Original Paper

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Improving Living Kidney Donor Follow-up Using Mobile Health: A Pilot Randomized Control Trial

Abstract

**Background:** Every year, more than 5,500 healthy people in the US donate a kidney for the medical benefit of another person. The Organ Procurement and Transplantation Network (OPTN) requires that transplant hospital monitor living kidney donors (LKD) for two years post-donation. However, the majority (57%) of transplant hospitals in the United States (US) continue to fail to meet nationally mandated requirements for LKD follow-up. A novel method for collecting LKD follow-up is needed to ease both transplant hospital and patient-level burden. We built a mobile health (mHealth) system, mKidney®, designed specifically for collecting and reporting required LKD follow-up data. The mKidney® mobile application was developed based on input elicited from LKDs, transplant providers, and thought leaders.

**Objectives:** The primary objective of this study is to evaluate the impact of the mKidney® smartphone application on LKD follow-up.

**Methods:** We are conducting a two-arm randomized control trial (RCT) with LKDs who undergo living kidney donor transplantation at Methodist Specialty and Transplant Hospital in San Antonio, Texas. Eligible participants will be recruited in-person by a study team member at their 1-week post-donation clinical visit. and randomly assigned to either the intervention or control arm (1:1). Participants in the intervention arm will receive the mHealth intervention (mKidney®) and participants in the control arm will receive the current standard of follow-up care. Our primary outcome will be policy-defined complete (all components addressed) and timely (60 days before or after expected visit date) 6-month, 1-year, and 2-year follow-up. Our secondary outcomes will be compliance at each of the three time points, evaluated separately. Data analysis will follow the intention-to-treat principle. Additionally, we will collect quantitative and qualitative process data regarding the implementation of the mKidney® system.
Results: We anticipate beginning recruitment for this study in May of 2018. We will recruit participants for 2 years, and follow-up with them for the 2-year mandated follow-up period.

Conclusions: This pilot study will determine whether use of the mKidney® system improves LKD follow-up rates at a large living kidney donor transplant hospital. It will provide valuable information on strategies for implementing such a system in a clinical setting, and inform effect sizes for future RCT sample size calculations.

Trial Registration: ClinicalTrials.gov NCT03400085

Keywords: mHealth, transplantation, living kidney donors, follow-up, care management
Introduction

Need for living donor kidney transplantation.

Almost 100,000 patients with end-stage renal disease (ESRD) in the United States (US) are currently on the waitlist for a deceased donor kidney transplant (DDKT). An additional 30,000 are added to the waitlist each year. In 2017, only 14,038 received a DDKT. Most patients who are listed for a kidney transplant today (who do not have a living donor) will have to wait 3-7 years to get an organ offer and the waitlist just continues to grow. Living kidney donation offers patients with ESRD a timely and therapeutic modality that has superior outcomes to DDKT and dialysis [1]. Living donor kidney transplantation has been recognized and promoted as the best treatment option for patients with kidney failure by the American Society of Transplantation Living Donor Community of Practice in a consensus statement [2].

Sequelae of living kidney donation.

Living kidney donors (LKDs) naturally experience a 50% nephron loss (i.e. one kidney) following donor nephrectomy with immediate consequence of a 25-40% loss of renal reserve as measured by glomerular filtration rate (GFR). This decline in GFR might also be consequential in the long-term, especially in the event of de novo disease [3]. Diseases of greatest concern to LKDs in the post-donation period are diabetes mellitus (DM), hypertension (HTN), and glomerulonephritis (GN), which account for over 60% of documented cases of ESRD in the LKD population [4]. Long before de novo diseases cause chronic kidney disease (CKD) and ESRD, they manifest as hyperglycemia, elevated blood pressure, and proteinuria/hematuria. In a recent study, where national data from the Organ Procurement and Transplantation Network (OPTN) was linked to private insurance medical claims, at 7 years post-nephrectomy significantly more (p=0.002) African-American LKDs had renal condition diagnoses compared to white LKDs. This included CKD (12.6% versus 5.5; adjusted hazard ratio [aHR] 2.32), proteinuria (5.7% versus 2.5%; aHR, 2.27), nephrotic syndrome (1.3% versus 0.1%; aHR, 15.7), and any
renal condition (14.9% versus 9.0%; aHR, 1.72) [5]. While the overall risk of developing renal disease is low [6], follow-up and self-care management are important.

**Living kidney donor follow-up is poor in general and incomplete.**

Among LKDs who donated in 2010-2012, complete clinical and laboratory follow-up data (serum creatinine and urine protein) were only successfully collected in 37%, 35%, and 33% of LKDs at 6 months, 1 year, and 2 years post-donation. This prompted a national policy that began requiring centers to collect these data beginning in 2013 [7, 8]. Implementation of even this requirement has shown limited improvement; LKDs between 2013-2015 had only 68%, 62%, and 53% successful follow-up at 6 months, 1 year, and 2 years post-donation. Transplant hospitals currently lack the tools to improve LKD engagement.

**Appropriate living kidney donor follow-up is likely to reduce progression to late-stage CKD and ESRD in kidney donors.**

Routine laboratory tests can screen for subclinical entities like hyperglycemia, elevated blood pressure, proteinuria, and hematuria, which present an opportunity for early detection and control of DM, HTN, and GN. Most importantly, appropriate LKD follow-up would provide an opportunity to detect early-stage CKD thus slowing ESRD progression. Routine screening is especially important for young donors who have many decades of post-donation life expectancy with reduced renal reserve. Moreover, there are racial disparities in post-donation outcomes. African-American LKDs have the highest absolute risk of ESRD post-donation as well as the highest risk attributable to donation (74.7 per 10,000 person-years) coupled with incidence of hypertension and diabetes [6, 9, 10]. Risk of ESRD in African-American donors was 3.1 times higher than matched African-American non-donors. The risk of HTN in African-American
LKDs was 1.52 times that of white donors, and African-American donors were 2.32 times more likely to develop CKD [9].

**Appropriate living kidney donor follow-up will also improve our ability to understand long-term sequelae of donation**

Given the limitations of the current system of LKD follow-up, alternative approaches are of utmost urgency to enable the medical community to uphold its obligation to care for living organ donors. To date, knowledge of health outcomes have been largely limited to perioperative mortality and long-term survival from living donor nephrectomy allowing for ESRD risk prediction, accounting for differences among racial and ethnic minorities [9, 11-15]. Because of the lack of follow up and long-term data, inferences on long-term donor morbidity have been historically limited including about longer-term mortality, cardiovascular disease, and CKD. In addition, only limited pilot data are available on the effect of donation on the pathophysiology of cardiovascular disease; more research to better define the effects of donation on cardiovascular disease surrogates and clinical events is needed [16].

**Preliminary data**

In our formative research of potential LKDs at the Johns Hopkins Hospital, mobile phone ownership was nearly 100%, and in a pilot study of 73 post-donation LKDs, engagement through even simple text communication exceeded 80% at 2 years, far higher than our traditional engagement. Fifty-two percent of LKDs we studied selected e-mail and 45% selected text message as their method of post-donation communication with the transplant hospital. There was no significant difference in the choice of preferred contact method by sex: text messaging was the chosen form of communication for 38% of males and 53% of females (P=0.3) [17]. Text messaging was the chosen contact method for 71% of African American LKDs, 39% of Caucasian LKDs, and 50% of LKDs of other races (P=0.1). E-mail was the
preferred contact method for the youngest (<30 years old) and oldest (>50 years old) donors and text messaging was preferred by LKDs 31-50 years old (p=0.02). This demonstrates feasibility for the use of electronic communications like mHealth to improve upon existing methods of post-donation communication with LKDs and was consistent with Pew Research Center findings that in 2015, 92% of adults in the United States owned a mobile phone [18].

Benefits of mHealth technology to patients and providers.

As mobile phone use has changed the way providers communicate with patients and each other, there is a need to develop the science of mHealth [19, 20](19). mHealth applications designed for smartphones can help empower high-need, high-cost patients to self-manage their health, and mHealth has been perceived to be an ideal tool to engage patient populations in chronic disease management [21].

Benefits of patient engagement.

Growing evidence suggests that healthcare is more efficient and effective when patients are actively engaged in their treatment [22]. Engaged patients collaborate with their providers, are better treated with respect and dignity, receive information related to their care, and are involved in decision-making [23]. LKDs who are better engaged and informed may be able to keep better track of their post-donation health, and may benefit from being able to visualize and summarize their health information, receive guidance on preventive care, and communicate with healthcare providers and the transplant system.

Significance summary.

LKDs experience a 50% nephron loss following nephrectomy with the immediate consequence of a 25-40% loss of renal reserve, and in the post-donation period could develop de novo disease that could lead to CKD and progress to ESRD. Follow-up of LKDs is critical, providing a mechanism for disease detection
and intervention, but current methods have not been successfully or adequately implemented. This mHealth intervention will help patients by early detection of CKD risk factors and therefore early intervention. This will help the long-term research of LKD health outcomes by providing more granular data on more donors. Preliminary data shows promise for the use of electronic communications to connect with LKDs in the post-donation period. New technology such as mHealth to improve follow-up and engagement in LKDs has not yet been explored. The proposed research will identify barriers to technological innovations for LKD follow-up and engagement and design the mHealth system thus informing clinical care management and risk mitigation. This is particularly important for African-American LKDs who have the highest ESRD risk attributable to donation as well as higher rates of post-donation HTN diagnoses [24].

**Innovation**

*The design and development of new technology.*

An effective method of follow-up communication with LKDs that does not place undue burden on either the patient or the provider, that allows for the monitoring and tracking of surgical recovery milestones, and that can detect the development of de novo kidney disease to intervene when possible is needed. We propose to design new mHealth technology to capitalize on available computing power and technologies available that can transform the reach of medical care and research [25].

**Novel approach to improve a health system failure.**

Text messaging, email-based, and mHealth are promising new approaches to rectify the striking gap in regular post-donation medical care for LKDs. Dialysis patients reported high interest in using mHealth to promote physical activity, and mHealth interventions have recently been evaluated in clinical trials for
self-management support, weight management, prevention and management of cardiovascular disease, and diabetes in other populations [26-32].

Benefit and innovation of mHealth for living kidney donor follow-up.

Despite the recent proliferation of mHealth technologies, few are currently used in research studies. The NIH strategic plan supports contributing to the mHealth evidence base because everyone can use this technology. With the national transplant advisory committee and among informal conversations with LKDs on Facebook, we identified five primary benefits to an mHealth system for LKD engagement and follow-up: 1) portability: mHealth goes beyond point of care clinical diagnostics thus following the LKD past transplant hospital visits, 2) scalability: mHealth platforms have been shown to be economical to scale [33], and with no current mechanism for reimbursement for required follow-up, transplant hospitals absorb the cost, 3) rich data input through continuous data sampling: devices and wearables are meant to integrate with daily functions making data collection convenient, which could make LKD follow-up automatic and seamless, 4) personalization capacity, and 5) real time data and feedback with the ability for automated analyses. An mHealth system will allow donors to medically engage with the hospital where they donated a kidney, including having opportunities to ask for medical record review, and even have built-in alert to primary care when laboratory tests or blood pressure measurements might be worrisome. Novel applications of inexpensive and automated electronic communication technologies such as mHealth could enhance patient follow-up and could be applied to other patient populations. In an environment of spiraling healthcare costs where paperwork is administratively expensive and burdensome, this technology could find broad application.
Overview and theoretical framework.

This research is based on the Donabedian 3-factor conceptual framework of care quality, as adapted to LKD follow-up [34, 35]. In the adapted conceptual framework the structures of care can be viewed as both the national organ transplant system as well as the individual transplant hospitals performing the living donor transplant surgery who are responsible for reporting follow-up to the OPTN. Processes of care for LKD follow-up can be viewed as both internal and external to the transplant hospital responsible for reporting. Outcomes for LKD follow-up can be viewed as both short and long-term and vary in measures based on policy requirements and principles of prevention. The development of an mHealth system for LKD engagement and follow-up care addresses both short and long-term outcomes and promote prevention.

Objective

To pilot an mHealth system (mKidney®) and design a future large-scale multicenter randomized control trial of this intervention. We will recruit 400 participants (200/year for 2 years) at the time of LKD to pilot test the intervention. We will compare our ability to achieve required follow-up at 6, 12, and 24 months against controls to help estimate potential effect sizes of the intervention (to inform subsequent RCT design and power calculations).
**Methods**

**Study design.**

An RCT pilot study with parallel group design that will analyze the impact of mKidney®, an mHealth system for living donor follow-up in preparation for a fully powered clinical trial (NCT03400085).

**Study population.**

We plan to enroll 400 LKDs who donate a kidney at Methodist Specialty and Transplant Hospital in San Antonio, Texas during the study period. LKDs (approx. N=200) randomized to the intervention arm will participate in the mHealth system. LKDs (approx. N=200) randomized to the control arm will receive the standard-of-care for follow-up. For the pilot we will limit participation to those who are English speaking; by national policy all donors are ≥18 years of age.

**Study Procedure.**

LKDs will undergo consent and randomization at the clinically required 1-week post-donation clinical visit. Study personnel who have undergone Human Subjects Training will use a written consent form to document consent (Supplemental Materials). Surgeon and clinician members of the study team will not participate in recruitment activities to avoid the potential for coercion and appearance of conflict of interest. Paradata will be collected on the number of acceptances, eligible enrollments, and refusals.

We will use block randomization to assign participants to the intervention or the control group using random block sizes ranging from 2 to 8. Block randomization will improve the probability of balanced groups over the course of the study as well as during shorter time horizons. A statistician, blind to the
group allocations, will generate a list of sequential group assignments using this method. The list will be used to create sequentially numbered, sealed envelopes that will be used to allocate consenting participants to the control or intervention arms of our study. Each patient will have a 50% chance to be in the intervention arm of the study. Patients, healthcare workers on the study team, and study team members responsible for data collection and analysis will be aware of which arm participants are randomized to. Therefore, this study will not be blinded to providers, patients, or study personnel.

Study personnel will assist participants assigned to the mHealth intervention arm with downloading the mKidney® application and explain its functioning. After enrollment in the study, participants in the intervention arm will complete a questionnaire documenting their remote standard of care clinic visit and the required laboratory values at 6 months, 1 year, and 2 years following donor nephrectomy using the mKidney® application. The control participants will be instructed to complete required follow-up as is standard of care, but will not use the mKidney® application to do so.

The primary outcome of interest will be the effectiveness of the mKidney® application by collecting whether or not participants in the intervention and control arms complete their 6-month, 1-year, and 2-year follow-up completely and within the 60-day window of their donation anniversary, as specified in national reporting guidelines. In order to understand logistical or demographic barriers to implementation, we will also collect process data and utilize routinely collected data on LKDs in the study. These data include age, sex, race, ethnicity, and educational level of LKDs.

**Sample size and power calculation.**

If we recruit a total of 400 LKDs over a 2-year period and the proportion of control arm LKDs with compliant follow-up is 50%, we will have 80% power to detect a difference of 13.8% and 90% power to
detect a difference of 15.9%. There is the possibility that we might face low levels of recruitment or high levels of dropout. If we are only able to recruit 300 LKDs over 2 years, then we will have 80% power to detect a difference of 15.9% and 90% power to detect a difference of 18.3%. If we are only able to recruit 200 LKDs over 2 years, we will have 80% power to detect a difference of 19.3% and 90% power to detect a difference of 22.1%.

Table 1. Power Size Calculations.

<table>
<thead>
<tr>
<th>Total N</th>
<th>Control Proportion</th>
<th>Intervention Proportion (80% power)</th>
<th>Delta (80% power)</th>
<th>Intervention Proportion (90% power)</th>
<th>Delta (90% power)</th>
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<td>0.183</td>
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<td>0.638</td>
<td>0.138</td>
<td>0.659</td>
<td>0.159</td>
</tr>
</tbody>
</table>

Figure 2. Power calculation of piloting mKidney® with 200 donors/year. If the projected follow-up rate of donors’ receiving the mHealth intervention is 67% (the minimum threshold for policy compliance), this study will have 79% power to detect a difference. If the follow-up rate in the intervention arm is 70%, this study will have 95% power.
Analysis.

Descriptive statistical methods will be used to analyze frequency of key variables including chi-squared and rank-sum tests. Follow-up rates between intervention recipients and controls will be compared using generalized linear regression. Additionally, we will perform subgroup analyses for younger donors (age at donation < 40), older donors (age ≥ 40), men, and women. The impact of mKidney® on follow-up compliance will be compared to historical follow-up with a difference-in-difference framework. All analyses will follow an intention-to-treat principle. Data will be analyzed with Stata 15 for Linux (StataCorp Inc., College Station, TX, USA).
IRB Approval

This study was reviewed and approved by both the Johns Hopkins School of Medicine Institutional Review Board (IRB00162212) and Methodist Specialty and Transplant Hospital Institutional Review Board (IRB12091661).

Results

We are anticipating beginning recruitment for our RCT pilot study in May of 2018 at Methodist Specialty and Transplant Hospital in San Antonio, Texas. We plan to recruit for 2 years, and follow-up with participants for the 2-year mandated follow-up period. Pilot findings will inform the development of a larger, multi-site proposal and will provide process measures, an initial comparison to standard or care, and will inform effect size estimation for a fully powered RCT.

Discussion

Potential limitations and proposed solutions

Insufficient recruitment.

One potential challenge may be participant recruitment. While we anticipate high participation, even with low recruitment we believe the study will be feasible. Given our expected living donor volume of approximately 800-1000 LKD transplants during the study period, the recruitment period can be extended if needed. If living donor volume at the pilot transplant hospital is insufficient, then we will leverage the existing study population, experienced research team, and resources associated with an NIH funded cohort study of living kidney donors. These resources will help to ensure timeliness, feasibility, and high likelihood of success. It is also possible that the effect size will be larger than estimate in the power calculations and that a smaller sample might provide adequate power.
Special populations.

Methodist Specialty and Transplant Hospital patients are mostly white and Hispanic, thus we might have limitations on recruitment of African-Americans and Asians. We will consider age-related issues to technology adaptation and use, which could be a limitation to implementation of mKidney®. Based on recent trends at our pilot site, we anticipate approaching patients with a wide distribution of age.

Technical infrastructure and connectivity.

We will leverage the robust resources of emocha Mobile Health Inc. and the Johns Hopkins University to limit possible challenges to interoperability and functionality. Future updates to mobile operating systems or related software might affect the function of mKidney®. We will continuously monitor the function of mKidney® and provide updates as necessary with the developer, emocha Mobile Health.

Need for tailoring for differences in adoption among different racial and ethnic groups.

Should we receive different feedback based on any factors including sex, age, or race/ethnicity that requires additional tailoring of mKidney® to address health disparities, there might be the need to design different mHealth systems or different system components to address health literacy or other concerns to reduce health disparities. The national transplant advisory committee has expertise in the design, development and culturally tailoring of transplant education materials and tools should the need arise to develop different versions.
Acknowledgements

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Conflicts of Interest

Three of the authors G.S., V.W., and S.S. are employees of emocha Mobile Health, Inc.

Abbreviations

CKD: chronic kidney disease
DDKT: deceased donor kidney transplant
DM: diabetes mellitus
ESRD: end stage renal disease
GFR: glomerular filtration rate
GN: glomerulonephritis
HTN: hypertension
LKD: living kidney donor
NIH: National Institutes of Health
OPTN: Organ Procurement and Transplantation Network
RCT: randomized control trial
UNOS: United Network for Organ Sharing
References


