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Sudden Death Risk in Type 2 Diabetic patients Post Myocardial Infarction: A “Sweet” Opportunity?

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Sudden cardiac arrest is a leading cause of death in the U.S., with over 300,000 victims per year.¹ Although the prevalence of SCA has fallen in tandem with cardiovascular events in recent decades due to improved management of cardiovascular risk factors and modern therapy for myocardial infarction,^{2–3} an opposing trend is the dramatic epidemic of metabolic syndrome and diabetes mellitus. Combined, these conditions affect an estimated 7.8% of the US population (23.6 million individuals),^{4–6} raising the disturbing possibility that the incidence of cardiovascular mortality⁷ and SCA may again start to rise over time.

Diabetes mellitus confers equivalent risk to coronary artery disease for many major adverse cardiac events⁸, yet its specific risk for SCA is not clear. SCA is the presenting feature in up to 1/3 of coronary disease patients,⁹ with an incidence of 1.2% in the first 30 days after an MI, rising to 3% and 7% at one and five years, respectively.^{10–11} However, it is unclear if diabetes alters the incidence of SCA^{12–13} due to mechanisms including autonomic dysfunction, altered cardiac repolarization or cardiomyopathy that may be distinct from the contributions of coronary disease.¹² Current guidelines for managing SCA risk in diabetics acknowledge their increased risk, but fall short of specifying guidelines due to lack of data. The data on whether diabetics suffer a higher incidence of SCA than non-diabetics are mixed, potentially because study populations have differed in their extent of documented coronary disease and length of follow-up.¹²

In this issue of *HeartRhythm*, Junttila et al¹⁴ compared the incidence and time course of post-MI SCA between Type 2 diabetics and non-diabetics in 3276 post-MI patients accrued in 2 prospective observational studies (MRFAT and ISAR- Risk). MRFAT studied the predictive value of various non-invasive arrhythmia markers for SCA in 700 consecutive MI survivors, of whom 19% were diabetic by WHO criteria.¹⁵ Over 5 years of followup, the incidence of SCA was 3.2% and the incidence of non-sudden cardiac death was 5.5%. ISAR-Risk enrolled 2343 MI survivors to study the predictive value of ECG indices of autonomic function for cardiac mortality.¹⁶ In 5 years of followup, the total mortality rate was 7.7%.

The authors found that the incidence of SCA (5.9% vs. 1.7%), non-sudden cardiac death (7.2% vs. 2.8%) and all-cause mortality (21% vs. 8.4%) were higher in diabetics than non-diabetics. In patients with preserved LV function, diabetics had higher rates of SCA and non sudden cardiac death than non-diabetics. However, the impact of impaired LVEF was additive. Accordingly, highest SCA incidence was observed in diabetics with LVEF<35%, lowest

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incidence in non-diabetics with preserved LVEF, and intermediate incidence in other groups. Notably, diabetics with preserved LVEF had a similar risk of SCA to non-diabetics with reduced LVEF (<35%). In addition, SCA occurred sooner post-MI in diabetics than non-diabetics. The incidence of non-sudden cardiac death was lower in diabetics with preserved LV function than non-diabetics with reduced LV function.

These results are particularly sobering in context of the twin epidemics of diabetes and metabolic syndrome, and the authors should be congratulated for dissecting out the relationship of diabetes to post-MI SCA risk. Nevertheless, the study must be interpreted with some caveats. For instance, its results were likely skewed by the higher risk profile of diabetic compared to non-diabetic patients. Diabetics were older, with a higher incidence of hypertension, numbers of prior MI, multi-vessel disease and lower LVEF than non-diabetics. On the other hand, the protean manifestations of diabetes may make it difficult to separate from these ‘comorbidities.’ The retrospective study design makes it difficult to ascertain whether the cohorts diverged further over time. For instance, functional heart failure status was similar between groups at baseline, yet diabetics are more likely to develop heart failure than non-diabetics,^{17–18} and intercurrent heart failure is more predictive than ischemia for SCA.⁹ The authors were similarly unable to evaluate the time-dependent contribution of altering LV function, MI and renal function between cohorts. Future prospective studies could address these areas, as well as the important issue of whether good glycemic control and lower HbA1c in diabetics reduces their SCA risk – as reported by Jouven et al.¹⁹

Most SCA victims currently have preserved LV function^{1,2}, and results of this study suggest that the growing diabetic population may further exaggerate this trend. Given our relative inability to predict SCA risk in patients with preserved LVEF²⁰, further studies on the mechanisms and risk factors for SCA in diabetics are clearly of critical importance. The authors report evidence of reduced heart rate variability and elevated heart rates, both markers of pro-arrhythmic autonomic dysfunction^{21–22} in diabetics compared to non-diabetics. However, reduced HRV did not predict SCA in diabetics, unlike prior mixed populations²³. Although heart rate turbulence was measured in the ISAR-Risk study, the authors did not report its predictive value for SCA in diabetics compared to non-diabetics. T-wave alternans predicts risk for SCA in many populations²⁴ and, if studied in patients with appropriate glycemic control, may have predictive value in diabetics.^{25–26}

In summary, Junttila et al.¹⁴ provide compelling data that MI survivors with type 2 diabetes mellitus are at substantially higher risk of SCA than non diabetics, and that the magnitude of risk conferred by diabetes may rival that of LV dysfunction. These issues warrant a large scale prospective study in diabetics, to better define their risk for SCA and non-sudden cardiac death, identify potential mechanisms for and modes of SCA, and thus identify risk stratifiers for these endpoints. Identifying new candidates for potentially lifesaving ICD therapy and revising current guidelines would be “sweet” indeed.

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