Letter Regarding Article by Koller et al, "Altered Dynamics of Action Potential Restitution and Alternans in Humans With Structural Heart Disease"

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Circulation 2006;113;e462
DOI: 10.1161/CIRCULATIONAHA.105.597310
Circulation is published by the American Heart Association. 7272 Greenville Avenue, Dallas, TX 72514
 Print ISSN: 0009-7322. Online ISSN: 1524-4539

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To the Editor:

In their recent publication, Koller and colleagues[1] found that the dynamic pacing protocol yielded significant differences in restitution kinetics between patients with and patients without structural heart disease, but no significant difference was observed using the S_2 pacing protocol. The authors speculated that the dynamic protocol may improve the predictive value of electrophysiological testing for ventricular fibrillation (VF) (p1546).

However, their dynamic pacing cycle length was not shortened to <250 ms for ethical reasons, and repolarization data were obtained from a single ventricular pacing site. Thus, the kinetics of dynamic restitution remained undetermined at diastolic intervals between 0 and approximately 50 ms, as well as at other ventricular sites. In another study in which dynamic pacing cycle length was reduced to 200 ms, a good correlation between dynamic and S_2 restitution characteristics at 2 ventricular sites was found.[2]

If the current hypothesis of VF[3] were to be tested in the human ventricle, the pacing technique should allow restitution kinetics measurement at very short diastolic intervals where conduction velocity restitution may also be engaged. The S_2 protocol could allow determination of electrical restitution at short diastolic intervals in vivo without the risk of inducing recurrent VF. In this regard, the study of restitution characteristics with the use of the S_2 protocol combined with 3-dimensional ventricular mapping[4,5] may have a role in advancing the understanding of VF mechanisms in humans.

Disclosures

Dr Yue has previously received research grants from St Jude Medical and Endocardial Solutions.

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Response

Dr Yue correctly points to an important limitation of the dynamic restitution protocol in human electrophysiological studies. Because the maximum pacing rate must be limited in vivo to avoid the risk of inducing recurrent ventricular fibrillation (VF), the kinetics of the dynamic restitution function cannot be determined directly at diastolic intervals (DIs) between 0 (or even negative DI values) and approximately 50 ms. He suggests that an S_2 protocol allows determination of electrical restitution at short DIs in humans without the risk of inducing recurrent VF. As we have shown in our previous in vitro experiments,[1] however, the S_2 restitution function may not adequately represent action potential duration (APD) dynamics at high heart rates. In particular, we found that the slope of the S_2 restitution curve was <1 in isolated Purkinje and endocardial muscle fibers, a finding that would preclude the occurrence of APD alternans at rapid heart rates. In concordance with our in vitro experiments, we found in our current study[2] that the slope of the dynamic restitution function is higher than the slope of the S_2 restitution function in human ventricular myocardium. More importantly, we did not find significant differences in S_2 restitution kinetics between patients with and those without structural heart disease, whereas there was a clear divergence of the dynamic restitution relations at short DI between the 2 patient groups. Taken together, these findings suggest that a dynamic restitution protocol more closely represents APD dynamics at high heart rates than a standard S_1S_2 protocol in the patient populations we studied. In addition, the dynamic protocol provides information regarding APD alternans magnitude and the range of DIs over which alternans occurs that cannot be obtained directly from the S_1S_2 protocol. Further studies in other patient populations are needed to determine whether these features of restitution are consistent across groups and to resolve the apparent differences between our results and those of Pak et al.[3]

Finally, we agree with Dr Yue that information on APD and conduction velocity restitution parameters combined with 3-dimensional ventricular mapping techniques may help to further elucidate the mechanisms leading to wave front destabilization as the initiating event for VF in human myocardium.

Disclosures

None.

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