2012

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DOI

http://dx.doi.org/10.1016/j.hrtlng.2012.02.012

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Published in final edited form as:
Heart Lung. 2012 ; 41(4): 368–373. doi:10.1016/j.hrtlng.2012.02.012.

Feasibility and Compliance with Daily Home ECG Monitoring of the QT Interval in Heart Transplant Recipients

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Introduction

About 13% of adult heart transplant recipients do not survive to one year and a major cause of death is acute cellular allograft rejection.[1,2] According to the 2009 annual United States data published from the International Society for Heart Lung Transplantation Registry, acute rejection occurs in 25 – 35% of transplant recipients within the first year following transplant surgery.[3] In order to detect the early stages of rejection so that more aggressive and early immunosuppressant therapy can be initiated, frequent biopsies of heart tissue are performed (typically, weekly or every other week in the first 3 months and then monthly or every other month during the first year). Although endomyocardial biopsy (EMB) is not a perfect "gold standard" for a correct diagnosis of acute allograft rejection, it is considered the best available test and thus, it is the current standard practice. Unfortunately, EMB is an invasive and costly procedure that is not without risk.[4,5] If a simple noninvasive biomarker could be identified to detect the early stages of acute rejection, it might be possible to reduce the number of invasive biopsy procedures and to initiate earlier therapy that might prevent death from severe rejection.

In a retrospective analysis by Tenderich et al, 12-lead ECGs were recorded in 200 heart transplant patients during the first three months following transplant surgery, prolongation of the QTC interval of >25 milliseconds predicted acute cellular allograft rejection with a sensitivity of 77% and specificity of 96%.[6] In normal individuals, there are two major influences on the duration of the QT interval: heart rate and autonomic nervous system activity. There is an inverse relationship between heart rate and the QT interval. In terms of the autonomic nervous system, sympathetic stimulation shortens whereas parasympathetic stimulation lengthens the QT interval. In the denervated cardiac allograft, both influences of heart rate and autonomic nervous system activity are almost entirely removed so there is little diurnal variation of the QT interval.[8] A potential major benefit of allograft denervation is that without the confounding influences of heart rate and autonomic nervous system activity, an observed increase in the QT interval is likely to indicate abnormal ventricular repolarization due to another cause such as acute allograft rejection.

No prospective study to date has investigated whether such increases in the QT interval could provide early detection of acute allograft rejection. We plan to conduct a prospective NIH-funded clinical trial (1RO1 NR012003) to determine whether daily monitoring of the transplant recipient's ECG using a simple home device would provide an early sensitive and specific biomarker for acute allograft rejection. In preparation for this clinical trial, the current pilot study was undertaken to: (1) determine whether heart transplant patients could

achieve compliance in transmitting a 30- second ECG every day for 1 month using a simple ECG device and their home telephone, (2) evaluate ease of device use and acceptability of time required for transmission by transplant recipients, and (3) evaluate the quality of transmitted ECG tracings for QT interval measurement.

Methods

Sample and Setting

In a 3-month period ending in May, 2010, we selected a convenience sample from three transplant centers: University of California, Los Angeles Medical Center, Cedars Sinai Medical Center, also in Los Angeles, and Columbia University-New York Presbyterian Medical Center in New York City. Institutional Review Board approval was obtained from these three institutions as well as the University of California, San Francisco (UCSF) Medical Center, which served as the ECG Core Lab for the study. The inclusion criteria were adult heart transplant recipients living independently who were clinically stable. Demographic characteristics are detailed in Table 1.

Instruments and Procedure

Home ECG Device—After a thorough search of the available technology, the HeartOne ECG recorder (Aerotel Medical, Israel) was selected (Figure 1, Top photograph). The ECG device is pocket size, lightweight, and stores up to four 30-second recordings of a bipolar ECG Lead.

ECG Lead and QT Measurement—The QT interval is measured from the onset of the QRS complex to the end of the T wave. T waves must be of sufficient amplitude to identify the T wave endpoint. Because normal T wave axis falls between 15–75 degrees in adults, Lead II which is at the 60 degree axis point often has the largest amplitude T wave. Lead II requires an electrode on the right wrist and left ankle. We used an expandable metal wristwatch type electrode for the right wrist and a C-shaped electrode for the left ankle, both of which could be easily slipped on and off (Figure 1, Middle and Bottom photographs). Subjects were given spray bottles of saline to spray on the electrode site to improve conductance without the need to use more permanent adhesive-type ECG electrodes.

ECG Acquisition and Transmission—Site investigators taught each patient at the time of enrollment on how to use the ECG device. Subjects were asked to perform a return demonstration in front of the site investigator and were provided a booklet with detailed photographs of each step of the recording and transmitting process, to take home with them. To minimize myopotential noise, patients were instructed to acquire the ECG while sitting quietly with their arms resting on a table/desk or supine in bed. After ECG data acquisition, recipients were instructed to transmit the data trans-telephonically (landline telephone required) using a toll-free number that guided the patient with voice prompts. A small subset (6%) of subjects who had mobile telephones but no landlines were allowed to participate in the study after it was confirmed by the investigators that their mobile devices were capable of transmitting an acceptable quality ECG.

ECG Analysis—The HeartLine Receiving Station (Aerotel Medical Systems, Israel) received ECG transmissions and stored each subject's ECGs into a separate file folder that contained all their daily ECGs. QT and RR intervals were made in a computer-assisted manner. The Aerotel measurement software provides a zooming feature to enlarge ECG waveforms for better visualization. In addition, electronic calipers are provided so that the researcher selects the appropriate waveform onset and offset points and the computer software provides the interval value in milliseconds (ms). The end of the T wave was

defined as the intersection of a tangent to the steepest slope of the last limb of the T wave and the isoelectric baseline (Figure 2).[7] One investigator (EVC) made all measurements for the current analysis. Criteria for acceptable QTc measurement were as follows: T wave amplitude >100 μV; minimal baseline artifact; non-noisy consecutive RR and QT intervals and no baseline wander.

Database Management and Statistical Analysis

All sites used a secure web-based data capture site, Research Electronic Data Capture (REDCap), which is sponsored by a consortium of 118 research institutions, including the institutions involved in our study. Stata 11 (StataCorp, College Station, TX) was used to calculate descriptive statistics (frequencies, means and standard deviations), Chi Square and ttests.

Results

Sample Characteristics

At Columbia University, all patients approached (n=15) were invited to participate and agreed to be in the pilot study; at UCLA, 19 of 27 patients approached participated. Reasons for non-participation were lack of interest (6), and being too busy (2). A total of 34 subjects (24 males; 10 females) were enrolled. After initiation of the study, two subjects (UCLA, 1; Columbia, 1) were excluded from the analysis because they were hospitalized and could not transmit ECGs from home. Additionally, a third subject (Columbia) decided to withdraw from the study due to personal reasons. The remaining 31 subjects comprised the pilot study and had a mean age of 55 ±13 years. Ethnicity and race reflected the demographics of urban Los Angeles and New York City with 37% of subjects being non-white (Hispanic-19%; Asian-12%, Black, 27%). Eleven subjects (35.5%) had visible extremity tremor and 17 subjects (55%) had ≥1+ peripheral edema involving the left ankle electrode site.

ECG Quality

There were a total of 644 ECGs successfully received by the ECG Core lab at UCSF during the study period. Due to construction, there was a period of several days in which power outages in the Core lab precluded ECG transmissions. Of the total 644 ECGs, 569 (89%) were acceptable for QTC measurement (i.e., non-noisy consecutive RR and QT intervals). There was no statistically significant difference in the proportion of acceptable quality ECGs in patients with and without extremity tremor (p=0.151) or peripheral edema (p=0.212).

The mean QT interval was 415 milliseconds (ms) in males and 426 ms infemales. We defined abnormal as a QT interval of >470 ms in females and >460 ms in males. In both sexes, the QT interval was within normal limits without any correction formula utilized. When utilizing the Bazett correction formula (bQTc), of the 569 ECG readings read, 415 ECG readings from the malesubjects (33%) had bQTc intervals >460 ms and 154 ECG readings from the female subjects (57%) had bQTc intervals > 470 ms. This small gender difference in bQTc (~10 ms longer in females compared with males) was statistically significant (p=0.000).

Patient Compliance and Ease of Device Use

Daily ECG transmission was achieved by 73% and all 32 subjects (100%) achieved at least a weekly ECG transmission. To the question, how difficult do you think it was to record and transmit your ECG by phone, 88.9% answered either “somewhat easy” or “extremely easy.” Some patients reported that recording their ECG was easy; however, transmitting their ECG by telephone was more difficult because sometimes the receiving computer was unavailable (power outages) and repetitive attempts had to be made. To the question, I would be willing

to use the HeartOne device every day for six months, 89% answered positively. In total, 644 transmissions out of a potential 976 ECG transmissions over the one-month pilot period. During this time 48 incidences of non-transmission due to power outages and 133 incidences of non-transmissions due to various patient reasons occurred. This represents approximately 18% (non-transmission/expected transmissions) of loss ECG data. As our primary aim was to test compliance and feasibility, we believe 18% represents a minor loss of data. Additionally, each patient provides multiple transmissions; we assume that due to the central limit theory, an increase in the number of transmissions would tend to lead more towards mean bQTc. Therefore the data described herein should be considered upper or lower bound sample estimates

Discussion

This pilot study demonstrates that transplant recipients can be compliant in recording their ECGs daily/weekly using a home device. Subjects achieved a nearly 74% daily and 100% weekly compliance in recording and transmitting their ECGs. The transplant population is especially well suited for applying novel technology. They are typically younger than other cardiac populations, with 86% of adult heart transplant recipients between 18-64 years of age. Moreover, patients are pre-screened to be free of conditions that would prevent adherence to the complex post-transplant regimen such as cognitive impairment, substance abuse, or psychological disorders.

Compliance would have undoubtedly been better in our study if patients had not been asked to transmit their ECGs by landline telephone 100% of the time. There is a growing trend for Americans to use mobile phones exclusively, especially in urban areas that are well saturated with cell phone towers. Unfortunately, the HeartOne ECG device used in our study is not recommended for use with mobile phones. We did permit two study participants to utilize mobile devices because they did not have a landline. In both cases, mobile telephone transmission did not impede the investigators' ability to analyze the transmitted ECG.

Another problem with telephone transmission is that any power surge or outage triggers the receiving computer to shut down until the computer can be rebooted. As a result, patients cannot connect to the receiving computer and have to make repeated attempts to transmit their ECG.

For these reasons, we will use a different ECG transmission system for our NIH clinical trial. The new ECG device will automatically seek, find, and upload the ECG by wireless Bluetooth communication to an Internet Transmitter located in the subject's home. Then, using mobile phone technology (subscriber identity module [SIM] card), the Internet Transmitter device will automatically seek, find, and send the digital ECG to a UCSF server via wireless General Packet Radio Services (GPRS) internet access. Thus, subjects will not have to dial a telephone to transmit their ECG; they will only need to record their ECG and the rest will be automatic. The ECG will be sent to a large UCSF server and investigators in the ECG Core Lab will access the ECG data via a Virtual Private Network (VPN).

Although we took measures to reduce noise in the ECG recordings, 12% of the transmitted ECGs were unanalyzable due to issues like myopotential noise. There are various causes for myopotential noise, with the most likely cause in the present study being due to the tensing of arm/leg muscles while the ECG was being acquired. We measured involuntary muscle movement due to tremor; however, because patients performed these recordings in their home, we were unable to control all sources of voluntary myopotential noise.

In future studies, we will ask patients to lie down to record their ECGs. Two conditions that we hypothesized might be associated with a poor quality signal were lower leg edema and extremity tremor; however, neither of these conditions were related to poor quality ECGs.

The QT interval in our cohort was shorter than normal (mean 387.63 ms, males; 340.32 ms, females) and this is in agreement with prior observations in the transplant population. In normal individuals, vagal dominance at rest prolongs the QT interval compared with transplant recipients who do not have such vagal tone. As a result, QT intervals are typically shorter than normal individuals

Conclusions

Adult heart transplant recipients are compliant with recording daily and weekly ECGs. Direct internet transmission of ECGs from a patient's home to an ECG Core Lab rather than telephone modem transmission would likely improve patient compliance further. Ankle edema and side effects of immunosuppressive drugs that can cause tremor are common but do not interfere with ECG quality. Whether an increase in the QT interval measured daily will prove to be an early and sensitive and specific biomarker for acute allograft rejection in the first six months following transplantation will be the subject of an ongoing clinical trial.

Acknowledgments

NIH/NCRR/OD UCSF-CTSI Grant Number TL1 RR024129-6 supported this publication. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH. Many thanks to Dr. Joel Palefsky, Dr. Peter Chin-Hong, Cecily Hunter and the rest of the PACCTR staff as well as UCLA and Columbia University for their work on this project.

References

1. Hershberger RE, Starling RC, Eisen HJ, et al. Daclizumab to Prevent Rejection after Cardiac Transplantation. N Engl J Med. 2005; 352(26):2705–2713. [PubMed: 15987919]
2. Stehlik J, Starling RC, Movsesian MA, et al. Utility of long-term surveillance endomyocardial biopsy: a multi-institutional analysis. J Heart Lung Transplant. 2006; 25(12):1402–1409. [PubMed: 17178332]
3. Taylor DO, Stehlik J, Edwards LB, et al. Registry of the International Society for Heart and Lung Transplantation: Twenty-sixth Official Adult Heart Transplant Report- 2009. J Heart Lung Transplant. 2009; 28(10):1007–1022. [PubMed: 19782283]
4. Fiorelli AI, Coelho GHB, Oliveira JL Jr, et al. Endomyocardial Biopsy as Risk Factor in the Development of Tricuspid Insufficiency After Heart Transplantation. Transplantation Proceedings. 2009; 41(3):935–937. [PubMed: 19376392]
5. Hamour IM, Burke MM, Bell AD, Panicker MG, Banerjee R, Banner NR. Limited Utility of Endomyocardial Biopsy in the First Year after Heart Transplantation. Transplantation. 2008; 85(7): 969–974. [PubMed: 18408576]
6. Tenderich G, Jahanyar J, Zittermann A, Schleithoff SS, Wlost S, Korfer R. Predictive value of ECG changes for acute cardiac rejections in heart transplant recipients. Med Klin (Munich). 2006; 101(2):99–106. [PubMed: 16501906]
7. Postema PG, De Jong JS, Van der Bilt IA, Wilde AA. Accurate electrocardiographic assessment of the QT interval: teach the tangent. Heart Rhythm. 2008; 5(7):1015–1018. [PubMed: 18598957]
8. Alexopoulos D, Rynkiewicz A, Yusuf S, Johnston JA, Sleight P, Yacoub MH. Diurnal variations of QT interval after cardiac transplantation. Am Cardiol. 1988; 61(6):482–485.

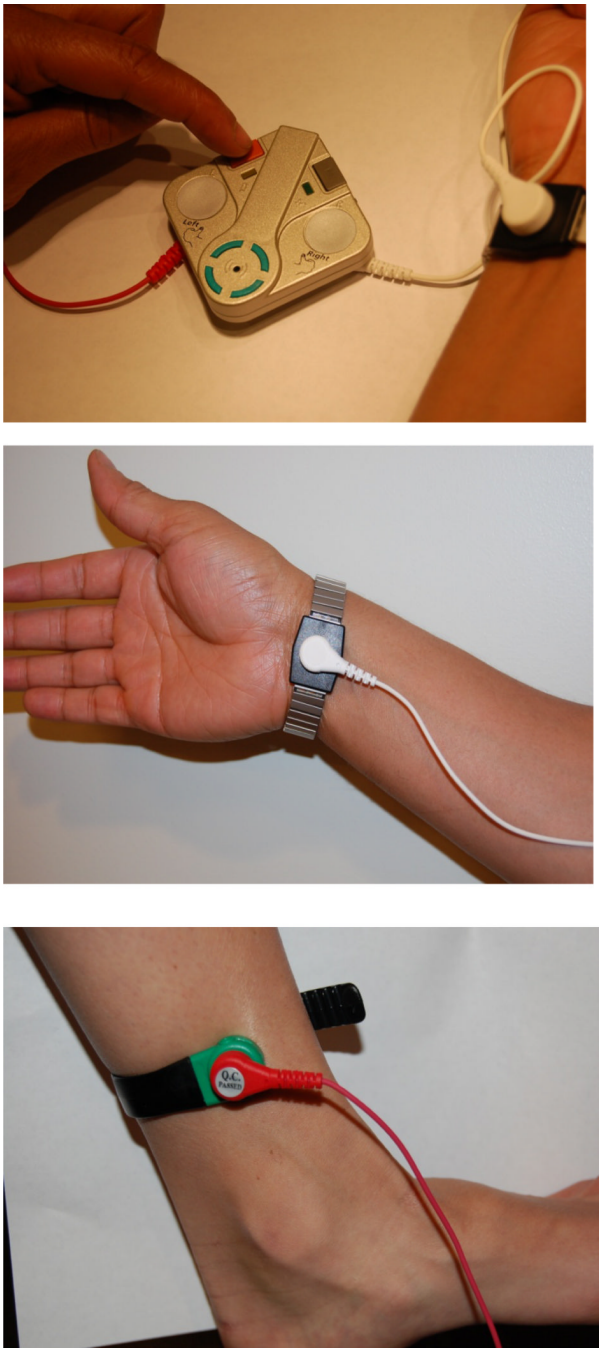

Figure 1.
Top: HeartOne ECG recorder (Aerotel Medical, Israel) Middle: Placement of expandable metal wristwatch type electrode for the right wrist. Bottom: Placement of C-shaped electrode for the left ankle

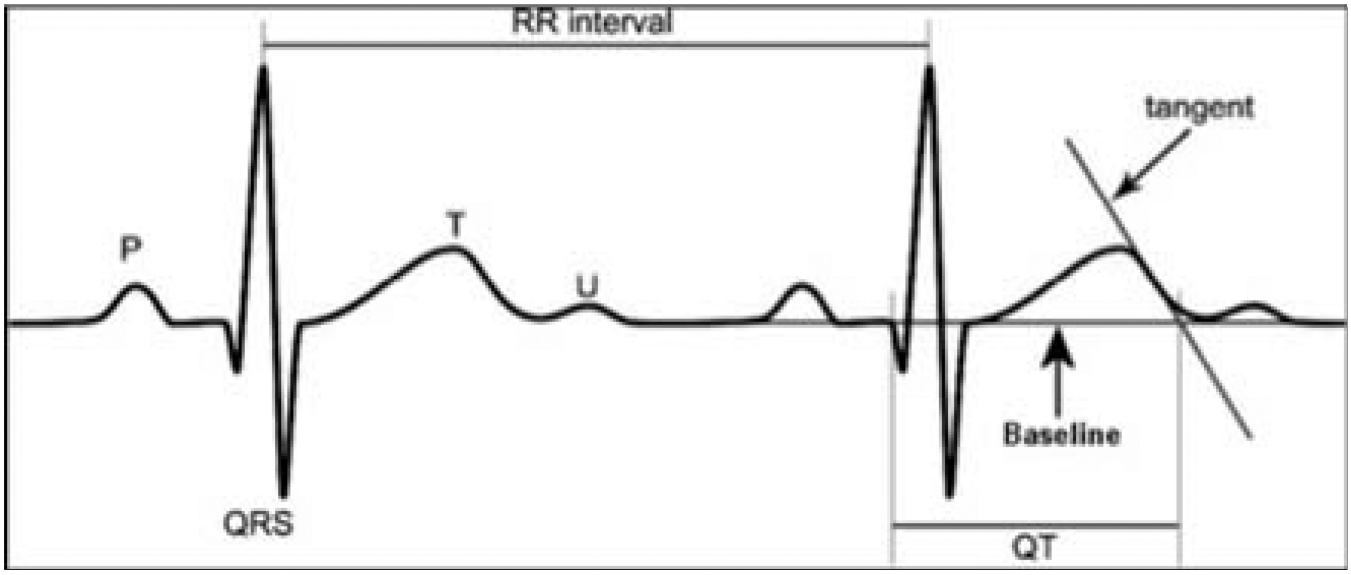

Figure 2.
A tangent is drawn to the steepest slope of the last limb of the T wave; the end of the T wave is the intersection of this tangent with the baseline.

Table 1

Demographics

Characteristics of the 31 Subjects Enrolled in the New Heart Pilot Study

	Men (n=22)	Women (n=9)
	mean±sd	*mean±sd*
Age (n=31)	*55±14*	54±14
	%	*%*
Ethnicity (non-Hispanic) (n=25)	81	78
Ethnicity (Hispanic) (n=6)	18	22
Race: (n=31)		
Black	9	45
White	59	33
Asian	14	0
Language spoke at home: (n=31)		
English	78	89
Spanish	14	11
Other	9	0
Etiology of HF (n=31)		
Ischemic	18	0
Viral/Bacterial	0	0
Cardiomyopathy	59	67
Congenital	5	0
Other	18	33
Type of CM: (n=31)		
Dilated	50	89
Restrictive	9	0
Hypertrophic	9	0
Non specific	32	11
Upper Extremity tremor (n=31)		
None	64	67
Barely visible	23	22
1 to <3cm	9	11
5 to <10cm	4	0
Lower Extremity edema (n=31)		
None	50	33
1+	27	22
2+	13	45

	Men (n=22)	Women (n=9)
	mean±sd	*mean±sd*
3+	5	0
4+	5	

HF=heart failure; CM=cardiomyopathy