (age, sex, left ventricular ejection fraction, NYHA class, ischemic vs. non-ischemic, previous myocardial infarction, and history of hypertension or diabetes) on the sudden cardiac death was also adjusted.

Sudden death was reported in 3583 patients, and they were more frequently male, older, with ischemic cardiomyopathy, worse cardiac function, lower systolic blood pressure, higher heart rate, worse heart failure symptoms, and had more frequently a history of myocardial infarction, diabetes or renal dysfunction, in comparison with those in whom the sudden cardiac death did not occur. Across trials there was a 44% decline in the rate of sudden death (from 6.5% annual rate of sudden death in the earliest trial: RALES, to 3.3% in the most recent trial: PARADIGM-HF). The cumulative incidence of death at 90 days after randomization was 2.4% in the earliest trial and 1.0% in the most recent trial. The rate of death was not related to the time between the diagnosis of the heart failure and randomization in the trials.

This study has demonstrated that rate of sudden cardiac death declines substantially over time among ambulatory patients with heart failure with reduced ejection fraction who were enrolled in clinical trials. The authors explain it by a cumulative benefit of evidence-based medications on death. The authors further remark that decreased risk of death in the contemporary trials in patients with heart failure and reduced ejection fraction, suggests that it would be difficult to show a significant benefit of implantable cardioverter defibrillator implantation for primary prevention in most patients with heart failure with reduced ejection fraction in the modern era. They underline that new efforts should be made to identify a high-risk subgroup of heart failure patients, who would benefit from implantable cardioverter defibrillator and in whom it would be cost-effective. Well developed and validated prognostic models would be of great use for this purpose.

ADDITIONAL ARTICLES OF INTEREST:

1. Elming MB, Nielsen JC, Haarbo J, Videbæk L, Korup E, Signorovitch J, Olesen LL, Hildebrandt P, Steffensen FH, Bruun NE, Eiskjær H, Brandes A, Thøgersen AM, Gustafsson F, Egstrup K, Videbæk R, Hassager C, Svendsen JH, Høfsten DE, Torp-Pedersen C, Pehrson S, Køber L, Thune JJ. Age and Outcomes of Primary Prevention Implantable Cardioverter Defibrillators in Patients with Non-Ischemic Systolic Heart Failure. Circulation. 2017 Sep 6.

2. Friedman DJ, Al-Khatib SM, Zeitler EP, Han J, Bardy GH, Poole JE, Bigger JT, Buxton AE, Moss AJ, Lee KL, Steinman R, Dorian P, Cappato R, Kadish AH, Kudenchuk PJ, Mark DB, Inoue LYT, Sanders GD.New York Heart Association class and the survival benefit from primary prevention implantable cardioverter defibrillators: A pooled analysis of 4 randomized controlled trials. Am Heart J. 2017 Sep;191:21-29

3. Køber L, Thune JJ, Nielsen JC, Haarbo J, Videbæk L, Korup E, Jensen G, Hildebrandt P, Steffensen FH, Bruun NE, Eiskjær H, Brandes A, Thøgersen AM, Gustafsson F, Egstrup K, Videbæk R, Hassager C, Svendsen JH, Høfsten DE, Torp-Pedersen C, Pehrson S; DANISH Investigators. Defibrillator Implantation in Patients with Nonischemic Systolic Heart Failure. N Engl J Med. 2016 Sep 29;375(13):1221-30.