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Intraoperative High-Density Global Mapping in Adult-Repaired Tetralogy of Fallot

Altered Left Ventricular and Right Ventricular Activation and Implications for Resynchronization Strategies

To the Editor: Activation delay due to right bundle branch block (RBBB) has been implicated in the pathogenesis of right ventricular (RV) dilation and dysfunction in patients with tetralogy of Fallot (ToF) (1). Accordingly, it has been proposed that RV apical pacing may improve RV function on the basis of resynchronizing late activated segments (2). Late manifesting left ventricular (LV) dysfunction, correlative with RV impairment, is associated with adverse outcomes in this population (3,4). Multiple mechanisms may contribute to late manifesting LV dysfunction, including the impact of early cyanosis on the LV myocardium, the effects of both palliative shunts and cardiopulmonary bypass surgery on the LV, residual shunts and valve lesions, and the effects of the RV on the LV (RV–LV interaction). Against this background, understanding the electrical activation pattern in adult-repaired ToF is critical to determining optimal treatment. As such, and using high-density intraoperative mapping, we evaluated electrical activation delays in the various regions of both the RV and LV in adults with repaired ToF and RBBB and compared these delays with those in a control group of patients with ischemic cardiomyopathy and left bundle branch block (LBBB).

Between 1995 and 2008, 15 patients (mean age 37 ± 9 years; 9 men) with repaired ToF underwent intraoperative mapping for ventricular tachycardia during redo pulmonary valve replacement surgery. A comparison group of 4 patients (mean age 59 ± 5 years; 1 man) with ischemic cardiomyopathy, severe LV dysfunction, and LBBB undergoing intraoperative ventricular tachycardia mapping served as control subjects for assessing LV epicardial activation delay. This study was approved by the University Health Network Ethics Review Board.

In this study, both an endocardial balloon electrode array and epicardial electrode mesh (sock) were used and have been described previously (5). During the recording process, simultaneous unipolar and bipolar electrograms were recorded from all electrodes overlying the RV and LV. Activation mapping was conducted manually, and activation time was measured during sinus rhythm using the onset of surface QRS as a reference point. Total activation time was defined as the first to last activation seen. RV balloon array electrodes were divided into 4 regions (right ventricular outflow tract [RVOT], free wall, septum, and apex) on the basis of their anatomical position of contact. The sock electrodes were assigned to either of 2 regions, the LV or RV, again on the basis of anatomical location. LV activation times were compared with those in the control group of patients with ischemic cardiomyopathy. To relate electrical activation delays to electrical substrate, we constructed myocardial substrate (scar) maps using standard bipolar voltage categories: 1) healthy tissue (>0.5 mV); 2) scar tissue (<0.25 mV); and 3) areas of abnormal myocardium ($0.25 < x < 0.5$ mV).

Activation times (mean ± SD) for the RV in the patients with ToF were 165 ± 10 ms in the RVOT, 132 ± 6 ms in the free wall, 126 ± 5 ms in the apex, and 121 ± 9 ms in the septum. The mean total activation time for all patients was 169 ± 8 ms. The RVOT was latest in 73% of patients (11 of 15) followed by the septum in 13% (2 of 15), and the apex and RV free wall were each individually late in only 1 patient. When the RVOT was the latest activating segment (n = 11), the apex was earlier than the RVOT by an average of 49 ± 7 ms ($p < 0.001$). The region with the greatest delay varied from patient to patient, but the RV apex and/or free wall was rarely the site of latest activation.

In the LV (Fig. 1), epicardial activation time was similar compared with the RV epicardium (156 ± 7 ms vs. 122 ± 14 ms, $p = 0.102$) and was not significantly different from the right endocardial mean total activation time (169 ± 8 ms, $p = 0.268$). LV epicardial activation delay in the patients with ToF and RBBB was comparable with that observed in the control patients with severe ischemic cardiomyopathy and LBBB (156 ± 7 ms and 165 ± 19 ms, respectively, $p = 0.660$), although a greater range was seen within the ischemic cardiomyopathy group. Areas of RV endocardial activation delay were not bound by areas of scar. The areas of endocardial scar were localized predominantly to the basal aspects of the free wall, RVOT (inclusive with the infundibulum), and septum, corresponding to the transannular and RV patch. In all patients with ToF, delayed LV epicardial regions were demarcated by low-voltage substrate. The majority of patients had electrocardiographic QRS duration (QRSd) >120 ms. In all patients, correlation analysis was performed between QRSd and total activation time in the RV, RVOT activation, RV apex activation, and RV free wall activation. Pearson's correlations were $R^2 = 0.34$ ($p = 0.22$), $R^2 = 0.19$ ($p = 0.11$), $R^2 < 0.01$ ($p = 0.90$), and $R^2 = 0.06$ ($p = 0.40$), respectively, indicating no significant correlation between QRSd and total activation time.

In patients (n = 3) whose R-wave axes were negative (i.e., northeast), there was marked LV activation delay. Of the study patients, 9 had normal LV function (defined as ejection fraction ≥60%), and 6 had mild to moderate LV dysfunction (defined as any ejection fraction <60%). In contrast, both QRSd (166 ± 10 ms vs. 166 ± 8 ms, $p = 0.72$) and total activation delay (181 ±

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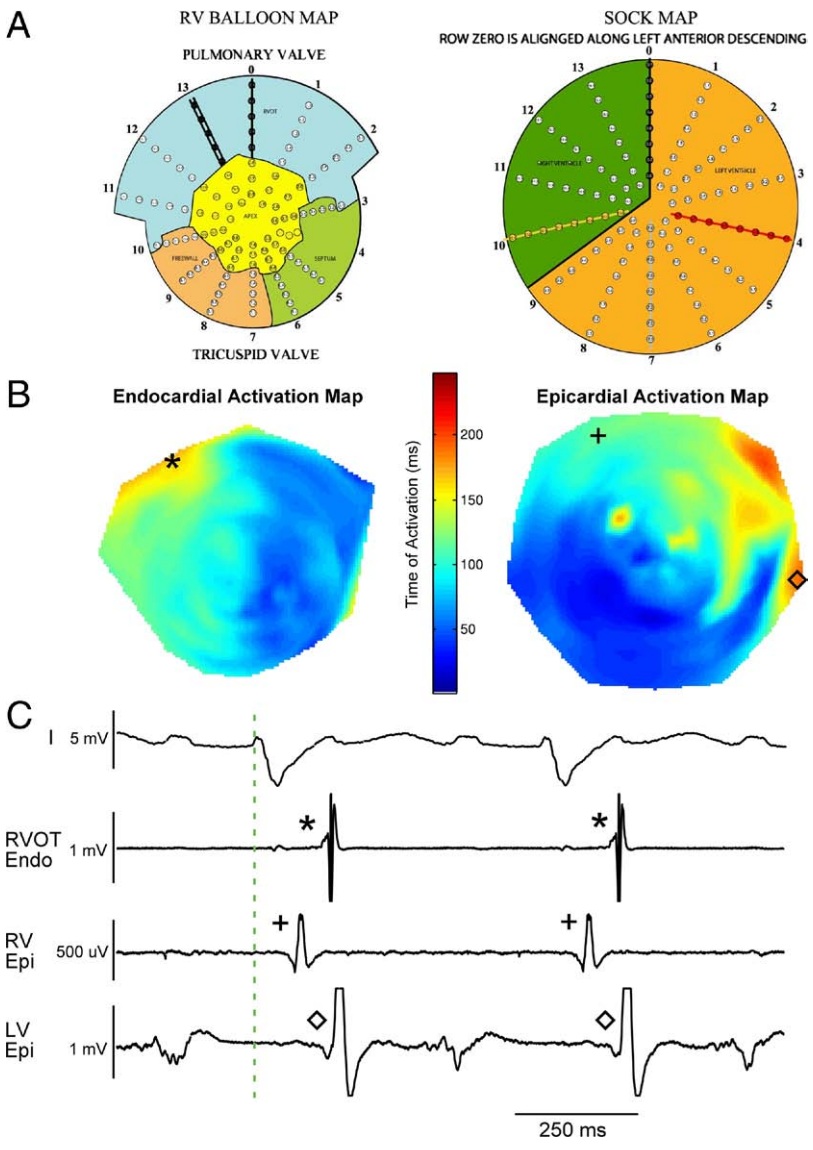

Figure 1 **Comparison of Endocardial and Epicardial Bipolar Activation Maps and Examples of Corresponding Electrograms**

(A) Each electrode array is made of 112 bipolar electrodes that serve as positions of contact with myocardium arranged in numbered rows. Each endocardial electrode consists of 2 silver beads (2 mm in diameter) separated 2.1 mm center to center. On the **left** is a 2-dimensional view of the unfurled right ventricular (RV) endocardial balloon array, and on the **right** is a 2-dimensional unfurled view of the epicardial sock array (**line through row 0** indicates site of the left anterior descending coronary artery, **color legend** indicates anatomical regions). **(B)** On the **left**, the RV endocardial activation map demonstrates the right ventricular outflow tract (RVOT) as the latest area to activate (**blue** indicates early activation, **red** indicates late activation). On the **right**, the epicardial activation map demonstrates that left ventricular (LV) activation was delayed compared with the RV. **(C)** Electrograms at locations of latest activation. From **top** to **bottom**, electrocardiographic lead I, latest RV endocardial electrode **(asterisks)**; latest RV epicardial electrode **(plus signs)**, and latest LV epicardial electrode **(diamonds)**.

9 ms vs. 162 ± 12 ms, p = 0.20) did not differentiate patients with abnormal LV function from those patients with normal LV function.

In this study of patients with adult-repaired ToF, in addition to RV activation delay, we have demonstrated previously unrecognized LV activation delays using high-density combined endocardial and epicardial mapping. The RVOT, not the RV apical region, appears the most delayed segment in the RV. LV epicardial activation was significantly delayed in all patients, even in the presence of RBBB, to a similar degree to that observed in patients with ischemic cardiomyopathy and LBBB. These LV epicardial delays appear to be explained by areas of low voltage, indicating abnormal substrate and conduction. These findings suggest that RV apical pacing alone may not be sufficient to rectify electrical delays in ToF and, further, underscore the importance of developing and refining alternative approaches to address activation delay in this population, especially that of the LV.

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