

Response to Letter Regarding Article, “Comparative Effectiveness of Implantable Cardioverter Defibrillators for Primary Prevention in Women”

Mareev and colleagues raise several important issues related to comparing findings from randomized clinical trials (RCTs) to observations from clinical practice cohorts as it relates to our recent article.¹ The effect size associated with implantable cardioverter defibrillator (ICD) therapy in our population was greater than that seen in RCTs, but this is not surprising. Indeed, our findings are consistent with other effect sizes associated with primary prevention ICDs in clinical practice cohorts.² There are reasons why effect sizes in RCTs may differ from those in less selected cohorts. In particular, RCT patients are known to be healthier and receive better overall care than patients in clinical practice, which can contribute to lower event rates and, thus, what might seem as less benefit from interventions. Furthermore, the large cohort and the longer follow-up period in our analysis provide greater power to detect differences. Another potential contributing factor is the selection bias related to offering an ICD to clinical practice patients who are most likely to benefit.

Mortality rates in our cohort were high, but in a previous analysis, when survival of clinical practice patients was compared with propensity score-matched patients from RCTs of primary prevention ICDs, it was not different even in patients ≥ 65 years old.³ In our study referenced by Mareev, we report a relative risk reduction associated with an ICD similar to that observed in Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT; hazard ratio 0.78 versus 0.77).⁴ However, when absolute risk is increased as in an older, sicker population like ours, absolute risk reductions are expected to be greater, despite similar relative risk reductions.

As was pointed out by Mareev et al and acknowledged in our article,¹ no statistical methods can adjust for all potential bias in an observational study. However, when questions about the effectiveness of interventions remain in important subgroups such as women, observational data may be informative.

Disclosures

Dr Fonarow report consulting from Medtronic. The other authors report no conflicts.

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References

1. Zeitler EP, Hellkamp AS, Schulte PJ, Fonarow GC, Hernandez AF, Peterson ED, Sanders GD, Yancy CW, Al-Khatib SM. Comparative effectiveness of implantable cardioverter defibrillators for primary prevention in women. *Circ Heart Fail*. 2016;9:e002630. doi: 10.1161/CIRCHEARTFAILURE.115.002630.
2. Khazanie P, Hellkamp AS, Fonarow GC, Bhatt DL, Masoudi FA, Anstrom KJ, Heidenreich PA, Yancy CW, Curtis LH, Hernandez AF, Peterson ED, Al-Khatib SM. Association between comorbidities and outcomes in heart failure patients with and without an implantable cardioverter-defibrillator for primary prevention. *J Am Heart Assoc*. 2015;4:e002061. doi: 10.1161/JAHA.115.002061.
3. Al-Khatib SM, Hellkamp A, Bardy GH, Hammill S, Hall WJ, Mark DB, Anstrom KJ, Curtis J, Al-Khalidi H, Curtis LH, Heidenreich P, Peterson ED, Sanders G, Clapp-Channing N, Lee KL, Moss AJ. Survival of patients receiving a primary prevention implantable cardioverter-defibrillator in clinical practice vs clinical trials. *JAMA*. 2013;309:55–62. doi: 10.1001/jama.2012.157182.
4. Bardy GH, Lee KL, Mark DB, Poole JE, Packer DL, Boineau R, Domanski M, Troutman C, Anderson J, Johnson G, McNulty SE, Clapp-Channing N, Davidson-Ray LD, Fraulo ES, Fishbein DP, Luceri RM, Ip JH; 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;352:225–237. doi: 10.1056/NEJMoa043399.

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