Time Dependence of Defibrillator Benefit Postcoronary Revascularization

In a recent issue of the Journal, Goldenberg et al. (1), in a subgroup analysis of MADIT-II (Multicenter Automatic Defibrillator Implantation Trial) (2), showed that in patients with ischemic left ventricular dysfunction who underwent coronary revascularization (CR), the efficacy of implantable cardioverter-defibrillator (ICD) therapy was not apparent when the device was implanted 6 months or less following CR. The authors concluded a time dependence of the ICD therapy efficacy and raised the question of the optimal timing of device implantation following CR. In our opinion, the issues raised by the study should instead focus on the reasons why the ICD benefit was only apparent when implanted after long time frames following revascularization.

In view of the elapsed time following CR by the time of patient enrollment, we can assume that the distinguishing feature between patients enrolled early and those enrolled late after CR resides in the probability of recurrent ischemia. This was moreover the rationale of the selected time frames based on the probability of coronary artery disease progression. Because several observations suggest a role for silent (or overt) ischemia as at least a contributing factor to sudden death (3,4), the lack of survival benefit of ICD therapy in the group characterized by a lower probability of ischemia may therefore be attributed to the prevention of recurrent ischemia by revascularization. This hypothesis is further substantiated by the CABG (Coronary Artery Bypass Graft)-Patch trial (5) where no survival benefit was conferred by prophylactic ICD in patients undergoing CABG with depressed left ventricular function.

Accordingly, this subgroup analysis (1) further confirms the importance of revascularization to lower the risk of sudden cardiac death. As it is reasonable to first treat the contributing factors rather than the consequences, a systematic evaluation of the coronary artery status with CR if required prior to prophylactic ICD implantation should be the conclusion to draw from this subset of the MADIT-II study. The investigators raised the question of the optimal timing of device implantation. However, considering time frames from up to and more than 5 years following CR, the “timing” for a significant life-saving benefit of ICD to become apparent also coincides with an increasing probability of progression of coronary artery lesions. We may then assume that a substantial proportion of patients in these time frames would actually have qualified for a coronary evaluation prior to ICD implantation.
The recruitment of patients with remote myocardial infarction and depressed left ventricular function without systematic coronary artery status evaluation was precisely one of the limitations raised by the MADIT-II study (6). Is it then appropriate to implement the MADIT-II in patients considered for prophylactic ICD after a coronary evaluation has been performed as warranted in clinical practice in light of the present observations? Indeed, Goldenberg et al. (1) observe that those patients who qualify for a revascularization procedure subsequently performed will not enjoy a significant survival benefit due to the ICD. Similarly, for those whom a revascularization procedure is not needed, hence without an ischemic substrate, the corollary of the study suggests that their risk of sudden death might be lower than expected and hence limit the detectable benefit of ICD.

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Reply

We agree with the suggestion of Drs. Pascale and Fromer that a coronary evaluation should be carried out in MADIT (Multicenter Automatic Defibrillator Implantation Trial)–II type patients with a history of remote myocardial infarction (MI) and depressed left ventricular dysfunction. This is also in agreement with current guidelines for the management of patients with heart failure, in which coronary angiography is recommended in patients who present with angina or significant ischemia (Class I) and to eligible asymptomatic heart failure patients with suspected coronary disease (Class IIa) (1). Our data, published in JACC, demonstrate that coronary revascularization (CR) by either coronary artery bypass graft surgery (CABG) or coronary angioplasty confers a significant reduction in the risk of sudden cardiac death (SCD) in this population (2). Furthermore, in the CABG-Patch trial (3) and in the current MADIT-II subgroup analysis (2), no implantable cardioverter-defibrillator (ICD) benefit was observed when the device was implanted at the time of elective CABG or in the immediate post-CR period.

Nevertheless, further studies are required to determine to what extent complete CR provides a long-term protective effect against SCD. In our analysis, the benefit conferred by CR was shown to be time-dependent, and was no longer evident six months after the revascularization procedure. Therefore, we continue to recommend primary ICD therapy in MADIT-II type patients because it is associated with a significant survival benefit in post-MI patients with left ventricular dysfunction (4). Coronary evaluation should be performed in eligible patients, and may be followed by complete or partial revascularization. However, our data suggest that defibrillator implantation may be deferred for only a limited time-period after CR in this high-risk population. In addition, Drs. Pascale’s and Fromer’s suggestion, namely that benefit of the ICD is limited in patients without an ischemic substrate, is not supported by findings from recent primary intervention trials (5,6).

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