Postinfarct Ventricular Arrhythmias
Should We Calm the Renal Nerves?

Jacob S. Koruth, MD; Srinivas R. Dukkipati, MD

The risk of sudden death from ventricular arrhythmias (VAs) in the early post–myocardial infarction period is well appreciated by clinicians who are often faced with varying degrees of uncertainty when it comes to assessing arrhythmic risk in their patients.[1] Effectively reducing this risk, therefore, has important clinical implications. In this issue of *Circulation: Cardiovascular Interventions*, we are directed by Jackson et al[2] to look once again in the direction of renal arterial denervation (RDN) as an approach to addressing this risk. Modulating the sympathetic nervous system to reduce cardiac dysrhythmias is well supported by several preclinical and clinical reports.[3–7] Cervical sympathectomy, for example, is one such modality that has been effectively used in the treatment of refractory VAs in certain clinical situations.[7] However, the pursuit of RDN for its antiarrhythmic properties has waned over the recent years in light of the negative SYMPLICITY HTN-3 trial (Renal Denervation in Patients With Uncontrolled Hypertension).[8]

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In the present study, the authors present a preclinical, randomized controlled experiment with a sham arm that examines RDNs effect on VAs in a swine infarct model. Infarcts were created by occluding the mid left anterior descending artery for only 45 minutes, resulting in infarcts that were relatively small (mean left ventricular ejection fraction of 55%). All animals were implanted with transvenous implantable cardioverter-defibrillators, and at 2 weeks after infarction, catheter-based RDN or a sham procedure was performed. Subsequently, animals were survived for another week at which point inducibility for VAs was assessed by electrophysiological study. Using implantable cardioverter defibrillator counters, the authors demonstrated that RDN resulted in a 100% reduction in spontaneous VAs in the RDN group and a 75% increase in the control group. However, the degree of appropriate shock reduction seen with RDN did not reach statistical significance compared with the sham group. Importantly, there was no impact on inducible VAs at the time of electrophysiology study. The method used for denervation in this study, catheter-based multielectrode radiofrequency ablation, was appropriately assessed for efficacy. The authors demonstrate reduced renal arterial wall neurofilament scores supporting effective radiofrequency lesion formation in the arterial wall and also provide us with evidence of how this affects the infarcted myocardium. They elegantly demonstrate reduced myocardial sympathetic nerve staining and reduced neuropeptide-Y expression in the infarcted myocardium of the RDN group.

RDN has been previously shown to have antiarrhythmic effects on the ventricles in the setting of acute cardiac ischemia in preclinical studies.[9,10] Jackson et al[2] now provide additional evidence of its antiarrhythmic effects and demonstrate that RDN can be effective in the early post–myocardial infarction period (<1 month) also. This study provides important insights into possible mechanisms that mediate reduction in VA via RDN. On the basis of the findings of this study, the predominant benefit of RDN seems to be through cardiac sympathetic nerve modulation of VAs related to abnormal automaticity and triggered activity, which are seen early post-infarct, rather than scar-related reentry, which tend to occur months to years after. This is supported by the observed reduction in spontaneous, but not induced, VAs in the RDN group. The lack of effect of RDN on inducible VAs in their study is consistent with findings from our group. We demonstrated in a randomized controlled porcine experiment using an ischemic cardiomyopathy model that VA inducibility at 60 days after infarction was not different between RDN (surgically performed) and sham groups.[11]

Overall, the findings of this study are noteworthy, particularly from a mechanistic standpoint, and the authors are to be commended for their efforts. However, the answer to the clinically relevant question of RDN's appropriateness in the postinfarct period as an antiarrhythmic is still unclear and to be answered. The relatively small infarcts, limited survival time (<1 month), and selective impact on spontaneous VAs are important factors to consider when attempting to extrapolate the results to a broader clinical population of post–myocardial infarction patients. Of note, the authors discuss that the antiarrhythmic effect of RDN could be equivalent to that of β-blockers as was shown by Linz et al[9] and then contend that RDN has the advantage of being a single intervention with cardiac effects that comes without the issues of per-oral drugs such as cost, compliance, etc. Although this argument may be thought provoking, these statements are not supported by the presented data and do not take into account procedure-related complications such as renal artery stenosis that has been previously reported with RDN. The present study is a small preclinical study with limited follow-up (1 week post RDN) and lacks a comparative β-blocker group. Further studies assessing RDN's effectiveness for longer timelines and in

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Disclosures

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KEY WORDS: Editorials ■ animal ■ arm ■ cardiomyopathy ■ infarction ■ tachycardia, ventricular

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