Electrophysiological Alterations After Mechanical Circulatory Support in Patients With Advanced Cardiac Failure

John D. Harding, BA; Valentino Piacentino III, BA; John P. Gaughan, PhD; Steven R. Houser, PhD; Kenneth B. Margulies, MD

Background—Recognizing that mechanical circulatory support with a left ventricular assist device (LVAD) induces changes in myocardial structure and contractile function, we examined whether there are changes in ventricular conduction and/or repolarization among failing human hearts after LVAD implantation.

Methods and Results—We examined 12-lead electrocardiograms before surgery, immediately after LVAD placement, and at a delayed (>1 week) postoperative time point in 23 patients who were receiving LVAD support for refractory heart failure. The immediate effects of hemodynamic unloading via LVAD placement included a decrease in QRS duration from 117 ± 6 to 103 ± 6 ms (P < 0.01), an increase in absolute QT duration from 359 ± 6 to 378 ± 8 ms (P < 0.05), and an increase in the heart rate–corrected QT interval (QTc) from 379 ± 10 to 504 ± 11 ms (P < 0.01). None of these immediate changes were observed among 22 patients undergoing routine coronary artery bypass grafting. With sustained cardiac unloading via LVAD support, there was a marked decrease in the QTc from 504 ± 11 to 445 ± 9 ms (P < 0.001). Studies in isolated cardiac myocytes, obtained at the time of transplantation, confirmed that delayed decreases in heart rate–adjusted QTc were the result of decreases in action potential duration after LVAD support.

Conclusions—Acute electrocardiogram responses to LVAD placement demonstrate the dependence of QRS and QT duration on load in the failing human heart. Delayed decreases in QTc and action potential duration reflect reversal of electrophysiologic remodeling in the failing heart. Shortening of the action potential duration likely contributes to the improved cellular contractile performance observed after sustained LVAD support. (Circulation. 2001;104:1241-1247.)

Key Words: heart failure ■ heart-assist device ■ QT interval ■ action potential ■ calcium

The hallmarks of the pathological phenotype observed in failing human cardiac myocytes include hypertrophy, slowed contraction and relaxation, abnormal calcium homestasis, impaired responses to adrenergic or frequency stress, and electrophysiological abnormalities. Electrophysiological abnormalities observed in failing myocytes from humans or animal models are manifested by a distortion of myocyte action potential shape and duration.1 Prolongation of the action potential delays myocyte repolarization and cellular relaxation. Because the QT interval is a direct measure of ventricular repolarization on the surface electrocardiogram (ECG), it is not surprising that many patients who have heart failure exhibit a prolonged QT interval. Moreover, both QT prolongation and conduction abnormalities, reflected by an increased QRS duration, have been associated with increased mortality among patients who have chronic heart failure.2 Effective as a means of sustaining medically refractory patients awaiting transplantation, clinical use of left ventricular assist devices (LVADs) also provides a novel opportunity to explore the pathophysiology of chronic heart failure, providing data on the effects of unloading on the myocardium. Highlighted in recent reviews,3,4 studies of LVAD-supported hearts have demonstrated striking structural, functional, and biochemical plasticity in human hearts with advanced heart failure. To date, no studies have examined the effect of unloading on the electrophysiological properties of the failing human heart. Therefore, the purpose of our study was to determine whether there were significant early or delayed changes in ventricular conduction and/or repolarization, as reflected by the surface ECG, among failing human hearts after LVAD implantation. We hypothesized that LVAD support would induce significant alterations in the cardiac electrophysiology of failing human hearts.

Methods

Patient Population

We retrospectively examined the medical records of 57 patients who received LVAD support between January 1993 and August 2000 at Temple University Hospital. From this set of patients, we identified 35 patients with archived 12-lead ECGs obtained within 4 days...
before LVAD insertion, immediately (≤6 hours) after LVAD placement, and at a delayed (>1 week) time after LVAD placement. A final set of 23 patients was obtained after excluding patients with atrial fibrillation, paced rhythms, and marked changes in heart rate (>20 bpm) immediately after LVAD placement. In all cases, the delayed ECG was used as the last archived ECG before cardiac transplantation.

To compare the immediate effects of mechanical unloading on the surface ECG, we selected a group of control patients who underwent cardiac surgery without mechanical unloading. Patients in this non-LVAD control group underwent coronary artery bypass grafting without valve replacement, device implantation, or aneurysmectomy. As in the LVAD group, control patients experienced general anesthesia, a median sternotomy, and cardiopulmonary bypass, and they were free of atrial fibrillation, paced rhythms, or marked changes in heart rate. From 348 patients screened, 22 patients meeting these criteria comprised the non-LVAD control group.

**Clinical Variables**

Patients’ charts and other archived materials were reviewed retrospectively to determine the etiology and duration of heart failure, medications at the time of their ECGs, and other pertinent features of their medical history. Left ventricular ejection fraction, measured with a balloon-tipped pulmonary artery catheter immediately before and after LVAD placement.

**ECG Analysis**

From archived 12-lead surface ECGs, we recorded the computer-derived average QT interval, heart rate, PR interval, and QRS duration. All ECGs included 10 seconds of digital data recorded at a 250-Hz sampling frequency to a resolution of 5 μV (GE-Marquette Medical Systems). Manual review of all ECGs (K.B.M.) was used to record the presence or absence of atrial fibrillation, right bundle branch block, or left bundle branch block and to assure that ectopic QRS complexes were not used for derivation of QT duration. From archived 12-lead surface ECGs, we selected a group of control patients who underwent coronary bypass grafting. The demographic data and clinical characteristics of the 23 patients who had nonischemic cardiomyopathy (11 idiopathic, 1 adriamycin-induced, and 1 valvular) and 10 patients who had ischemic cardiomyopathy.

**Myocyte Action Potential Measurements**

In an effort to relate whole-heart repolarization changes to single-cell repolarization, action potentials were recorded in isolated left ventricular myocytes from LVAD-supported and non-LVAD-supported hearts. Myocyte isolation was performed by using a previously described protocol. Briefly, at the time of transplant, the aortic root was perfused in situ with a cold blood-buffered cardioplegic solution. Within 30 minutes of cross clamping, an epicardial artery was cannulated and perfused sequentially with a Krebs-Henseleit Buffer rinse solution, a collagenase digestion solution, and a final rinse solution for 20, 30, and 10 minutes respectively. Midmyocardial myocytes were filtered, centrifuged (75g), and resuspended in a Krebs-Henseleit solution containing 1% wt/vol bovine albumin, taurine (10 mM/L), and CaCl2 (0.2 mM/L). All solutions were maintained with 95% O2, and 5% CO2 at 37°C.

Myocytes were placed in a chamber on the stage of an inverted microscope. The chamber was superfused with Tyrode solution containing 150 mM/L NaCl, 10 mM/L dextrose, 5.4 mM/L KCl, 1.2 mM/L MgCl2, 2.0 mM/L Na pyruvate, 5 mM/L HEPES, and 1.0 mM/L CaCl2. By using the whole-cell patch-clamp technique, action potentials were recorded in current-clamp mode (Axoclamp 2, Axon Instruments). To induce action potentials, current was passed through the patch electrode at 10% above threshold. The stimulus artifact was isolated to assure accurate membrane recordings. The pipette-filling solution contained 130 mM/L K aspartate, 20 mM/L KCl, 5 mM/L K2ATP, 1 mM/L MgCl2, 10 mM/L NaCl, and 10 mM/L HEPES. All experiments were performed at a chamber temperature of 37°C. Data were recorded online with pClamp software (Version 7.0, Axon Instruments). For each cell, the action potential duration at 50% repolarization (APD50) was derived from 3 action potentials at 0.2 Hz.

**Statistics**

A retrospective analysis of the ECGs from 23 LVAD patients meeting inclusion criteria as defined above was performed to determine if the ECG intervals changed across the 3 time periods measured, ie, pre-LVAD, immediate post-LVAD, and delayed post-LVAD. The following ECG intervals were analyzed: PR interval, QRS duration, absolute QT duration (QTabs), and QT duration corrected for heart rate. The heart rate–adjusted QT duration was determined by using 3 separate approaches. The first approach used Bazett’s formula (QTcBazett = QT/RR1/2) which, despite its known shortcomings, is used in the great majority of published studies requiring a heart rate–adjusted QT duration. The second approach used Fridericia’s cube-root formula (QTcFridericia = QT/RR1/3) which has been shown to better model the heart rate dependence of the QT interval. Lastly, we used analysis of covariance with QT duration adjusted on the basis of heart rate to determine whether apparent changes in the QT interval could be attributed to changes in heart rate alone. With the exception of QRS, all data were normally distributed. For that reason, a log transformation of QRS was performed before analysis.

The LVAD group’s data were analyzed as a single-factor experiment with repeated measures. An ANOVA was performed followed by pairwise between-time comparisons by using the Dunn-Bonferroni adjustment. Subgroup analyses explored possible differences based on various clinical parameters such as the duration of heart failure, etiology, sex, the presence of a bundle branch block, or the use of antiarrhythmics. Changes in cardiac hemodynamic parameters resulting from LVAD support were analyzed by using a paired Student t test. Comparisons with the coronary artery bypass graft control group were analyzed by using a two-factor ANOVA with repeated measures on time. For the comparison of APD50 between LVAD-supported and non-LVAD-supported myocytes, unpaired t tests were used. All data reported in text and tables are expressed as mean±SEM. A P value less than 0.05 was considered statistically significant.

**Results**

**Clinical Characteristics**

The demographic data and clinical characteristics of the 23 LVAD-supported patients are presented in Table 1. These individuals had a mean age of 48 years (range, 26 to 65), and most were men. The average duration of heart failure before LVAD placement was 30 months (range, 1 to 80). The sample included 6 patients who had heart failure with a duration of less than 3 months. The sample was relatively balanced with respect to heart failure etiology including 13 patients who had nonischemic cardiomyopathy (11 idiopathic, 1 adriamycin-induced, and 1 valvular) and 10 patients who had ischemic cardiomyopathy. Both nonischemic and ischemic subgroups had severely depressed systolic function with an average ejection fraction of 9±1% and 11±1%, respectively. All but 2 patients required both milrinone and dobutamine intravenously before LVAD placement, and 18 of 23 received intra-aortic balloon pump–support before LVAD placement. All patients were receiving vasodilator...
therapy at the time of LVAD placement. The 4 patients who were receiving antiarrhythmic therapy were administered amiodarone before and immediately after LVAD placement. One patient (No. 2) was receiving a β-blocker at the time of LVAD placement.

Hemodynamic Effects of LVAD Support

Hemodynamic measurements in the operating room at the time of LVAD placement were available in 21 of 23 patients. LVAD placement was associated with an immediate decrease in pulmonary artery systolic pressure from 54±2 to 36±1 mm Hg (P<0.0001) and a decrease in pulmonary artery diastolic pressure from 31±1 to 17±1 mm Hg (P<0.0001). These marked reductions in pulmonary artery systolic and diastolic pressures reflected immediate left ventricular decompression induced by the LVAD as documented by echocardiography in previous studies.9 In our patients, LVAD placement did not significantly reduce right atrial pressure (18±1 to 16±1 mm Hg), which is also consistent with previous studies.9,10

Immediate ECG Responses

The electrocardiographic changes observed immediately after LVAD placement are presented in Table 2. After the initiation of LVAD support, there was a significant decrease in average QRS duration (−13±4 ms). As shown in Figure 1, immediate decreases in QRS duration after LVAD support

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<th>TABLE 1. LVAD Patient Demographics and Clinical Characteristics</th>
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48±3 | 19 | 13 | 30±6 | 2 | 2 | 10±1 | 4

| **Male** | **Nonischemic** | **Female** | **Ischemic** |

CHF indicates congestive heart failure; RBBB, right bundle branch block; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction.

<table>
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<th>TABLE 2. Immediate and Delayed Changes in ECG Parameters After LVAD Support</th>
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<td><strong>Parameter</strong></td>
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<td>Heart rate (bpm)</td>
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<td>QTc-Bazett (ms)</td>
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<td>QTc-Fridericia (ms)</td>
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*P<0.05 vs preceding period; †P<0.01 vs preceding period; ‡P<0.001 vs preceding period; §P<0.05 Pre-LVAD vs Delayed Post-LVAD; ||P<0.001 Pre-LVAD vs Delayed Post-LVAD.
were observed in all but 5 patients, and 3 of these patients had a complete right or left bundle branch block. As shown in Table 2, placement of the LVAD also resulted in immediate increases in the absolute QT interval and the heart rate–adjusted QT interval, regardless of whether the formula of Bazett or Fridericia was applied. In addition, analysis of covariance further demonstrated that increases in QT duration immediately after LVAD placement were not related to changes in heart rate.

To better define the relative effects of LVAD support versus cardiac surgery per se on the immediate ECG changes, we compared the ECG changes in our LVAD cohort with those from 22 patients who underwent conventional on-pump coronary artery bypass grafting. As shown in Figure 2, changes in QRS duration, absolute QT duration, and corrected QT duration observed immediately after LVAD placement are clearly different from the electrocardiographic changes observed immediately after coronary artery bypass grafting.

Subgroup analyses of LVAD patients indicated that immediate decreases in QRS duration and increases in absolute and corrected QT duration were observed regardless of sex, heart failure etiology, heart failure duration, or the presence of antiarrhythmic therapy. However, we observed differential responses of QRS duration depending on the presence or absence of a bundle branch block. Specifically, QRS duration did not decrease among the 4 patients with a right or left bundle branch block (148±17 to 152±18 ms; P=not significant [NS]), whereas QRS duration decreased significantly among the 19 patients without a bundle branch block (110±5 to 93±3 ms; P<0.001). There was also a nonsignificant tendency (P=0.08) toward more striking immediate decreases in QRS duration among the 4 patients treated with antiarrhythmic therapy (ΔQRS, −27±5 ms) than among the 19 patients without antiarrhythmic therapy (ΔQRS, −10±4 ms).

**Delayed ECG Responses**

As shown in Table 2, with sustained cardiac unloading via LVAD support, we observed additional changes including decreases in heart rate, increases in the PR interval, and marked decreases in the heart rate–adjusted QT interval. The changes in the heart rate–adjusted QT interval were significant regardless of whether Bazett’s or Fridericia’s formula was applied. Moreover, analysis of covariance confirmed that delayed decreases in QT interval during LVAD support were not attributable to changes in heart rate. As illustrated in Figure 1, a biphasic change in the QTc during LVAD support (an initial increase followed by a later decrease) was observed in the majority of patients.

Subgroup analysis revealed no significant impact of sex, heart failure etiology, or heart failure duration on delayed changes in any ECG parameter. Likewise, when patients were subdivided based on their duration of LVAD support between the immediate and delayed post-LVAD ECGs (<1 month, 1 to 2 months, >2 months), no significant differences in any ECG parameter were observed between subgroups. An increase in PR interval between immediate post-LVAD ECGs and delayed post-LVAD ECGs was observed among the 19 patients without previous antiarrhythmic therapy (ΔPR 16±5 ms; P<0.01), but not among the 4 patients who had received antiarrhythmics (ΔPR, −7±10 ms; P=NS). However, the decrease in QTc-Bazett between early post-LVAD and delayed post-LVAD ECGs was observed with or without previous antiarrhythmic therapy (−69±16 versus −57±10 ms; P=NS). Similarly, the delayed decrease in QTc-Bazett was observed in the presence or absence of a bundle branch block (−42±17 versus −63±9 ms; P=NS).

**Myocyte Action Potential Measurements**

To examine the cellular mechanism of delayed changes in QTc, whole-cell APD30 values were compared between 7 isolated left ventricular myocytes from 3 LVAD-supported hearts and 7 myocytes from 6 non-supported hearts. As shown in Figure 3, at 0.2 Hz, the average myocyte APD30 was considerably longer among myocytes from hearts without previous LVAD support than in LVAD-supported myocytes (863±37 versus 529±154 ms; P<0.005).

**Discussion**

The major findings of this investigation are that mechanical circulatory support of the failing human heart with a LVAD

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Figure 1. Immediate and delayed changes in QRS interval and heart rate-adjusted QT duration (QTc-Bazett) after LVAD placement in failing human hearts.

Figure 2. Average changes in surface ECG parameters between preoperative recordings and immediate postoperative recordings among 23 patients undergoing LVAD placement (solid bars) and 22 patients undergoing coronary artery bypass grafting (CABG, open bars). Data are presented as mean±SEM. *P<0.05 between groups; **P<0.01 between groups; ***P<0.001 between groups.
induces both immediate and delayed changes in cardiac electrophysiology. LVAD placement was associated with an immediate decrease in the QRS interval, indicating load-dependent changes in intraventricular conduction. Immediate effects of unloading also included an unexpected increase in the QT interval, reflecting slowed myocardial repolarization. Neither of these changes was observed among patients undergoing coronary artery bypass grafting without myocardial unloading. Over a period of weeks to months after LVAD placement, our findings indicate further electrophysiologic remodeling with a delayed decrease in the heart rate–adjusted QT interval consistent with acceleration of myocardial repolarization. In vitro data from hearts explanted at the time of transplantation suggests that this secondary change in QT duration may reflect a shortening of cardiac myocyte action potential duration compared with failing myocytes without antecedent LVAD support. Shortening of action potential duration during sustained myocardial unloading suggests one mechanism contributing to the increased rate of myocyte relaxation previously observed after sustained LVAD support.5

**Early Decreases in QRS Duration After Unloading**

One of the most striking and consistent findings observed immediately after LVAD placement was a decrease in QRS duration. The absence of such immediate decreases in QRS duration among the patients undergoing coronary artery bypass grafting suggests that reduced cardiac distension, rather than other aspects of cardiac surgical intervention (eg, anesthesia, sternotomy, cardiopulmonary bypass) was responsible. Previous studies have described myocardial distension on impulse conduction. Studies in isolated cardiac muscle preparations from mammalian and non-mammalian species suggested that overstretching could reduce conduction velocity. Recent studies in the normal rabbit heart11 and normal and myopathic canine hearts12 have failed to identify changes in conduction velocity after cardiac distension induced by volume loading. Because the dimensions of the failing heart are known to decrease significantly immediately after LVAD placement,9 it is possible that the reduction in QRS duration reflects a decrease in conduction distance rather than an increase in conduction velocity. Because a decreased QRS duration was not observed among the 4 patients with bundle branch blocks, it is also possible that reduced ventricular distension could reduce QRS duration primarily via effects on specialized cardiac conduction tissues.

**Early Increases in QT Duration After Unloading**

We observed that LVAD placement induced consistent increases in QT and QTc intervals, which suggests prolongation of overall myocardial repolarization caused by altered conduction and/or increased average action potential duration. The absence of similar effects in coronary artery bypass graft patients suggests that reduced cardiac distension, rather than other aspects of cardiac surgical intervention, was responsible for changes in repolarization. The increases in QT and QTc occurred despite significant decreases in QRS duration that would be expected to shorten myocardial repolarization. Thus, QT and QTc prolongation probably reflect acute increases in myocyte action potential duration immediately after cardiac decompression rather than a defect in cardiac conduction. While Pye and Cobbe13 demonstrated shorted action potential duration with increasing load, Zhu et al12 observed a prolonged effective refractory period with reduced preload. Both observations were more pronounced in failing hearts; therefore, in the present study, it seems likely that acute mechanical unloading with LVAD placement acutely increases action potential duration.

Small changes in the ionic currents during the plateau phase of the action potential can either hasten or delay cellular repolarization.14 At least two possible explanations could explain the acute prolongation of action potential by reduced cardiac distension. Inactivation of the swelling-activated chloride channel (Icl,swell), that is present in heart failure15 could cause a prolongation of action potential duration. As an outward rectifying current, Icl,swell tends to shorten action potential duration when activated by cell swelling or mechanical distension.16 Icl,swell has been shown to be present in human myocardium15 and is increased in a canine model of tachycardia-induced heart failure.17 Inactivation of Icl,swell in severely failing hearts may induce an immediate increase in action potential duration.

Increased forward-mode Na+:Ca++ exchange might also produce an inward current that would prolong QT and QTc with immediate unloading. Acute unloading of the ventricle, reflected by intraoperative hemodynamic measurements, is likely associated with a decrease in overall sarcomere length during the cardiac cycle. Previous studies have demonstrated that shorter sarcomere length decreases myofilament Ca++ sensitivity.18 Such decreased Ca++ sensitivity would decrease Ca++ binding to myofilaments and increase the cytosolic free Ca++ concentration thereby increasing forward-mode Na+:Ca++ exchange (3 Na+ in:1 Ca++ out) and increasing action potential duration after cardiac decompression. Of course, such putative mechanisms for immediate changes in QT and QTc after LVAD placement are speculative at this point.

**Decreases in QTc and APD During Sustained Unloading**

Despite sustained cardiac unloading, the delayed effects of LVAD support on myocardial repolarization were distinct and opposite from the acute effects. We observed significant reductions in the heart rate–corrected QT interval regardless
of which methodology of heart rate correction was used. Our in vitro data strongly supports the hypothesis that delayed decreases in QTc reflected decreases in average action potential duration among myocytes from LVAD-supported hearts. Action potential prolongation is one of the signature abnormalities in failing human hearts. Delayed decreases in QTc and action potential duration, observed during sustained LVAD support, suggests a reversal of the electrophysiologic remodeling characteristic of the failing human heart. In previous studies, chronic LVAD support has induced the regression of left ventricular and myocyte hypertrophy and LVAD support has been associated with improvements in contractile performance. Cellular relaxation, Ca²⁺ homeostasis, and adrenergic responsiveness compared with failing hearts without LVAD support. The present study adds to a growing body of evidence that LVAD support induces recovery of failing hearts and provides a novel model system for identifying pivotal mechanisms of myocardial plasticity and recovery.

Interestingly, electrophysiologic remodeling with sustained ventricular unloading appears to occur within the first month after LVAD placement. Specifically, the 7 patients with LVAD durations of <1 month showed significant reductions in QTc which were not different from those observed with longer durations of LVAD support.

Potential Significance of Electrophysiological Reverse Remodeling

Although changes in the surface ECG clearly reflect changes in conduction and repolarization at the tissue level, to our knowledge, this is the first demonstration of parallel shifts in the QT interval and cellular repolarization in human hearts. In addition to its role as a marker of pathological hypertrophy and failure, increasing evidence indicates that increased action potential duration contributes to abnormal excitation-contraction coupling in the failing heart. Through direct actions on voltage-dependent processes, such as Ca²⁺ entry through the L-type Ca²⁺ channel and Na⁺:Ca²⁺ exchange, action potential duration has a profound impact on both the amplitude of cellular contraction and the timing of cellular relaxation. Shortening of action potential duration after LVAD support likely contributes to the faster cellular relaxation and improved force-frequency relationship. Given that Ca²⁺-dependent processes have been implicated in pathological gene expression in the failing heart, decreases in action potential duration could also contribute to LVAD-induced changes in myocardial gene expression.

Prolonged depolarization, as well as heterogeneous depolarization (QT dispersion), contributes to arrhythmogenesis in failing hearts. This is clearly demonstrated by the increased risk of sudden death associated with both familial long QT syndromes and drug-induced QT prolongation. Previous studies have demonstrated that QT prolongation is associated with increased QT dispersion. We may therefore speculate that the LVAD-induced decreases in action potential and QTc durations could reduce the risk of spontaneous ventricular arrhythmias. However, changes in medications, chamber distension, and neurohormonal activation typically associated with sustained LVAD support will render it difficult to define a cause-and-effect relationship between faster repolarization and arrhythmia risk during LVAD support.

To date, most of the physiological and molecular evidence of reverse remodeling with LVAD support has relied on tissue-based analyses, particularly applied to heart tissue obtained at the time of transplantation. Therefore, another implication of the present studies is that a set of noninvasive parameters, including those derived from the surface ECG, could inform assessments of myocardial recovery and guide therapeutic strategies.

Study Limitations

In most cases, we were limited to a single delayed ECG to demonstrate the time course of decreases in QTc. Similarly, although recent studies highlight the prognostic importance of abnormalities in QT dispersion, our retrospective study did not permit demonstration of alterations in temporal QT dispersion that would require prolonged rhythm analysis. Because conduction velocity was not measured directly, we could not determine if immediate decreases in QRS duration were the result of changes in cardiac geometry versus changes in intraventricular conduction velocity. There is no ideal method of heart rate adjustment of the absolute QT interval. However, it is reassuring that all the changes in QTc were observed regardless the method used. We could not exclude the possibility that changes in medications or secondary neurohumoral changes contributed to the delayed electrophysiological changes we observed. Our findings support the concept of early and delayed load-dependent changes in cardiac electrophysiology among patients with medically refractory end-stage heart failure. These results may not be applicable to individuals with less advanced heart failure.

Conclusions

Many of the defects associated with advanced heart failure are modulated and sustained by increased hemodynamic loading conditions. Abnormalities of ECG and action potential shape and duration demonstrated consistent and striking improvements with sustained mechanical circulatory support. Parallel observations at the cellular and organ level validate the use of in vitro techniques for discerning the bases of defects in failing hearts and demonstrate the potential to translate such insights into clinically relevant diagnostic and therapeutic strategies.

Acknowledgments

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References


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