Published in final edited form as:

J Electrocardiol. 2013 ; 46(6): . doi:10.1016/j.jelectrocard.2013.05.005.

NONINVASIVE MAPPING OF VENTRICULAR ACTIVATION IN PATIENTS WITH TRANSPLANTED HEARTS

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Abstract

This is the first reported study of ventricular activation patterns after cardiac transplantation, using Electrocardiographic Imaging (ECGI), a noninvasive method for electrophysiologic mapping. This study of ten patients reveals that transplanted hearts have unique ventricular activation patterns in sinus rhythm, activating early in the epicardial aspect of the anterior or inferior septum, with intact right and left bundle branch conduction. They have late activation with slowing of conduction near the right ventricular (RV) basal free wall, causing a mild QRS prolongation and an rSr' pattern in lead V1 of the ECG. PVCs arise from both endocardial and epicardial locations in both ventricles.

Keywords

Electrocardiographic Imaging; ECGI; Cardiac Transplantation; Right Ventricle; Conduction; Premature ventricular complexes

BACKGROUND and METHODS

Transplanted hearts are electrophysiologically unique; they lack external innervation and have altered electrophysiologic substrate from graft ischemia during transplantation and from transplant vasculopathy. Invasive mapping data on the electrical activation in patients post cardiac transplantation are lacking and difficult to obtain. We therefore sought to study the ventricular activation patterns in transplanted hearts using Electrocardiographic Imaging (ECGI), which combines 256 ECGs with a non-contrast thoracic CT scan to noninvasively map the electrical activity on the hearts epicardial envelope [see ^(1,2,3) for details]. Initiation sites of focal activation have been shown to be localized with an accuracy of 6mm with ECGI⁽²⁾. Patients 3 months after cardiac transplantation were recruited, allowing time for

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Conflict of Interest: Y.R. co-chairs the scientific advisory board of and holds equity in CardioInsight Technologies, which does not support any of his research, including that presented here.

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sternal healing. We excluded patients in acute rejection due to the many complex electrophysiologic changes that occur in these hearts⁽⁴⁾. All protocols were approved by Washington University Human Research Protection Office and written informed consent was obtained from all patients.

RESULTS

Ten adults (7 males and 3 females), age 20-68, were studied at least 3 months post cardiac transplantation (median duration 7 ½ months), mapped during sinus rhythm (QRS duration 74-110 msec, average 90 msec). The donors were young, healthy males aged 18 to 54 (median age 28 years) who died from head trauma, drowning or stroke, with no prior cardiac history and normal echocardiograms. Exceptions were the donor for patient Tr8 who had LV ejection fraction (LVEF) of 35% that recovered to normal post transplant, and donor for patient Tr2 who had mild LVH but a normal LVEF. All donors had normal ECGs with QRS durations ranging from 71 to 90 msec (average 80 msec). The average QRS duration increased significantly from 80 msec in donor's prior to transplant, to 90 msec in recipients post transplant ($p=0.045$, two tailed paired t-test). Average graft ischemic time was 2hrs and 39min. Patients received either bicaval or caval-atrial anastomosis during surgery, thus having donor-recipient anastomotic lines in the atria or great vessels. There were no anastomotic lines in the ventricles that could affect conduction. **Echocardiograms post transplantation** were performed at a median time of 7 months post transplant. All patients had normal to low-normal LV systolic function, except patient Tr4 with mild global systolic dysfunction (LVEF 45%) due to a prior mild rejection episode, which had resolved 7 months prior to the study. The RV size and function were normal in 7 of 10 patients, but RV size was slightly dilated in 3 patients (Tr2, Tr8, Tr9). The RV filling pressures were normal in all patients, except patient Tr2 who was on Sildenafil therapy for pulmonary hypertension.

ECGI findings

1) Late activation of the RV basal free wall—9 of the 10 patients had late activation in a segment of the RV basal free wall with slowing of conduction in this region, as shown in FIGURE 1. Eight of these patients had an rSr' morphology in lead V1 of their ECG, reflecting this late activation. In 1 patient (Tr9) the late activation was not evident on the 12 lead ECG. In 1 patient (Tr4), latest activation was on the LV (basal inferior lateral region). There was no slowing of LV activation in any patients.

2) Early activation of the epicardial aspect of the Anterior and Inferior septum—As shown in FIGURE 1, four patients had earliest activation in the epicardial aspect of the anterior septum (Tr2, Tr4, Tr7, Tr9), while one patient (Tr10) had early activation in the septal RV outflow tract. The remaining five patients had abnormal earliest activation in the epicardial aspect of the inferior septum (Tr1, Tr3, Tr5, Tr6, Tr8), followed closely by activation of the epicardial aspect of the anterior septum. These five patients also had a left superior QRS axis on ECG, ranging from zero to minus 82 degrees, due to early activation of the inferior septum propagating in a left superior direction. There were minor differences in the earliest point of activation along the septum between patients.

3) Endocardial and Epicardial origin of ventricular premature beats—Four patients had monomorphic PVCs during ECGI (FIGURE 2). None had history of syncope or sustained VT. Based on ECGI derived electrogram morphology^(1,2), in 2 patients these PVCs were of endocardial origin (Tr1, Tr3), while 2 patients had epicardial origin of the PVCs (Tr9, Tr10).

DISCUSSION

Normal ventricular activation^(5,6) is characterized by earliest activation and epicardial breakthrough in the anterior paraseptal regions of the RV, with subsequent RV and LV activation, and latest activation in the LV base or RV outflow tract. This differs from the earliest ventricular activation in transplanted hearts which starts in the septum, either anteriorly (suggesting right bundle branch participation), inferiorly (suggesting left posterior fascicle participation) or in the septal RV outflow tract (suggesting right bundle branch participation). The large regions of simultaneous early activation of the epicardial aspects of the anterior and inferior septum suggest that the right bundle and left posterior fascicle are intact and functioning normally. Most transplant recipients display latest activation in the RV basal free wall post transplantation, producing an rSr' pattern in lead V1 of the ECG and prolonged QRS duration. Thus, post-transplantation, the activation sequence is different from that of intact (non-transplanted) normal hearts in specific ways. Delayed conduction in the RV base along with PVCs originating from various RV locations (despite normal RV filling pressures) point towards an altered RV substrate from surgical or thermal injury during transplantation, or from increased RV afterload immediately post transplant. This indicates increased susceptibility of the RV to injury from transplantation as compared to the LV that showed normal conduction in all cases. The PVCs originated from a wide range of endocardial and epicardial locations, including the LV and RV free walls and outflow tracts, which are not biopsy sites. These PVCs could be secondary to high circulating catecholamine levels, loss of parasympathetic tone to the heart, cardiac allograft vasculopathy or graft ischemia encountered during transplant surgery⁽⁷⁾.

Study Limitations

Being a pilot project, this observational study was conducted on a small number of patients using published normal controls^(5,6) for comparison. A larger study with matched controls paired with other imaging modalities is needed for definitive conclusions. This study does not serve to provide additional validation to that of previous studies on ECGI.

Acknowledgments

FUNDING: Y.R. is the Fred Saigh Distinguished Professor at Washington University in St Louis. This study was supported by Grants 1UL1 RR024992-01, 1TL1 RR024995-01 and 1KL2 RR 024994-01 from the National Center for Research Resources (NCRR) of the NIH.

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FIGURE 1. Activation sequences of transplanted hearts in native sinus rhythm

All patients show fast LV conduction and latest activation in the basal RV free wall with slow conduction in the RV. The asterisks show the sites of earliest epicardial activation. The dark grey regions depict the Pulmonary Artery (PA), which is presumed to be electrically silent. A. Early activation of the epicardial aspect of the inferior septum: Tr1, Tr8, Tr3 demonstrate abnormal earliest activation in the epicardial aspect of the inferior septum (light pink region) which collides with a second early activation wave front from the epicardial aspect of the anterior septum (dark pink), before spreading to the LV and basal RV. B. Early activation of the epicardial aspect of the anterior septum: Patients Tr7 and Tr9 show early activation in the epicardial aspect of the anterior septum, while pt. Tr10 shows early septal RVOT activation.

FIGURE 2. Activation maps show the site of origin (asterisk) and direction of propagation of PVCs

In Tr1 and Tr3, PVCs are of intramural origin (ECGI derived rS electrogram at the earliest epicardial activation site, indicating initial activation propagating towards that site^(1,2)). **Tr1** had monomorphic PVCs originating from the anterior RV free wall. **Tr3** had monomorphic PVCs originating from the anterior basal LV near the superior mitral valve annulus, with two regions of early epicardial activation appearing simultaneously (asterisks). This broad wavefront of early activation, in addition to the ECGI derived rS epicardial electrogram, indicates intramural origin of the PVC. There is fast activation of the LV with slow conduction along the septum causing late RV activation. In Tr9 and Tr10, PVCs are of epicardial origin (ECGI derived Q wave electrogram at the earliest epicardial activation site, indicating activation spreading away from that site^(1,2)). **Tr9** had monomorphic PVCs originating from the inferior-basal RV. The PVC activates the inferior wall, and then spreads to the apex and LV, with the RVOT activating last. **Tr10** had monomorphic PVCs originating from the outflow tract near the left coronary cusp. The 12 lead ECG determined PVC initiation site was consistent with the ECGI mapped initiation site for patients **Tr1** and **Tr3**, but there was minor disagreement in the initiation site for patients **Tr9** and **Tr10**, though these locations were not far apart. The 12 lead ECG localized the PVC initiation site to the inferior basal RV septum for **Tr9** and the RV outflow tract (free wall) for **Tr10**. Being on the heart surface, ECGI epicardial maps provide greater spatial resolution and accuracy for localizing initiation sites than the body surface ECG.