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Research Article

Postoperative Telemonitoring Following Kidney Transplantation: Effects on Early Hospital Readmissions and Graft Outcomes

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Abstract

Background: Telemonitoring has been recently shown to improve outcomes and reduce hospital admission rate in cardiac patients. Effect of telemonitoring on early hospital readmission and graft outcomes in kidney transplant population is not well studied.

Methods: In this retrospective observational study, we compared 167 kidney transplant recipients who were discharged with telemonitoring to 191 historic controls with no telemonitoring. All telemonitored patients were monitored with the use of CardioCom device, by a registered nurse trained in transplant and home care. To assess the impact of the telemonitoring on readmission rate, logistic regression analysis was performed. Survival analysis was conducted to assess impact on one-year graft and patient survival.

Results: Of 358 total patients, 32.1% (n=115) had early readmission. Of these, 56 of the 167 patients (33.5%) with telemonitoring experienced early readmission, compared to 59 of 191 controls (30.9%). Telemonitoring was associated with slightly higher early readmission compared to control group, which was not statistically significant (OR=1.13, 95% CI=0.72-1.76, p=0.59). Telemonitored and control patients had comparable one-year graft and patient survival, 97% vs. 94.2% (HR: 0.51; 95 CI: 0.18-1.48, p=0.22) and 98% vs. 96.3% (HR: 0.32; 95 CI: 0.07-1.55, p=0.14) respectively.

Conclusions: Early post kidney transplant telemonitoring did not show significant reduction in early hospital admission rate or improvement in 1-year patient/ graft survival.

Keywords: Kidney transplantation; Telemedicine; Graft outcome; Hospital re-admission

Abbreviations: CMS: Centers for Medicare Services; ED: Emergency Department; HER: Early Hospital Readmission; MI: Myocardial Infarction; TKP: Telemonitoring Kidney Program; UHCMC: University Hospitals Cleveland Medical Center

Introduction

Early hospital readmission, defined as readmission within 30 days after discharge, is a common metric for hospital quality that may indicate care transition failure or premature discharge. In 2013, the Centers for Medicare and Medicaid Services (CMS) initiated Hospital Readmission Reduction Program (HRRP) as a permanent component of Medicare's inpatient hospital payment system to most acute care hospitals. The current focus in the HRRP is readmissions occurring after initial hospitalizations for selected conditions namely, heart attack, heart failure, pneumonia, chronic obstructive pulmonary disease, elective hip or knee replacement, and coronary artery bypass graft. As part of HRRP, Medicare can penalize hospitals with higher than national average of readmission rates for these diagnoses, with a maximum rate of penalty of 3% in 2017. For the fiscal year of 2017, CMS estimated that these penalties will be \$528 million [1]. Although this penalty is currently restricted to the above diagnoses, it is possible that the penalty will be expanded to other conditions. As such, transplant centers are focusing on assessing causes and implementing strategies to reduce readmission after kidney transplantation.

The kidney transplant population has markedly high early readmission rate, when compared to the general Medicare population

[2-4]. In 2013, 17,600 kidney transplantations were performed [5], and ED visits and readmission rates within the first 30 days post transplantation were reported to be as high as 12% and 31% respectively [2,4]. Readmission after kidney transplant has been a focus for several studies that sought to identify predictors of readmission, and also strategies to reduce it. High readmission rates are associated with various center, recipient, and donor factors [2]. Furthermore, readmission has been associated with high patient burden in hospitals, increased costs, and worse graft survival for kidney transplant recipients-perhaps due to improper coordination of care and immunosuppression medications errors [6-8]. Strategies to reduce readmissions are gaining prominence, in an effort to improve hospitals' quality of care and health outcomes and to decrease costs [9,10]. Telehealth is one of such strategies that had been studied in the context of non-transplant related hospitalizations.

Telehealth is utilization of telecommunication technology in health

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care delivery across distance. According to The Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services, it includes activities involving telecommunications and electronic information to support and promote long-distance clinical health care, patient and professional health-related education, public health, and health administration. Telehealth services can be diverse and include telecheck-ups (e.g., phone calls to ensure that the patient is doing well), telemonitoring by recording physiological data, teleconsultation, and teletreatment [11]. Remote patient monitoring, also sometimes referred to as telemonitoring or telehomecare, has been recently shown to improve outcomes and reduce readmission, mainly in congestive heart failure (CHF) patients. In a meta-analysis that included thousands of patients with CHF, telemonitoring has reduced all-cause mortality by 34%, all-cause hospitalizations by 9% [12]. In our own health system, telemonitoring has been effective in reducing 30-day hospitalization by 50% among patients with CHF (unpublished data). Studies are lacking on the influence of telemonitoring on outcomes following kidney transplantation. In this study, we explored our experience with telemonitoring in the early post-operative period after kidney transplant surgery, and studied its impact on readmission, rejection rates, and one-year graft and patient survival.

Materials and Methods

Study design

This retrospective observational study included adult patients (Age>18 years) who underwent kidney alone transplant at University Hospitals Cleveland Medical Center (UHCMC), between January 1, 2012, and December 31, 2015. Patients who were discharged to acute rehabilitation, or died prior to discharge were excluded. The study protocol was approved by the UHCMC Institutional Review Board (IRB # 01-17-16), and adheres to the Declaration of Helsinki and Istanbul.

Telemonitoring protocol

Starting in November 2013, UHCMC instituted the Telemonitoring Kidney Program (TKP) in which all kidney transplant recipients discharged to their homes from UHCMC were offered telemonitoring services, unless they lived in a zip code that is not in the coverage area of UHCMC home health services.

We used the Commander Flex^{*} monitoring system by Cardiocom (Medtronic, Minneapolis, Minnesota) as our telemonitoring system. The telehealth monitor is able to transmit through an internal Wi-Fi, has branching logic, and has the ability to be programmed with specific questions for each patient, thus individualizing care. All telehealth patients are monitored seven days a week for the first 30 days post discharge, or until the patient is deemed stable per the nurse monitor and physician involved. The UHCMC telemonitoring team is composed of a doctoral-level nurse, a staff registered nurse (RN), and two part time equipment technicians. The staff RN received education from a full-time, experienced transplant nurse coordinator prior to implementation of this protocol.

TKP included two parts-an intensive home visit, followed by continuous monitoring. The initial one-time intensive home visit made by a homecare RN includes the installation of the telehealth monitor and instruction on its use. The home visit also includes reviews of the patient's new medication regime, especially immunosuppression medications, education on diet and hydration requirements, and training on checking blood pressure and vital signs. Continuous monitoring includes a daily phone call by a nurse. The incision is visualized daily through a webcam as part of a limited physical assessment. The patient is asked about temperature, blood sugar if applicable, urination, hydration, appetite, level of pain, and incision problems, including any drainage. Vital signs and other data are transmitted to the clinical team (transplant nephrologist, surgeon, and nurse coordinator) daily *via* the transplant charting system and the homecare electronic medical record. Emergent issues generate direct contacts with the transplant physician. This mode of monitoring is in addition to the direct channel of contact between patient, and clinical transplant nurse coordinator. The patient is informed to primarily contact the clinical transplant nurse coordinator and not the telemonitoring nurse for any questions or health related issues.

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Patients who participated in the TKP were compared to patients who underwent transplant between January 2012 and November 2013 and thus did not receive telemonitoring. We excluded patients who were discharged to a skilled nursing or acute rehab facilities. We also excluded three patients who died during the hospitalization for kidney transplant. There were 10 patients who refused and another 15 patients who lived outside of the geographical area of coverage who were included in the control group. In all, 358 adult kidney transplant recipients were discharged home with complete follow-up data. Of these patients, 191 were in the control group and 167 were in the TKP group (Figure 1). Overall, there was good adherence to protocol, with a compliance of over 90% with transmission of vital signs, and telephone call.

Immunosuppression and routine post-transplant care

All patients received induction therapy with either 20 mg of Basiliximab, or Anti-thymocyte globulin (ATG). Our center uses ATG for all deceased donor transplant recipients and living donor recipients under 50 years of age. All patients received Tacrolimus and Mycophenolate Mofetil as maintenance immunosuppressive agents unless they experienced side effects from them. Solumedrol at 500 mg IV is also used as induction agent, followed by 60 mg IV twice daily for four additional days. Following this steroid induction, patients who don't have history of high PRA>80, are not re-transplants, and don't experience delayed graft function, are maintained steroid free. After discharge from initial hospitalization, patients are seen in post-transplant clinic by nephrologist, and transplant coordinator within



1-2 weeks. Routine laboratory testing includes renal function panel, complete blood count, and tacrolimus level. This is done twice weekly for the first three months after transplant.

Outcomes

Primary exposure was assignment of telemonitoring at discharge. Primary outcome was readmission within 30 days of discharge. Patients with multiple readmissions within 30 days were counted as having one. There were four different transplant nephrologists during the study period, and criteria for determining admission were based on the judgment of transplant nephrologist actively involved. Secondary outcomes were ED visits, acute rejection episodes that were identified by for cause biopsies and according to contemporary BANFF criteria, patient survival, and graft survival through 1-year of followup. All demographic data, hospital admission and discharge dates, immunosuppression, and outcomes data were abstracted from the electronic medical record.

Predictor variables

All variables used to predict re-admission or other outcomes were obtained from the electronic medical record. These variables included demographics, comorbidities, and prior transplantation history, as well as various measures specific to transplant status. Such measures included cause of end stage renal disease (ESRD), organ type (living *vs.* deceased donor), dialysis vintage (pre-emptive transplants were given a value of zero), class I and II panel reactive antibodies (PRA), HLA mismatch, type of induction agent used (ATG, or Basiliximab, or no induction for HLA identical kidney transplant), calcineurin inhibitor (cyclosporine, or tacrolimus), steroid maintenance versus withdrawal, occurrence of delayed graft function (DGF), and transplant ureteral stent use. We also collected length of stay for index hospitalization of kidney transplant and number of office visits in the first 30 days.

Statistical analysis

Statistical tests were used to compare distribution of covariates across TKP and controls. Since the 2 groups were comparable in demographics, we did not run propensity score matching. We used Chi-Square test for categorical variables, and t-test or Wilcoxin rank sum test for continuous variables. To assess the impact of the TKP on readmission rate, logistic regression analysis was performed. We also performed logistic regression analysis to compare ED visits, and rejection rates between TKP and control groups. Patient and graft survival were compared between TKP and control group using Kaplan-Meier estimation and logrank testing [13]. For this survival analysis, transplant day was considered as day zero. All patients were censored at one-year post transplant. For graft loss, we considered death with kidney function as graft loss. Cox proportional hazard models were used to estimate the relative hazard associated with TKP for patient and graft survival outcomes [14]. Patient and graft survival were also compared between readmitted patients and those not readmitted. For multivariate models, we included baseline variables whose p-values between both groups were lower than 0.2. R version 3.4.0 (The R Foundation, Vienna, Austria) was used to perform the analysis.

Results

There were 358 kidney transplants included in the analysis. Of these, 191 were discharged without telemonitoring (controls), and 167 with telemonitoring (Figure 1).

Baseline characteristics

Table 1 illustrates baseline characteristics of patients, stratified by Telemonitoring. In the Telemonitoring group, there were more African Americans, with higher hypertension co-morbidity, dialysis vintage and Hepatitis C compared to control group. The two groups were otherwise similar in other baseline characteristics: age, gender, etiology of ESRD, BMI, donor source, heart disease, history of previous transplant, delayed graft function, induction agent, Tacrolimus use, PRA, steroid maintenance, HLA mismatch, and length of stay for kidney transplant.

Impact of telemonitoring on outcomes

Readmission: Of 167 Telemonitoring patients, 56 had experienced readmission (33.5%), compared to 59 of 191 controls (30.9%). In univariate model, telemonitoring was associated with 13% higher likelihood of readmission compared to controls, which was not statistically significant (OR=1.13, 95% CI=0.72-1.76, p=0.59). In multivariate model, no statistically significant difference in rate of readmission between the 2 groups was noticed (OR=0.97, 95% CI=0.60-1.58, p=0.92) (Table 2).

ED Visits in the first 30 days: Of 167 Telemonitoring patients, 35 had presented to ED (21.0%), compared to 32 of 191 controls (16.8%). In univariate model, telemonitoring was associated with 32% higher likelihood of ED visits in the first 30 days compared to controls, which was not statistically significant (OR=1.32, 95% CI=0.77-2.24, p=0.31). In multivariate model, rate of ED visits among the 2 groups was not statistically significant (OR=1.09, 95% CI= 0.61-1.96, p=0.71) (Table 2).

Acute Rejection First Year: Of 167 Telemonitoring patients, 16 patients had BPAR in the first post-transplant year (9.6%), compared to 24 of 191 controls (12.6%). In univariate model, telemonitoring was associated with 27% lower likelihood of BPAR in the first one year, compared to controls, which was not statistically significant (OR=0.73, 95% CI=0.38-1.44, p=0.37). In multivariate model, difference in BPAR incidence was not statistically significant (OR=0.68, 95% CI=0.33-1.40, p=0.29) (Table 2).

Graft and Patient survival (Figure 2 and Figure 3)

Five out of 167 of the Telemonitoring patients experienced graft loss within one year, with a graft survival of 97%, compared to 11 out of 191 in the control arm with a graft survival of 94.2% (HR=0.51; 95% CI=0.18-1.48, p=0.22). In multivariate Cox model for graft survival, no statistically significant difference was noticed between the 2 groups (HR=0.46; 95% CI=0.15-1.46, p=0.19). Two out of 167 of the telemonitoring patients died at one year, with a patient survival of 98.8%, compared to 7 out of 191 patients in the control arm, with a patient survival of 96.3% (HR=0.32; 95 CI=0.07-1.55; p=0.16). In multivariate Cox model, no statistically significant difference was noticed (HR=0.29; 95% CI=0.05-1.66, p=0.17). These results are illustrated in Table 2.

Impact of readmission on one-year patient and graft survival

Of 358 patients, 115 (32.1%) were readmitted within 30 days of discharge. Acute kidney injury was the most common cause for admission, followed by infection and fluid collection (Table 3). The reason for readmission was extracted from the primary diagnosis for admission using ICD code 10. Nine out of 115 of the readmission patients experienced graft loss at one year, with a graft survival of 92.2%, compared to 7 out of 243 of patients who didn't have readmission, with a graft survival of 97.1% (HR=2.78; 95 CI= 1.04-7.47; p=0.04). Among readmitted patients who lost grafts at one-year, telemonitoring was not associated with statistically significant better graft survival (HR=0.12; 95 CI=0.02-1.0; p=0.05). Five out of 115 of the readmitted patients died

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	Telemonitoring	No Telemonitoring	p value
Total number	167	191	
Median Age (IQR)	53.0 (40.5, 62.0)	51.0 (43.0, 61.0)	0.98
Males (%)	107 (64.1)	107 (56.0)	0.15
Black Race (%)	66 (51.5)	67 (35.1)	<0.01
Etiology (%)			0.09
Other	23 (13.8)	27 (14.1)	
Diabetes	35 (21.0)	47 (24.6)	
Glomerulonephritis	34 (20.4)	32 (16.8)	
HTN	65 (38.9)	59 (30.9)	
PKD	10 (6.0)	26 (13.6)	
Median BMI (IQR)	28.4 (24.8, 33.0)	28.81 (24.8, 33.3)	0.7
Living Donor (%)	34 (20.4)	50 (26.2)	0.2
Heart Disease (%)	34 (20.4)	25 (13.1)	0.1
Hypertension (%)	134 (80.2)	117 (61.3)	<0.001
Mean Dialysis Vintage (years)	5.0 (2.2, 7.0)	3.7 (1.8, 5.4)	<0.01
Retransplant (%)	22 (13.2)	36 (18.8)	0.19
Delayed Graft Function (%)	40 (24.0)	36 (18.8)	0.29
Induction (%)			0.1
None	3 (1.8)	1 (0.5)	
Basiliximab	8 (4.8)	19 (9.9)	
ATG	156 (93.4)	171 (89.5)	
Tacrolimus (%)	163 (97.6)	190 (99.5)	0.29
HCV (%)	13 (7.8)	4 (2.1)	0.02
Mean Class I PRA (SD)	17.1 (28.7)	19.9 (31.9)	0.39
Mean Class II PRA (SD)	14.6 (29.8)	17.1 (29.7)	0.43
Mean HLA mismatch (SD)	4.2 (1.4)	4.1 (1.5)	0.57
Mean Length of Stay (SD)	8.0 (4.6)	8.1 (7.2)	0.91
Steroid Use	87 (52.1)	100 (52.4)	1

 Table 1: Baseline characteristics of the kidney transplant recipients, stratified by assignment to telehealth.

Telmonitoring group included kidney transplant recipients who were transplanted between November 2013 and December 2015 while controls were transplanted between January 2012 and October 2013. Heart Disease was defined as having history of coronary artery disease, or congestive heart failure or valvular disease or valvular surgeries. Hypertension was defined as either history of hypertension or being on anti-hypertensives. Four patients who underwent HLA identical kidney transplants didn't receive any induction. Stent refers to the use of stent in transplant ureter. Continuous variables are described using mean and SD (standard deviation), and median and IQR (interquartile range) for normal and non-normally distributed variables respectively. Categorical variables are described using frequency. Comparisons between two groups are made using the Wilcoxon rank-sum test, t-test for continuous variables and Chi-Square test for categorical variables.

at one year, with a patient survival of 95.7%, compared to 4 out of 243 who didn't have readmission, with a patient survival of 98.4% (HR: 2.70; 95 CI: 0.72-10.05; p = 0.14) (Table 2).

Unadjusted Adjusted¹ Outcome Effect Size 95 % CI Effect Size 95 % CI Early Readmission 1.13 0.72-1.76 0.97 0.60-1.58 Early ED Visits 1.32 0.77-2.24 1.09 0.61-1.96 RPAR 0.68 0.33-1.40 0.73 0.38-1.44 Graft Survival 0.51 0.18-1.48 0.46 0.15-1.46 Patient Survival 0.07-1.55 0.29 0.05-1.66 0.32

Table 2: Impact of telemonitoring on outcomes.

¹Adjusted for baseline variables with p-values less than 0.2 between telemonitoring and control groups. These were race, hypertension, dialysis duration in years, transplant ureter placement during operation, hepatitis C Virus antibody, and number of clinic visits in the first 30 days after discharge. For early readmission, ED (emergency department) visits, and BPAR (biopsy proven acute rejection), the odds loaistic effect sizes are ratios rearession from modeling. graft and patient For survivals. effect the sizes are hazard ratios from Cox modeling.



Discussion

In our observational study, telemonitoring patients were more blacks, had longer dialysis vintage, more Hepatitis C, and more hypertension. Although there were slightly higher emergency room (ER) visits, early hospital readmission (EHR) and 1-year graft survival rate in the telemonitor group, all were not statistically significant.

Reporting bias might be responsible for the observed higher ER visits and EHR in the Telemonitoring group due to closer patient observation. In addition, it should be noted that the introduction of new Kidney Allocation System (KAS) coincides with introduction of Telemonitoring protocol in our study. That might explain the differences in baseline variable for dialysis vintage. Also, introduction of new anti-viral treatment for Hepatitis C happened around the same time that allowed us to transplant Hepatitis C patients with Hepatitis C in the intervention group.

In this study, we report 32.1% incidence of readmission rate within 30 days after kidney transplantation which was similar to the higher

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end in prior studies [2]. We considered patients who were admitted under 'observation status' as having an inpatient admission. Unlike some other transplant centers, our center does not have an outpatient transplant procedure unit that would administer intravenous fluids, and other immunosuppressive medication infusions. Such variations in practice might explain wide range in the readmission rates at different transplant centers that were found in prior studies [2].

McAdams-Demarco, et al. has shown that early hospital readmission is a strong predictor of late hospital readmission. In general, hospital readmission among kidney transplant population was associated with 50% higher risk of graft loss and mortality, when compared to patients without early readmission owing to improper coordination of care and immunosuppression medications errors [6-8]. In our study, readmission was associated with almost 3 to 4 times higher likelihood of graft failure, and patient death at one year.

There is mixed evidence in literature about impact of telemonitoring on patient outcomes. A randomized controlled study involving chronic heart failure (CHF) patients with six-months of Telemonitoring showed that all-cause mortality was significantly lower in the telemonitoring group as compared with the control group (5% vs. 17.5%, P=0.01). Furthermore, the total number of hospitalization, dialysis, or death was significantly lower for the telemedicine group compared with the control group [15]. Similarly, a Cochrane meta-analysis of studies assessing the benefits of telemonitoring in heart failure clinics has also shown that it is associated with reduced all-cause mortality [16]. However, two other large studies involving CHF patients have not shown any significant reduction in all-cause mortality [17, 18]. Fewer data are available for acute myocardial infarction (AMI) patients. A small retrospective observational study reported that telemonitoring was associated with lower readmission rate (5.8 vs. 28%) [9]. Proposed mechanisms in literature for improving patient outcomes in cardiac patients due to telemonitoring include early detection of disease deterioration and prompt medical intervention and increasing active patient participation in health care management, with movement towards personalized health care planning [19,20]. The key to success of this approach is the predictive value of the monitored variables [21].

Remote patient monitoring or telemonitoring, as in our study, is only one aspect of telehealth. Other aspects of telehealth include

Dessen for Deedwinsion	Number of Readmissions (115)	
Reason for Readmission	N (%)	
AKI	32 (28%)	
Fever and Infection	16 (14%)	
Fluid Collection	12 (10%)	
Dehydration	11 (10%)	
Wound Complication	10 (9%)	
Volume Overload	7 (6%)	
Hyperkalemia	4 (3%)	
Pain	3 (3%)	
Atrial Fibrillation	2 (2%)	
Anemia	1 (1%)	
Other	17 (14%)	

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Table 3: Reason for Readmission.

telemedicine where physicians are present at both locations, usually an expert providing consultation at main hospital center and patient and general physician at the remote location. This dual provider approach allows for a comprehensive virtual visit replacing the need for the patient to travel long distances. A recent systematic review reported utility of telehealth during post-surgical care [22]. Telehealth was analyzed by one of three timetables in post-surgical care: during scheduled follow up, as ongoing monitoring (like in our study), or on an "as needed" basis. Of the 21 studies included in the review, only one study involved kidney transplant patients, with primary end points of adherence to anti-hypertensive medications and adequate blood pressure control [23]. These studies did not look at effect on readmission rates or analyzed clinical outcomes in heterogeneous patient populations (pediatric urologic procedures, orthopedic trauma, laparoscopic inguinal hernia repair, cholecystectomy, knee and hip arthroplasty, and parathyroidectomy), making application to kidney transplant somewhat difficult. Similar to our study, there was no significant difference in many of the outcomes but there was a trend towards more complications in the telehealth group (2.8 vs. 0.4), which could be due to a reporting bias associated with closer monitoring. Reported advantages of Telemedicine protocols were less work time off per patients and caregivers [24,25]. Reduced costs associated with pretransplant evaluations and post-transplant care [26-28].

To our knowledge, this study is the first to report the impact of early Telemonitoring on hospital readmission and graft outcomes in kidney transplant population.

In contrary to prior studies included cardiac patients, our study suggests that Telemonitoring following kidney transplantation does not significantly reduce the risk of readmission, or improve one-year graft or patient survival. The contradictory results between the two populations might be due to the significant difference in the management protocols and symptomatic improvement after early intervention in certain disease such as CHF. Cardiac patients benefit from daily monitor and adjustments of medication based on cardio-vascular parameters (volume, blood pressure, heart rate, etc.) which is not the case for the kidney transplant population.

Owing to the retrospective observational design, our study might have potential hidden and overt bias. The small number in each group may have resulted in errors associated with hypothesis testing (type I and type II errors). In addition, the duration of telemonitoring for one month may have been too short to impact the one-year outcomes. Training patients and care providers on device use, collection and interpretation of results, as well as incorporation of the remote data into routine clinical practice are also some of the reported limitations

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of Telemonitoring studies [29-31].

In conclusion, early hospital readmission rates are high in kidney transplantation, and early Telemonitoring protocol does not show benefits. Larger prospective randomized studies that extend the telemonitoring to a longer post-transplant period, and study qualitative outcomes such as patients' perception of quality of care are warranted.

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Authorship

- Nagaraju Sarabu, Joshua J Augustine, Edmund Q Sanchez- Participated in study design.
- Nagaraju Sarabu, David Ngendahimana, Thomas E Love- Participated in data analysis.
- Nagaraju Sarabu, Nissreen Elfadawy, Kenneth J Woodside, Vanessa R Humphreville, CTS, Donald E Hricik- Participated in manuscript writing.
- Nagaraju Sarabu, Mohammad Abdalla- Participated in chart review and data collection.

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