Large randomized trials have demonstrated unequivocally that implantable cardioverter defibrillators (ICDs) improve outcome for individuals with defined clinical characteristics known to be associated with a high risk of ventricular arrhythmias. However, less is known about outcomes of patients receiving ICDs in the "real world." The National Cardiovascular Data Registry provides extensive and detailed clinical information about patients receiving ICDs at the time of implant, but does not include longitudinal data on mortality or shocks except in a small subset. Industry databases of ICD patients undergoing remote (transtelephonic) monitoring, which provide extensive information on therapies received, thus present a unique opportunity to fill this gap in knowledge.

In this issue of Circulation, Saxon et al describe data on 69,556 patients followed remotely (in addition to in-office) and 124,450 patients followed in-office alone, which was generated by the Altitude project, a prospectively designed database generated by a single ICD manufacturer to store data regarding patients receiving its devices. Survival data are obtained through cross-referencing with the Social Security death index, and data on treated arrhythmias are obtained from the transtelephonic transmissions. The authors use this database to answer four distinct questions: (1) whether remote monitoring impacts survival; (2) whether shocks are associated with mortality; (3) how survival compares among patients receiving ICDs, ICDs with cardiac resynchronization (CRT) capability (CRT-D), and CRT devices without defibrillation capability; and (4) how survival of "real-world" patients compares with that of patients enrolled in trials. The study is limited by lack of detailed information about the patients’ clinical characteristics. However, as the largest series by far of ICD patients with survival and shock data available, this study sheds interesting light on each of these questions from the 5000-foot view.

Most striking among the data presented, and also most novel, is the demonstrated higher survival in the patients followed remotely via the transtelephonic network, with a 50% relative reduction in mortality in the networked patients. The analysis is limited by the lack of detailed clinical data which would allow adjustment for any clinical differences between networked and non-networked patients that could potentially confound the results in this nonrandomized study. However, as a creative approach to this limitation, the investigators performed a sensitivity analysis, which showed that risk-factor burden would need to have been 5 times greater in the non-networked patients to confound the results, suggesting that the association between monitoring and survival is likely robust.

There are many potential routes by which remote monitoring could improve patient outcomes. More timely detection of both clinical and device-related issues may improve care, for example, by immediate notification of healthcare providers of new atrial fibrillation or changes in thoracic impedance indicating fluid status. The authors postulate that enhanced engagement by both patient and physician may be what underlies the improved outcomes, supported by the fact that the patients with highest survival were those also recording weight and blood pressure. However, because the use of remote monitoring was self-selected by both physicians and patients, the possibility also exists that use of monitoring may be a marker for an engaged, motivated physician and an engaged, motivated patient, whose outcomes are known to be better. Adherence even to placebo is associated with improved outcome, and it is possible that the improved mortality in those in compliance with remote monitoring may be an example of the "healthy adherer effect." Several prior small studies have evaluated the benefits of remote monitoring with overall promising results. In general, surveys reveal that patients prefer home to in-office monitoring, and that physicians find the systems user-friendly. The recently published TRUST trial (Lumos-T Safely Reduces Routine Office Device Follow-Up) randomized 1339 patients to receive home monitoring with a continuous-monitoring system with event-notification capability versus conventional in-office follow-up. Remote monitoring reduced the total number of in-person evaluations, improved adherence, and resulted in more rapid evaluation of events with more rapid initiation of indicated therapeutic interventions such as medications or programming changes. There was no difference in survival or clinical outcomes between the groups. Another small randomized study also did not show a survival benefit with remote monitoring, although only intermittent transmissions were uploaded, rather than the continuous monitoring evaluated in Altitude.
one very small study suggested remote monitoring to be cost-effective,7 other studies have not.10 The ongoing CONNECT study (Clinical evaluation Of remote NotificatioN to rEduCe Time to clinical decision) 4 will randomize 2000 ICD patients to continuous remote monitoring with automatic transmission of diagnostic data versus in-office follow-up. Primary outcome is the time from clinical event to clinical decision-making with secondary outcomes of cardiovascular healthcare utilization, patient quality of life, and heart failure status. Like previous prior randomized studies, however, that study is not powered to detect differences in survival or other “hard” clinical outcomes. Only a larger, randomized study will determine whether the use of remote monitoring improves survival.

Another provocative contribution of this data is the finding that both appropriate and inappropriate shocks predict mortality, but shocks for nonrhythm-related reasons (oversensing) did not. Many studies, including MADIT 211 and SCD-HeFT,12 have shown an increase in mortality after both appropriate and inappropriate shocks. However, it is not easy to tease apart cause and effect. Troponin increases after shock,13 and postshock decreases in left ventricular function have also been reported,14 suggesting potential detrimental effects of shock on the myocardium. It is possible that shocks, appropriate or inappropriate, are a cause of poor outcome, due to direct adverse effects on the myocardium13 or activation of adverse signaling pathways as has been postulated.15 However, it is also possible that shocks could rather be a marker for clinical conditions associated with poor outcome, such as ventricular arrhythmia, atrial fibrillation,16 or sinus tachycardia.17 One study suggested shock-treated but not ATP-treated fast ventricular tachycardia events were associated with mortality, although the effects of arrhythmia versus of the shock itself were difficult to differentiate.15 A previous single-center study showed that patients who receive shocks for noninvasive defibrillation threshold testing but had never received spontaneous shocks did not have an increase in mortality, suggesting that spontaneous shocks may be a marker of underlying conditions carrying poor prognosis, rather than being causative.18 In the Altitude study presented in this issue of Circulation, shocks for oversensing were not associated with mortality, although appropriate and overall inappropriate shocks were, also suggesting that shocks may be a marker rather than causative. The number of shocks for nonrhythm-related reasons in this report from Altitude was not high—133 shocks in 101 patients—but the finding that these shocks were not related to mortality suggests that the relationship between shocks and mortality may be due to the underlying rhythm, rather than due to damage from the shocks themselves. Additional reports from this project as data continue to accrue may shed more light on this question.

A final notable aspect of this study is the author list, which includes a combination of academic investigators known for their rigorous approach to data analysis and industry employees. Physician “relationships with industry” have come under increasing scrutiny, with calls to eliminate these relationships as potential sources of conflict of interest.19,20 Although some relationships may indeed create conflict, this fruitful collaboration exemplifies the type of high-integrity relationship in which the complementary expertise of academics and industry employees, working together, can forward scientific knowledge and quality of care for patients.

Disclosures

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References


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