Federal Coordinating Council on Comparative Effectiveness Research
Submission for Consideration

Sudden Cardiac Arrest

Sudden Cardiac Arrest (SCA) is a leading cause of mortality in the US, accounting for an estimated 325,000 deaths each year – more than stroke, lung cancer and breast cancer combined.[1,2] Out-of-hospital survival is 5%, making prediction and prevention critically important.[1,2]

Prophylactic ICD Therapy for SCA

In the last several years, indications for ICD therapy have expanded significantly to include prophylactic implantation in patients identified to be at increased risk primarily on the basis of reduced ejection fraction (EF).[3,4] Recently, however, current guidelines for ICD implantation have been critically examined in terms of clinical benefit and cost-effectiveness.[5] Because the majority of patients who receive an ICD never receive therapy from the device, the criteria used to select candidates has been questioned.

While reduced EF is associated with higher mortality, it is not a specific marker of arrhythmic risk.[6] Moreover, although low EF identifies a group with relatively increased risk, the substantial majority of SCAs occur in patients with more preserved EF, highlighting the limited sensitivity of this stratification method.[7]

Concerns about surgical risks of ICD implantation, inappropriate shocks, quality of life and device reliability are additional parameters that can lead physicians and patients to question the need for such an intervention.[8,9] Recent studies show that many at-risk patients, particularly women and minorities, are often not referred for evaluation or do not receive appropriate therapy.[10]

Clinical Benefits of Risk Stratification

Focused risk stratification paradigms that more accurately identify at-risk individuals can be used to guide ICD therapy to the most appropriate patients, thereby improving the therapeutic efficacy and cost-effectiveness of ICDs. Directing ICD therapy to those at highest risk protects low-risk patients from the inherent morbidity and mortality associated with implantation, and will likely bolster overall acceptance of the therapy.

Microvolt T Wave Alternans (MTWA) testing is a non-invasive tool that can be used in conjunction with other clinical factors to help physicians more accurately assess arrhythmic vulnerability. It may improve SCA risk stratification protocols by providing an additional piece of objective information.

Microvolt T Wave Alternans

MTWA refers to a subtle beat-to-beat fluctuation in the T-wave segment of the electrocardiogram. It is a specific, non-invasive marker of arrhythmic vulnerability and SCA risk.

Several large-scale studies have confirmed the predictive value of MTWA in various patient groups including those with left ventricular dysfunction, ischemic cardiomyopathy, non-ischemic cardiomyopathy and history of myocardial infarction.[11-15] Most recently, a meta-analysis of 13 studies (~6,000 pts) showed that patients with an abnormal MTWA result are 13.6 times more

likely to experience SCA than those with a normal test result.[16] This analysis also concluded that a negative MTWA test confers an extremely low annual risk of experiencing SCA (0.3%).

The ACC/AHA/ESC guidelines for Management of Patients with Ventricular Arrhythmias and Prevention of Sudden Cardiac Death state that it is reasonable to use MTWA testing to improve the diagnosis and risk stratification for those who are at risk of developing life-threatening ventricular arrhythmias (Class IIa).[17] MTWA testing is reimbursed by Medicare and several private payers when the analytic spectral method is used.

Improving the Therapeutic Efficacy of ICD Therapy

In a study of 768 patients with ischemic cardiomyopathy, Chow et sought to determine the value of ICD therapy in patients with negative and non-negative MTWA tests.[18] Results showed that ICD therapy was associated with a 55% relative reduction in mortality in patients with a non-negative MTWA test ($p = 0.0003$).[18] In contrast, ICD therapy had no significant effect on mortality in patients who tested MTWA negative. The authors concluded that MTWA may be an effective risk stratification tool in identifying patients most and least likely to benefit from ICD therapy, with potential policy implications for ICD coverage.

Recently, Chan et al extended this analysis to an expanded cohort of 965 primary prevention patients and found that MTWA was the only one of fourteen pre-defined clinical variables able to distinguish a high-risk group who benefited from ICD therapy from a low-risk group who did not ($p=0.02$).[19] An MTWA-directed approach toward ICD implantation has also been shown to be significantly more cost-effective.[19,20]

Interventional Trials

Multiple observational studies of MTWA have demonstrated its prognostic value. However, it has been suggested that to broaden the utility of any risk stratification tool, it is critical to have studies that address whether intervention based on that tool reduces the incidence of SCA.[7] In this regard, an interventional trial that evaluates ICD therapy based on MTWA status would greatly improve the current knowledge base and potentially result in a more refined risk stratification paradigm for SCA in the primary prevention population.

We propose that federal funding be provided to conduct a trial that assesses the impact of non-invasive risk stratification, specifically MTWA, on the effectiveness of ICD therapy for primary prevention of SCA.

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