To the Editor:

The recent article by Medina-Ravell et al1 addresses a potentially harmful effect of cardiac resynchronization therapy on ventricular repolarization. The authors found that single epicardial and biventricular pacing in patients with congestive heart failure increased the QT interval and the transmural dispersion of repolarization (interval from the peak to the end of the T wave, Tpeak-end). However, probably as a result of the ECG signal quality (the authors did not provide any details about ECG registration and analysis), Tpeak-end was not estimated at baseline and during biventricular pacing. We think that this information is of great importance.

In a preliminary study of our cohort of patients with congestive heart failure, we assessed ventricular repolarization with a high-resolution 65-lead surface ECG.2 Using signal-processing techniques, such as the total 65-lead root mean square curves,3,4 even low-amplitude signals (eg, onset and offset of the P wave4) can be precisely determined. With respect to the QT duration, our findings are in accordance with those of Medina-Ravell et al1; any pacing increases QTc. However, with respect to the Tpeak-end interval, we observed a significant decrease after biventricular pacing, as compared with baseline (baseline 100%, biventricular pacing 86±17% [P<0.05], right ventricular pacing 115±19%, left ventricular pacing 105±13%).

We fully agree that the epicardial-endocardial spread of activation during biventricular pacing may be a potential risk in a subset of these quite sick patients and that risk stratification is important. However, with respect to the presented QRST analysis, further refinements in methodology in addition to the correlation with the excellent animal experiment, especially assessment of Tpeak-end5 at baseline and during biventricular pacing, may be warranted.

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To the Editor:

In their recent article, Medina-Ravell et al1 investigated changes in QT interval and transmural dispersion of repolarization in surface ECG in patients after implantation of a resynchronization device under right, left, and biventricular stimulation. Pacing-site–dependent changes in a rabbit left ventricular wedge preparation were also examined.

On the basis of individual observations and supported by a surface ECG (Figure 4 of their article1), the authors suggest that epicardial pacing might lead to the development of torsade des pointes (TdP) in a subset of patients.

Critical review of Figure 4 in their article1 identifies a potentially different mechanism of TdP induction. None of the premature ventricular beats shown fulfill the definition of an R-on-T phenomenon according to the literature.2–4 Because of an unexplainable left ventricular asynchronous stimulation (VVO mode), left ventricular premature beats (almost the same morphology as left ventricular-paced beats) are upcoming, and the stimulus is delivered several times into the T wave (beats 46, 48, 50, and 54) before catching the vulnerable period of the premature ventricular beat following beat 55 and inducing TdP.

Although the manufacturer and the manner of programming of the cardiac resynchronization therapy devices of the 29 patients are not mentioned, it has to be assumed that biventricular pacemakers with separated right and left ventricular channels were used in this study. In these devices, only the right ventricular channel is used for sensing, whereas both are used for pacing. This may produce 2 phenomena. First, a left ventricular premature beat might be sensed too late to inhibit a left ventricular stimulus due to the propagation time from the left ventricle to the right ventricular lead. Second, the amplitude might be too low, resulting in undersensing. In both cases, TdP might be initiated by a stimulus in the T wave of the left ventricular premature beat. The interaction might be more complicated and unpredictable if 2 devices (biventricular pacemaker and implantable cardioverter defibrillator) are implanted in a patient, as mentioned in the case report.

In conclusion, caution must be exercised in transferring the interesting experimental data into clinical considerations or warnings. An analytical review of the device technology and programming is first required to judge every episode.

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Response

The comments provided by Butter and Schlegl and Roithinger et al in response to our recently published article1 are most welcome.

We believe that the premature ventricular beats in Figure 4 of our article1 fulfill the definition of an R-on-T phenomenon. The R-on-T phenomenon was first described by Smirk2 in 1949 as “R waves interrupting T waves.” Butter and Schlegl, themselves, cite one of the most commonly referenced papers on this issue by Engel et al.,3 in which the R-on-T phenomenon is defined as the superimposition of an ectopic beat on the T wave of a preceding
beat. In Figure 4 of our article,1 the premature ventricular beats with a coupling interval of \( \approx 530 \) to 540 ms clearly originate in the terminal portion of the T wave of the previous beats (QT interval=580 ms). The terminal limb of the T wave encompasses the vulnerable window representing the interval of time during which some ventricular myocytes are refractory, whereas others are not.4 Therefore, an impulse arriving during the terminal limb of the T wave (by definition R on T) could potentially initiate polymorphic ventricular tachycardia.

The second point raised by Butter and Schlegl is that the development of torsade de pointes (TdP) reported in our article may be due to a sensing problem. The multiple episodes of TdP shown in Figure 3 were initiated by properly sensed ectopic beats (as emphasized in the Figure 3 legend). In Figure 4A, the device was programmed in VOO mode. Although the possibility that stimuli delivered during the T wave of the ectopic beats could cause TdP cannot be absolutely excluded, the development of TdP in this particular case was most likely initiated by spontaneous ventricular ectopic beats. It is noteworthy that the ectopic beats only appeared during LV epicardial (Figure 4A) or biventricular pacing (Figure 4D) and were inhibited by RV endocardial pacing. Moreover, multiple episodes of nonsustained TdP in the same patient at the same office visit were observed during LV epicardial pacing with adequate sensing.

As noted by Roithinger et al, the \( T_{\text{peak-end}} \) interval at baseline and during biventricular pacing was not reported in our article.1 We pointed out in the Methods section that it was not feasible to measure the \( T_{\text{peak-end}} \) interval because of T-wave flattening at baseline and during biventricular pacing. In addition, measuring the \( T_{\text{peak-end}} \) interval during biventricular pacing may not yield reliable information regarding transmural dispersion of repolarization. The combined repolarization vectors encountered during biventricular pacing could lead to collision of these repolarization wavefronts that would render the \( T_{\text{peak-end}} \) interval invalid as an accurate index of transmural dispersion of repolarization. The

\[ T_{\text{peak-end}} \] interval encountered during epicardial pacing would be expected to provide a more reliable index. In the case presented in Figure 4 of our paper, the \( T_{\text{peak-end}} \) increased from 92 to 133 ms when pacing was switched from RV endocardial to LV epicardial pacing. We wholeheartedly agree with Roithinger et al that further QRST analysis, including measurement of the \( T_{\text{peak-end}} \) intervals during RV and LV pacing, may prove helpful in assessing the impact of biventricular pacing in individual patients.

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Effect of Epicardial or Biventricular Pacing to Prolong QT Interval and Increase Transmural Dispersion of Repolarization
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