ASSESSMENT OF PHYSICAL ACTIVITY IN POST RENAL TRANSPLANT PATIENTS USING ACCELEROMETERS

by

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ABSTRACT

Background: Post kidney transplant patients have numerous complications after transplantation due to their underlying co-morbid conditions and post transplant medications. These complications include reduced kidney function, high blood pressure, weight gain, and hyperlipidemia. While many of these issues are believed to be at least partially associated with being a post transplant patient, the possibility that they are caused, either directly or indirectly, to being physically inactive has yet to be explored. Research has shown that most of these issues tend to improve once a person becomes physically active. In order to find if prescribing physical activity to post renal transplants is a viable method of reducing these complications, it will be necessary to identify factors that may impact the ability of transplant recipients to be physically active, such as reduced kidney function. By evaluating the relationship between kidney function and physical activity, future protocols can be designed to address the problems of physical activity in post renal transplants.

Methods: Twenty post renal transplant patients who were 3 to 18 month post treatment wore a digital accelerometer for one week after a clinic visit to monitor their daily activity. In addition to the data collected from these instruments, demographic and laboratory data such as blood pressure, heart rate, age, blood urea nitrogen, and creatinine were collected at the date monitoring was initiated. Medical records were reviewed and their most recent blood urea nitrogen and serum creatinine values were recorded

Results: Only one subject met the Center for Disease Control and Prevention's criteria for being physically active. Using correlation analysis, serum creatinine was found to be positively associated with the number of minutes of activity ($p = 0.018$), while blood urea nitrogen ($p = 0.347$) was not associated. These associations were persistent even after adjusting for confounders that are known to be associated with physical activity such as age, gender blood pressure, and resting heart rate.

Conclusions: This pilot study suggests that kidney function does play some role in the level of physical activity. While the models did adjust for some confounders, other factors that could have impact on physical activity like medications and diet need to be controlled for in future studies. It is suggested that these variables, along with a larger sample size, may yield an understanding of how post renal transplant patients' kidney function has impact on their physical activity levels.

1. INTRODUCTION

1.1 Complications in Post Transplants

The United Network for Organ Sharing (UNOS) in conjunction with The Organ Procurement and Transplant Network (OPTN) has been tracking organ transplants since the middle of 1987. Their data show that between January 1st, 1988, and August 31st, 2008, there were 440,537 organ transplants performed in the United States. The most common transplant being kidney transplants (261,803 procedures) followed by liver transplants (92,370 procedures). While a majority (406,683) of these transplants was in adults, even children under the age of one have had transplants (5,399) including heart transplants (1,683). Improving the long term survival for all transplant recipients, there is the possibility of long term survival. For example, over 90 percent of those receiving a kidney transplant from living donors survive at least five years post transplantation. This creates a large and growing segment of the population with chronic health concerns that require constant monitoring and specialized care to prevent post transplant complications, which makes their care a public health issue (1).

The nature and type of complications after an organ transplant varies widely. Due to the risk of organ rejection, physicians frequently prescribe anti-rejection drugs that lower the immune response. Drugs like cyclosporine (Neoral or Gengraf), prednisone, Tacrolimus (Prograf), and mycophenolate mofetil (Cellcept) are some of the most widely used anti-rejection drugs. Each of these medications has unique side effects that patients need to be aware of and monitor. Hypertension, hyperlipidemia, diabetes and weight gain are all side effects related to many of these drugs. Because the immune system of these patients is suppressed, antibiotics are also prescribed initially after transplant

recipients to prevent infection. These drugs also have side effects, but not they are prescribed only for the short term. Over time patients will be able to reduce the amount of medications they take and some stop medications, but most of them will be required to take some form of ant-rejection medication for the rest of their lives (2-4).

There are an estimated quarter of a million people in North America who are living with a transplanted kidney (1). These post transplant patients tend to have complications related to their condition. These issues include reduced kidney function, high blood pressure, weight gain, and hyperlipidemia (4). While waiting for a transplant, a potential kidney recipient tends to be on dialysis. In 2004, a young adult could expect to wait a median time of 1,788 days for a kidney transplant (1). Renal transplant patients tend to have complications due to being on dialysis for an extended period of time (6). After the transplant, the drug regime can be highly variable (2-4). As stated, the side effects of post-transplant medications can include hypertension, weight gain, and hyperlipidemia and reduced renal function. All these medical complications need to be monitored for in post renal transplant patients.

1.2 Benefits of Physical Activity

The lack of physical activity by Americans has been widely reported in the scientific literature. The United States Department of Health and Human Services reported in year 2000, the amount of lost wages to employers for overweight and obese employees was over $117 billion. Department of Health and Human Services research shows that increases in physical activity in people have the following benefits (7):

- Decreases the risk of heart disease

- Decreases the risk of developing diabetes;
- Decreases the risk of developing high blood pressure while reducing blood pressure level in people who already have high blood pressure;
- Helps to maintain a healthy weight and lowers body weight in those who are overweight.

These conclusions are not only supported by the Surgeon General, but the Surgeon General goes further to advocate the promotion of more physical activity in teenagers, senior citizens, and those who are at risk for health related issues like people with cancer or diabetes (8). The 1999 Centers for Disease Control (CDC) physical activity guidelines state that in order to receive benefit from physical activity, a person needs to have five periods a week of moderate activity lasting 30 minutes or more; or three periods of vigorous activity lasting twenty minutes or more (9). Studies have shown that the more people know of these CDC guidelines, the more likely they will self report enough activity to meet these guidelines (10). Most self report physical activity surveys have been reported with high levels of reliability and/or liability (11 -15). But recently, studies have shown that many physical activity self report surveys, such as International Physical Activity Questionnaire (IPAQ), actually over-estimated the amount of physical activity people do when compared to other forms of measurement tools such as fitness testing, pedometers, and accelerometers (13, 16–19). This raises the issue that while people should be aware of the health benefits of physical activity, the most accurate method of capturing the level of physical activity may not be the self-reported survey method (20).

1.3 Physical Activity in Post Renal Transplants Recipients

As stated, it is unknown if it is the change in activity levels, the medications, or a combination of the two that leads to post transplant complications; or if the post transplant complications create a level of low of physical activity. The National Kidney Foundation recommends that people with kidney disease keep themselves healthy with exercise, particularly before transplant (2, 5-6, 21-23). After surgery, post kidney transplants patients are advised to exercise to avoid complications (2, 24-25). But reports show that most post renal transplants are not following these recommendations. Some research groups are attempting to utilize direct intervention techniques to improve activity levels in this specialized population (26-31).

1.4 Proposed Research

A pilot study was conducted to find whether the physical activity levels of post renal transplants are associated the level of kidney function. The hypothesis of the study was "There is a relationship between the physical activity levels and renal function in post kidney transplant patients." The aims of the study were:

1. To define renal function as Serum Creatinine and Blood Urea Nitrogen.
2. Find the level of physical activity in post renal transplants using the IPAQ survey and digital accelerometer.
3. Find an association between renal function and physical activity in post renal transplants after adjusting for confounders.

Because self reported physical activity levels have been shown to be inaccurate, digital accelerometers were used to measure the level of physical activity.

2. MATERIALS and METHODS

2.1 Selection and Recruitment of Subjects

Adult subjects for this study were recruited from the Oregon Health & Sciences University Kidney Transplant Clinic. Pediatric subjects were recruited from the Pediatric Kidney Transplant Program at Doernbecher Children's Hospital. For this protocol, subjects under the age of twenty-one years were classified as pediatric participants. Due to the structure of the clinics at Oregon Health & Sciences University there is an overlap in patient care between the adult and pediatric clinics. Pediatric patients may continue to see their transplant physician after the age of eighteen, while the patients in the adult clinic may be as young as eighteen. Most pediatric kidney transplant patients at Doernbecher Children's Hospital are followed by their transplant physicians, while almost half of the renal transplant patients in the Oregon Health & Sciences University Kidney Transplant Clinic are followed by their local nephrologists and are referred back to the transplant clinic at OHSU on a regular basis for post transplant management.

Eligibility criteria for this study protocol were similar to other studies of this type. This was done to create standards that had strong external validity. Mini Mitter digital accelerometers have been validated in children as young as thirteen. Because of this, the lower age limit for the study was set at thirteen years old. The accelerometers do not have an upper age range, but research has shown that age does not become a factor in

physical activity until about the age of sixty years old (32 – 34). Because of this, an upper age limit was set at sixty years old. The IPAQ survey has been used in research with subjects as young as fifteen and in those over sixty years old, but has not been validated in people thirteen or fourteen year olds. For this study, age at the time of study was based on the first day of wearing the accelerometer.

Potential subjects were limited to those between 3 to 18 months post transplant. The lower time limit was selected for a number of reasons. The first reason was to allow post treatment subjects time to heal after transplant. The second reason was to allow for the subject to be on a stable post transplant medication regime. The third reason was to allow the subject time to enter a normal life cycle after transplant. The upper bound was selected since most patients have rejection episodes within the first 18 months and the study will attempt to capture the relationship between activity and complications.

In addition to age and time after post transplant, subjects were required to meet three other criteria. The first was the ability to ambulate. This requirement was set since the accelerometer was created specifically for people who could walk and/or run. The second requirement was that the subject did not have heart and/or lung disease. The third requirement was that the subjects do not have a fever or show signs of an illness. These criteria were used since they could be potential confounders. Potential subjects were identified by co-investigators and sub-investigators from their clinics. These potential subjects were met in clinic after their scheduled visit and asked to join the study. Those who joined the study were advised to maintain their normal activity level during the monitoring week. No advertising was done for this study and no compensation given.

2.2 Equipment

2.2.1 Protocol and Consent

The study protocol was created using the Oregon Health & Sciences University General Clinical Research Center (GCRC) short protocol template [Appendix A]. Study protocol was submitted to the Oregon Health & Sciences University Research Integrity Office for approval by the Institutional Research Review Board (IRB) on March 19th, 2007. Enrollment began when both clinics were briefed on the study.

2.2.2 International Physical Activity Questionnaire (IPAQ)

The International Physical Activity Questionnaire (IPAQ) is a survey instrument used to assess a person's activity level. The questionnaire asks the subject a number of questions about their specific types of activity over the past three or seven days. The three day recall questionnaire and seven day recall questionnaire differ little except the number of days the survey covers. The survey can also be in either long or short form format. The short form only details three specific types of activity (walking, moderate, vigorous) in four domains of activity. These four domains are:

1) Leisure time physical activity
2) Domestic and gardening activities
3) Work-related physical activity
4) Transport related physical activity

The long form asks more detailed questions in each of these four domains. The results of the survey details the amount of energy used in each of the four domains by

each of the activity levels. The activity levels are rated using a physical activity measurement called Metabolic Equivalent (MET) Level. The definition of one MET is that "1 MET = the energy (oxygen) used by the body as you sit quietly, perhaps while talking on the phone or reading a book" (9, 35). By using METS as a unit of measurement, the data from the survey will allow for external validity since the amount of energy used is done in a ratio format instead of a total energy amount such as using kilocalories. Based on the assessment of METS a subject can be classified as "No or low activity", "Moderate Activity", or "High Activity".

2.2.3 Digital Accelerometer and Reader

Physical activity was monitored using an Actical accelerometer (Mini Mitter Co., Inc, Bend, Oregon). The Actical activity monitoring device utilizes a multidirectional accelerometer to monitor the occurrence and intensity of motion. The Actical device measures 28 mm by 27 mm by 10mm, weighs 17.0 grams (see Figure #1), and is securely attached to a waistband and placed around the waist. The device can be worn and collect data for 44 days using one minute epochs. For this study the subject was required to wear the monitor for 7 days. Data was uploaded and downloaded using an ActiReader from Mini Mitter. ActiReader requires a computer with a standard serial port and enough hard drive space to save the data. This data includes Daily Active Energy Expenditure and Total Daily Energy Expenditure which is measured in kilocalories. The Actical's activity data was converted into minute-by-minute energy expenditure using Metabolic Equivalent Levels (METS). This is the same form of METS that the IPAQ uses, which allows direct comparisons between the accelerometer and the survey. The raw data from

the accelerometer was transferred to an Excel workbook for data management and analysis.

Figure #1: The Actical Digital Accelerometer
By Mini-Mitter

2.2.4 SPSS BASE 15.0 and SPSS BASE 16.0 for Windows

The statistical software package SPSS 15.0 and SPSS 16.0 was used for statistical analysis. The software is the product of SPSS Inc. and was licensed to Oregon Health & Sciences University. Data for the subjects was entered directly into SPSS.

2.3 Procedures

Potential subjects were found by using the EPIC patient tracking and records system. The potential subjects were reviewed to find if they met the age and post transplant time requirements for the study. Medical records were also reviewed to determine if the potential subject had any findings that could prevent them from entering study

Adults were consented in clinic and were given a copy of the consent form to take home so they could refer to it later if they had questions. The contact number of the coordinator was provided on the consent form. Subjects under the age of eighteen years old were asked to sign both a consent and an assent. In addition, their parents were asked to sign the consent and the assent. Due to the simplicity of the requirements to be a subject and the procedures that they would need to perform as a subject, subjects under eighteen years old were allowed to read and sign the consent. This is not a typical procedure for the Oregon Health & Sciences University, but the consent was written at an eighth grade level and the study activities for subjects were straight forward. The Oregon Health & Sciences University Institutional Research Review Board also requires subjects under the age of 18 to sign the assent.

After consent (and assent in the case of children), an accelerometer was programmed to the subject's height, weight, and gender using the Actical reader and laptop. Within two minutes of the programming, the subjects starting wearing the instrument. The subjects were then given a prepaid FedEx box that would allow them to send the instrument back to study staff after wearing it for one week. In addition to the box, subjects were given an instruction sheet, packing slip, and IPAQ survey.

Subjects were briefed on the requirements for wearing the accelerometer over the next week. They were advised to wear the accelerometer exactly one week. The placement of the accelerometer was to be on their right hip. While the Actical accelerometer is made to be worn on the wrist, ankle and hip; the manufacturer recommends that it be placed on the hip for the most accurate information. Because of this, subjects were asked to wear the instrument on their right hip anytime they were

awake. The only times they were not to wear the accelerometer while awake was when they were swimming, changing, or bathing. After wearing the accelerometer for one week, they wear asked to remove the instrument and place it into the provided FedEx box. After noting the time on the packing slip, the subject filled out the IPAQ survey and placed it in the box with the accelerometer.

After the box was returned to the university, the raw data from the accelerometer was down loaded to the laptop computer using the ActiReader. Raw data was then transformed into a METS assessment over time by the Actical software. This information was transferred onto Excel spreadsheet for later review. All three data files created were then transferred to a secure directory on the Oregon Health & Sciences University internal system drives.

2.4 Data Management

Only the METs data file from the Actical accelerometer was used in this study. The data was imported into an Excel file for manipulation using the software associated with the ActiReader. Each Actical was set to record activity in minute intervals (epochs). Because of this, each file had in excess of 10,080 lines of data to be reviewed (60 minutes times 24 hours times seven days). Each file was examined to find periods of activity. A period of moderate activity was considered as 30 minutes or more of activity at a METS level of 3 to 6. A period of vigorous activity was classified as one lasting twenty minutes or more at a level of over 6 METS. If a person has five or more moderate periods of activity in a week, they were considered satisfying the CDC guidelines for moderate activity (9, 35). If the person has three or more periods of vigorous activity, they were

considered satisfying the CDC guidelines for vigorous activity (9, 35). Because the data file was examined visually for these periods, each file was examined three times. The data files were also examined in the same method for longest period of activity.

For total time of activity for each of the two activity groups, the same Excel data file was implemented. For total amount of vigorous activity, the following function was used to determine if the epoch minute was at 6 or more METS:

If (*CELL* > 5.9999, 1, 0)

The reporting cells for this function were then added together to find the total number of minutes at vigorous activity. For the total number of minutes of moderate activity, the following function set was used to find if the epoch minute was from 3 METS to 5.9999 METS:

If (*CELL* > 2.9999, 1, 0) MINUS If (*CELL* > 5.9999, 1, 0)

The reporting cells were added together to find the total number of minutes of moderate activity.

The International Physical Activity Questionnaire (IPAQ) was scored according to the seven day scoring assessment for the long form survey. The guidelines suggest a cap of 3 hours per activity per day in scoring of each activity group. Because the survey used did not use a daily assessment diary, it was not possible to find the amount of time spent per day in each of the activity groups. In addition to the scoring structure suggested by the IPAQ scoring guidelines, the surveys were returned with a return slip that was filled in with the time and date the accelerometer was removed. This allowed for assurance that the survey covered seven days. This time and date was also used to limit the accelerometer data to only when the instrument was worn.

A SPSS data file was created to hold the study's data. The results of the Excel spreadsheet was added to the data file along with demographics from the EPIC patient tracking system. The IPAQ survey was scored using the approved IPAQ scoring system to determine the type and amount of activity. The results were entered into the SPSS data file. Overall a total of 77 variables were created for analysis [Appendix C]. Of the 77 variables, only the first 27 were used in this study. The remaining 50 variables were created for future studies as more patients are enrolled. The variable "Body Mass Index" was the only variable that was required to be computed. This number was created using the formula provided by the ActiReader software.

2.5 Statistical Analysis

Initial analysis on the SPSS database included frequencies on categorical variables and descriptive statistics on continuous variables. Because of the limited sample size (n = 20) non-parametric methods were used to compared variables. Linear regression modeling was used to predict minutes of physical activity. An association between two continuous variables was assessed using Spearman's Rho correlations. An association between two categorical variables was assessed using Pearson Chi-Square and Fisher's Exact Test (where appropriate). Mann-Whitney tests were used to find median differences between the groups. To predict binary outcomes, logistic regression was used in either the standard (Enter) method or using a forward stepwise method. For predictions of continuous variables, both standard and forward stepwise regressions were used. Both regression modeling techniques allowed for adjustment of confounders.

Of the twenty-seven variables examined in this study, twenty-three were used in statistical analysis. The variables (see Appendix C) included the following:

Table 1. Study Variables

Number	Name	Type	Description
1	CDC Activity Level	Categorical	Coded as either the subject meet CDC guidelines as either moderate activity, vigorous activity or none
2	Meets CDC guidelines of activity	Binary	Defined as “yes” the subject did meet one of the requirements for activity groups or “no” the subject did not meet requirements.
3	Age at time of testing	Continuous	Age at the time the subject started using the accelerometer.
4	Age Group	Binary	Subjects under the age twenty-one years old were classified as pediatric subjects.
5	Gender	Binary	Subjects were classified as either “male” or “female”
6	Height (in inches)	Continuous	Height in inches at time of start of accelerometer.
7	Weight (in pounds)	Continuous	Weight in pounds at time of start of accelerometer.
8	Blood pressure (systolic)	Continuous	Systolic blood pressure at time of start of accelerometer.
9	Blood pressure (diastolic)	Continuous	Diastolic blood pressure at time of start of accelerometer.
10	Heart rate	Continuous	Number of heart beats per minute.
11	Reason for transplant	Categorical	Listed reason for transplant at time of transplant operation.
12	Serum Creatinine	Continuous	Serum Creatinine found during blood testing during the last blood draw. Typically done one to seven days before start of the accelerometer.
13	Blood Urea Nitrogen	Continuous	Blood Urea Nitrogen (BUN) found during blood testing during the last blood draw. Typically done one to seven days before start of the accelerometer.
14	Minutes of Moderate activity per accelerometer	Continuous	Minutes of activity on accelerometer that had a METS level of 3 to 5.99.
15	Minutes of Vigorous Activity per accelerometer	Continuous	Minutes of activity on accelerometer that had a METS level of 6.0 or greater.
16	Minutes on accounted for on accelerometer	Continuous	Total number of minutes accounted for during the week of observation.
17	Minutes of Moderate activity per IPAQ	Continuous	Minutes of activity scored in IPAQ that had a METS level of 3 to 5.99.
18	Minutes of Vigorous Activity per IPAQ	Continuous	Minutes of activity scored in IPAQ that had a METS level of 6.0 or greater.
19	IPAQ activity level	Categorical	Coded as either the subject meet IPAQ guidelines as either “No or low activity”, “Moderate Activity”, or as “High Activity”.
20	Longest period of moderate activity	Continuous	Created using the raw data from the digital accelerometer.
21	Periods of CDC recognized moderate activity	Continuous	Number of periods of moderate activity as defined by the CDC.
22	Body Mass Index	Continuous	Body mass as described by the CDC using their formula.
23	Days since Transplant	Continuous	Days after kidney transplant.

3. RESULTS

3.1 Sample Population

Patients were recruited between April 16th to December 4th, 2007. Approximately 90 potential subjects were identified from clinical scheduling. Of the 90 potentials, only twenty entered the study under the study's inclusion and exclusion criteria and comprised the study group. All potential subjects who were asked to enter the study agreed to participate. The primary reason for subjects not qualifying was that they simply did not show up for their clinic visit (roughly 50% of the excluded patients). The reasons the remaining subjects did not qualify due to illness and lacking the ability to ambulate.

Of the twenty, eight of the subjects were male and twelve were female. Thirteen of the twenty were twenty-one years of age or older at the time they started wearing the digital accelerometer. The average age of the male subjects was 43.3 (15 - 59, s.d. = 14.7) years and the average age of female subjects were 29.1 (15 – 58, s.d. = 15.6) years. There was no statistical difference in ages (p= 0.057) between genders. There was no statistical association between gender and age group (p= .158). Of the twenty, only one subject met the CDC guidelines for physical activity standards. That subject had 5 periods of moderate activity during the seven days. Only eighteen subjects returned the IPAQ survey. Of these eighteen subjects, five were classified as "No or low activity", ten were classified as "Moderate Activity", and three were classified as "High Activity" by the IPAQ scoring guidelines.

Results from the subjects' initial visit to clinic were evaluated along with the data from the accelerometers and IPAQ scores (see Table 2.). The age range for the study participants was from 15 to 59 years olds which provided a good spread. Blood

pressures, both systolic and diastolic, were (overall) normal. Heart rate was a little high, but subjects were attending a physician's visit to find out about the health of the kidney transplant, so this would be expected. The average amount of time of moderate activity was surprisingly high considering that all but one subject did not meet CDC guidelines for activity. On average, 10 hours of moderate activity per subject was done. Compared to the IPAQ survey, with an average of 44.7 hours of activity, it appears that there is a four to one ratio of assumed activity by the subject to actual activity. When applying the same ratio method to vigorous activity, the ratio is 26.5 between actual activity and assumed activity by the subject.

Table 2. Descriptive Statistics of Study Variables

Factor	N	Minimum	Maximum	Median	Mean	Standard error of mean	Standard Deviation
Age at time of testing (in years)	20	15	59	35	34.8	3.7	16.5
Systolic Blood Pressure	20	106	146	121.5	122.7	2.3	10.5
Diastolic Blood Pressure	20	55	88	71	72.1	1.9	8.3
Heart Rate (beats per minute)	20	57	94	80.5	78.7	2.3	10.2
Serum Creatinine (µmol/L)	20	0.9	1.8	1.2	1.2	0.06	0.27
Blood Urea Nitrogen (mg/dL)	20	6	37	19.0	18.2	1.4	6.3
Minutes of Moderate Activity[1] (Accelerometer)	18	18	1,366	650.5	567.2	84.9	379.9
Minutes of Moderate Activity[1] (IPAQ)	18	30	10,560	1160	2,684.8	767.7	3,257.2
Minutes of Vigorous Activity[2] (Accelerometer)	18	0	95	0	6.1	4.8	21.5
Minutes of Vigorous Activity[2] (IPAQ)	18	0	2,520	210	549.0	182.5	774.2
Longest Time of Activity[4] in minutes (Accelerometer)	18	1	68	12.0	18.2	4.0	17.7
Periods of moderate activity[5]	18	0	5	0	0.65	0.34	1.50
Body Mass Index (BMI)	18	18.8	37.7	27.18	27.4	1.20	5.38
Days since transplant	18	86	505	213.5	267	29.4	131.5

1 Moderate Activity defined as 3.0 to 5.99 METS over a period of a minute

2 Vigorous Activity defined as 6.0 or more METS over a period of a minute

3 Only 18 of the 20 subjects returned the IPAQ survey

4 Activity was defined as a METS of 3.0 or more over a period of a minute

5 A period of moderate activity was defined under the CDC guidelines as one having a METS of 3.0 or more over a period of 30 minutes of more.

The variable of "longest period of activity" was created after study analysis started. This variable was created by looking for the longest period of activity during the observation week. While the average of 18.2 minutes does look impressive, the standard deviation of 17.7 minutes showed that there was a lot of variation among the twenty subjects in this area. Body Mass Index (BMI) range was from 18.8 to 35.7, which suggested that the subjects were in the low end of the healthy scale to being well into the obese category according to the CDC (36). Days since transplant also had a wide range. The lowest number of days, eighty-six, was created when a subject came in for their three month post operation evaluation. The longest was 1.4 years after transplant. After applying a standard deviation of 131.5 days, it appears that a good variance in post transplant time was achieved.

Spearman's Rho correlation analysis was performed to identify potential co-linearity issues with independent variables in modeling. Spearman's Rho correlations were found to be statistically significant ($p \leq 0.05$) between the following pairs of continuous variables. The results were:

- Serum Creatinine and Age at the Time of Testing ($r = 0.516$, $p = 0.020$)
- Blood urea nitrogen and Age at the Time of Testing ($r = 0.522$, $p = 0.018$)
- Minutes of Moderate activity per accelerometer and Age at the Time of Testing ($r = 0.466$, $p = 0.038$)
- Body Mass Index and Periods of CDC recognized moderate activity per accelerometer ($r = 0.479$, $p = 0.033$)

- Body Mass Index and Blood pressure (systolic) ($r = 0.616$, $p = 0.004$)
- Longest period of moderate activity per accelerometer and Heart Rate ($r = -0.607$, $p = 0.005$)
- Longest period of moderate activity per accelerometer and Minutes of Moderate activity per accelerometer ($r = 0.763$, $p < 0.001$)
- Minutes of Moderate activity per IPAQ and Minutes of Vigorous Activity per accelerometer ($r = 0.714$, $p = 0.001$)
- Periods of CDC recognized moderate activity per accelerometer and Minutes of Vigorous Activity per accelerometer ($r = 0.462$, $p = 0.041$)
- Body Mass Index and Minutes of Vigorous Activity per accelerometer ($r = -0.487$, $p = 0.029$)
- Longest period of moderate activity per accelerometer and Periods of CDC recognized moderate activity per accelerometer ($r = 0.657$, $p = 0.002$)

Age was grouped per Federal Guidelines that those under the age of twenty-one were classified as a child. Analysis was done to find if there was an association between gender and age group (see Table 3).

Table 3. Association Between Gender and Age Group

Gender	Age Group		Total
	21 years old or older	Under 21 years old	
Female	6	6	12
Male	7	1	8
Total	13	7	20

Pearson Chi-Square showed there was not an association between Gender and Age Group ($\chi^2 = 2.967$, $p = 0.085$). While this p value was close to be being statistically significant, Fisher's Exact Test showed no association ($p = 0.158$).

Mann-Whitney tests were performed to find if there was a difference in the continuous variables (Blood pressure, Heart Rate, Serum Creatinine, Blood Urea Nitrogen, Body Mass Index, results of the accelerometer, and results from IPAQ) between the two age groups. The Mann-Whitney compares the ranks of each group. Results shown for age groups in Table 4.

Table 4. Age Group by Continuous Variables

Variable	Age Group	N	Mann - Whitney			
			Mean Rank	Sum of Ranks	Z	p Value
Blood Pressure (Systolic)	21 years old or older	13	11.81	153.5	-1.351	0.177
	Under 21 years old	7	8.07	56.5		
Blood Pressure (Diastolic)	21 years old or older	13	12.15	158.0	-1.711	0.087
	Under 21 years old	7	7.43	52.0		
Heart Rate	21 years old or older	13	11.12	144.5	-0.637	0.536
	Under 21 years old	7	9.36	65.5		
Body Mass Index	21 years old or older	13	12.46	162.0	-2.021	*0.043*
	Under 21 years old	7	6.86	48.0		
Serum Creatinine	21 years old or older	13	12.15	158.0	-1.732	0.083
	Under 21 years old	7	7.43	52		
Blood Urea Nitrogen	21 years old or older	13	13.23	172.0	-2.846	*0.004*
	Under 21 years old	7	5.43	38.0		
Minutes of Moderate Activity (accelerometer)	21 years old or older	13	12.46	162.0	-2.846	*0.004*
	Under 21 years old	7	6.86	48.0		
Minutes of Vigorous Activity (accelerometer)	21 years old or older	13	10.12	131.5	-0.567	0.571
	Under 21 years old	7	11.21	78.5		
Minutes of Moderate Activity (IPAQ)	21 years old or older	12	8.92	107.0	-0.656	0.512
	Under 21 years old	6	10.57	64.0		
Minutes of Vigorous Activity (IPAQ)	21 years old or older	12	9.17	110.0	-0.379	0.705
	Under 21 years old	6	10.17	61.0		
Longest Period of Moderate Activity (accelerometer)	21 years old or older	13	11.23	146.0	-0.754	0.451
	Under 21 years old	7	9.14	64.0		
Periods of CDC recognized Activity (accelerometer)	21 years old or older	13	10.69	139.0	-0.283	0.777
	Under 21 years old	7	10.14	71.0		

Mann-Whitney were performed to find if there was a difference in the continuous variables (Blood pressures, Heart Rate, Serum Creatinine, Blood Urea Nitrogen, Body Mass Index, results of the accelerometer, and results from IPAQ) between genders. Results shown for age groups in Table 5.

Table 5. Gender by Continuous Variables

Variable	Age Group	N	Mann - Whitney			
			Mean Rank	Sum of Ranks	Z	p Value
Blood Pressure (Systolic)	Female	12	8.58	103.0	-1.780	0.075
	Male	8	13.38	107.0		
Blood Pressure (Diastolic)	Female	12	7.33	88.0	-2.944	*0.003*
	Male	8	15.25	122.0		
Heart Rate	Female	12	9.54	114.5	-0.891	0.373
	Male	8	11.94	95.5		
Body Mass Index	Female	12	9.33	112.0	-1.080	0.280
	Male	8	12.25	98.0		
Serum Creatinine	Female	12	8.75	105.0	-1.647	0.100
	Male	8	13.13	105.0		
Blood Urea Nitrogen	Female	12	9.67	116.0	-0.781	0.435
	Male	8	11.75	94.0		
Minutes of Moderate Activity (accelerometer)	Female	12	9.08	109.0	-1.312	0.190
	Male	8	12.63	101.0		
Minutes of Vigorous Activity (accelerometer)	Female	12	11.13	133.5	-0.828	0.408
	Male	8	9.56	76.5		
Minutes of Moderate Activity (IPAQ)	Female	11	8.91	98.0	-0.589	0.556
	Male	7	10.43	73.0		
Minutes of Vigorous Activity (IPAQ)	Female	11	8.18	90.0	-1.327	0.185
	Male	7	11.57	81.0		
Longest Period of Moderate Activity (accelerometer)	Female	12	10.00	120.0	-0.463	0.643
	Male	8	11.25	90.0		
Periods of CDC recognized Activity (accelerometer)	Female	12	10.25	123.0	-0.331	0.741
	Male	8	10.88	87.0		

3.2 Primary Outcome (Study Aim)

The purpose of this study was to find if there was a relationship between kidney function and physical activity. Kidney function was measured by blood test within the week before first wearing the digital accelerometer. Serum creatinine and blood urea nitrogen scores were compared to physical activity as measured by the digital accelerometer. Serum creatinine was measured in milligrams per deciliter (mg/dL). Blood urea nitrogen was measured in milligrams per deciliter (mg/dL). Physical activity was measured in Metabolic Equivalent Levels (METS). The METS epoch setting was METS per minute since this allowed for conversion to CDC standards. Using these standards, subjects were classified as meeting CDC standards if they met either moderate activity and/or vigorous activity for the week. The original plan of analysis was to attempt to predict if a subject would meet guidelines based on the two kidney function scores. Because only one subject of the twenty meet CDC standards, no models could be created under the structure set by the study protocol.

Modeling was done using correlation analysis to predict the amount of minutes of moderate activity in the sample week. The relationship between kidney function and minutes of moderate activity is shown in Figures 2 and 3.

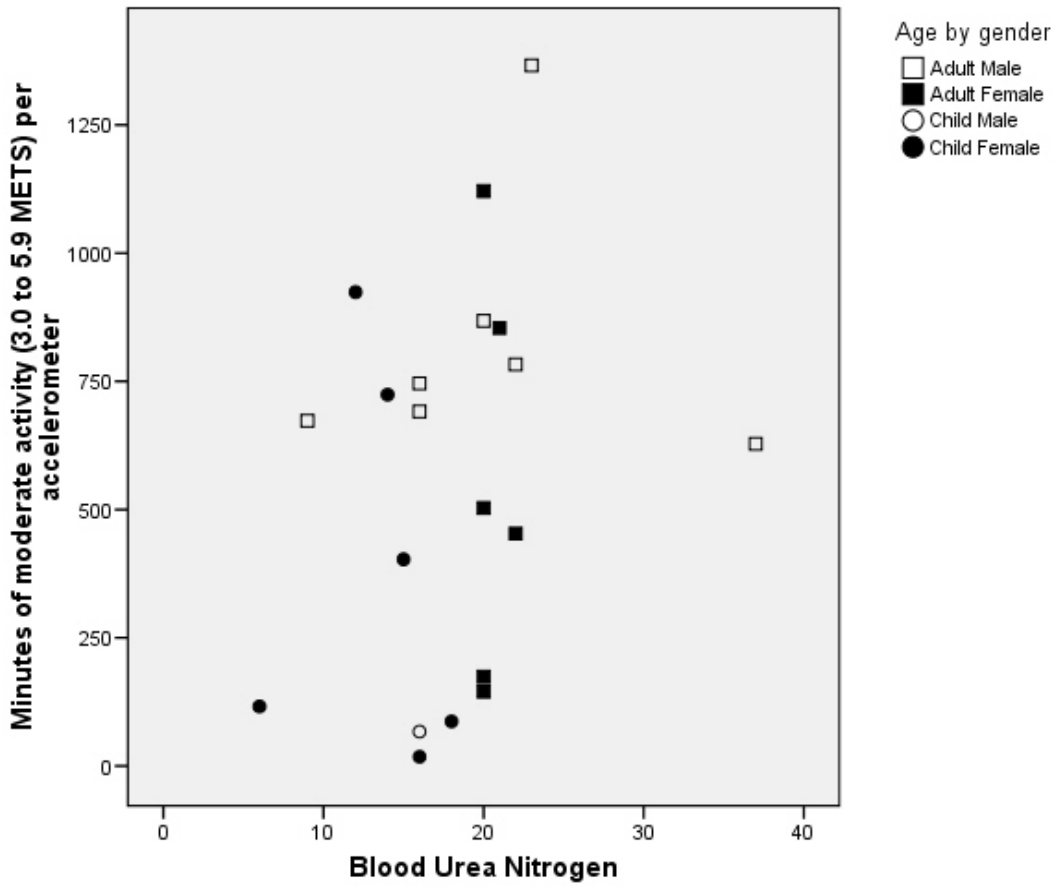

Figure 2. Blood Urea Nitrogen compared to Minutes of Moderate Activity in a week (accelerometer)

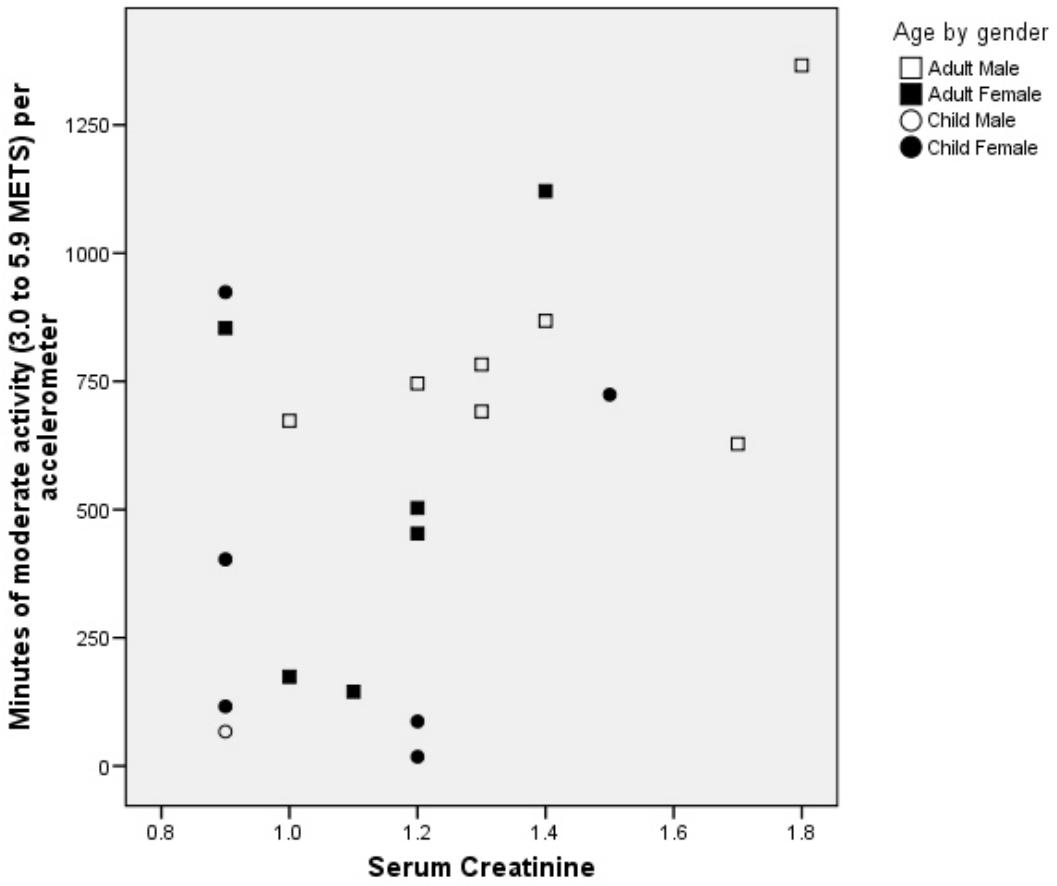

Figure 3. Serum Creatinine compared to Minutes of Moderate Activity in a week (accelerometer)

Blood urea nitrogen is normally 10 to 20 milligrams per deciliter (mg/dL). As shown in Figure 1, half the subjects were at 20 or greater. Normal serum creatinine is 0.8 to 1.4 milligrams per deciliter (mg/dL). This places fives subjects at or over the 1.4 threshold.

The correlation analysis was done to find the relationship between kidney function, blood pressure and heart rate has on minutes of moderate physical activity. This was followed by a stepwise regression model to predict minutes of moderate activity

using kidney function, being a minor, gender, blood pressure and heart rate has on minutes of moderate physical activity. Results are shown in Tables 6 and 7.

Table 6. Factors Associated with Minutes of Moderate Activity on Accelerometer

Variable	Pearson Correlation		Spearman's Rho	
	Correlation	p value	Correlation	p value
Blood Pressure (Systolic)	0.189	0.425	0.081	0.735
Blood Pressure (Diastolic)	0.183	0.439	0.039	0.869
Heart Rate	-0.300	0.199	-0.285	0.224
Serum Creatinine	0.523	0.018	0.430	0.059
Blood Urea Nitrogen	0.222	0.347	0.268	0.254

Table 7. Minutes of Moderate Activity on Accelerometer Model

(Stepwise Method)

Model	R	R^2	Adj. R^2	ANOVA	
				F value	Sig. of F Value
Predict "Minutes of moderate activity on accelerometer"	.523	.274	.233	6.788	0.018
Variables in Equation	**Unstand. B**		**SE B**	***t* value**	**p value**
(Constant)	-331		353	-0.938	0.360
Serum Creatinine	748		287	2.605	0.018
Variables not in Equation	**Beta**			***t* value**	**p value**
Age Group	-0.313			-1.499	0.152
Gender	0.175			-0.792	0.439
Blood Pressure (Systolic)	0.011			0.051	0.960
Blood Pressure (Diastolic)	-0.026			-0.116	0.909
Heart Rate	-0.091			-0.397	0.696
Blood Urea Nitrogen	-0.162			-0.624	0.541

The correlation analysis (Table 6) did not allow for adjustment for confounders to find if either of the two renal function lab tests were associated with minutes of moderate activity. The correlation analysis showed that serum creatinine was the only predictor of minutes of moderate activity on the accelerometer under the Pearson correlation and was close to being a predictor using the Spearman's Rho correlation. The stepwise regression model (Table 7) was used to find the best predictors for moderate activity. This showed that only serum creatinine was a predictor for moderate activity. For every for every milligram per deciliter (mg/dL) of serum creatinine, the subject had 748 minutes of moderate activity.

Modeling was also done to predict the amount of minutes of vigorous activity during the study week and longest time of activity. The relationship between kidney function and minutes of moderate activity is shown in Figures 4 and 5. Note that due to

the lack of vigorous activity in the sample group, no modeling was done on this type of activity.

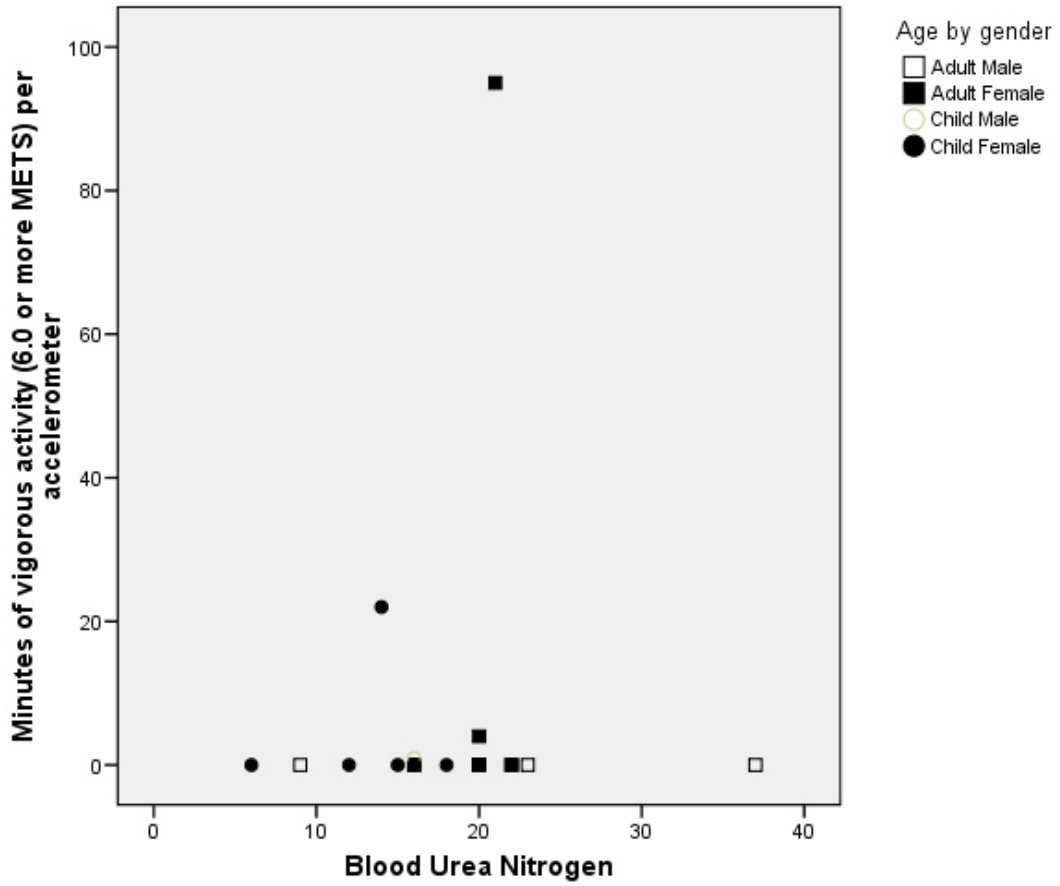

Figure 4. Blood Urea Nitrogen compared to Minutes of Vigorous Activity in a week (accelerometer)

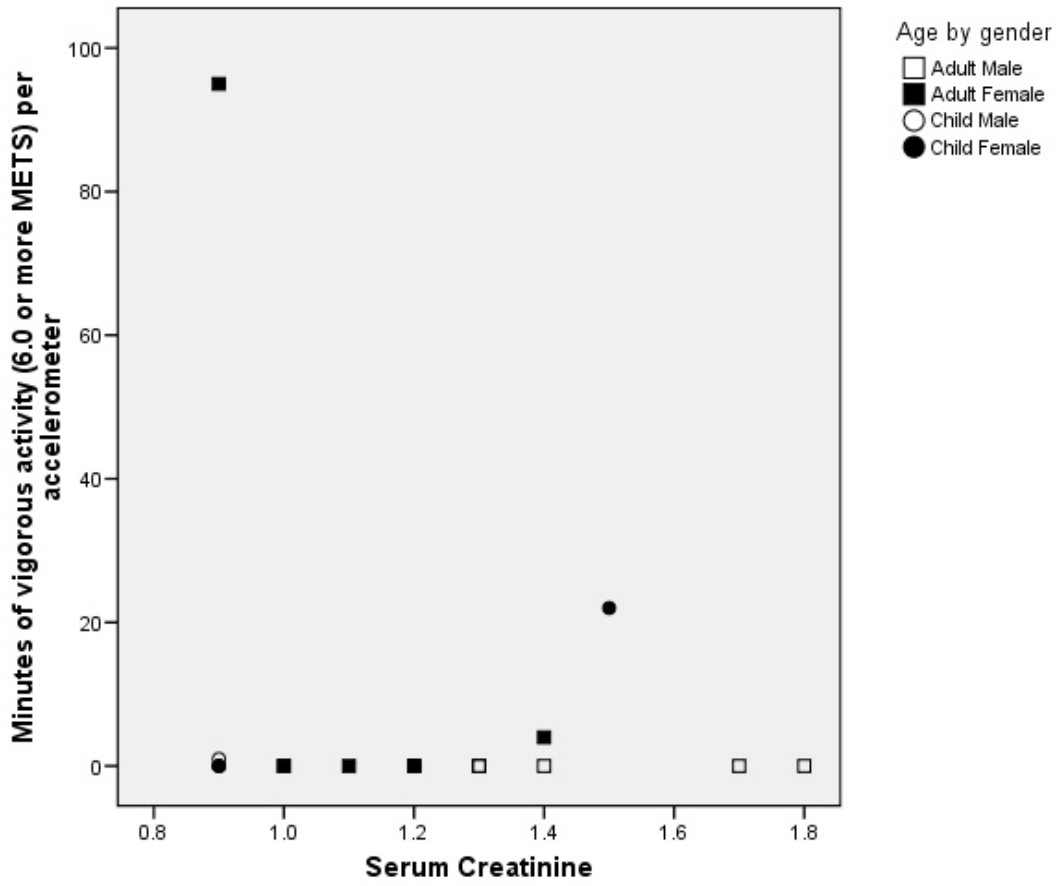

Figure 5. Serum Creatinine compared to Minutes of Vigorous Activity in a week (accelerometer)

The correlation analysis was done to find the relationship between kidney function, blood pressure and heart rate has on minutes of vigorous physical activity. This was followed by a stepwise regression model to predict minutes of vigorous activity by the same predictors. Results are shown in Table 8 for correlation analysis. The Stepwise model using the same variables showed no supporting factors and therefore was considered inconclusive. Both models were deemed as being insufficient in providing any accurate conclusions.

While serum creatinine was associated with minutes of moderate activity and BUN was not (see Table 6), it could be suggested that renal function is associated with moderate activity. If they are, the next issue would be what other factors could be associated after adjusting for these two. Because of this a new model was created with serum creatinine and blood urea nitrogen already in the model and a stepwise regression was used to apply the remaining variables. Results for the new model are shown in Table 9. This model showed that serum creatinine was a predictor of minutes of vigorous while blood urea nitrogen, along with the possible confounders, were not predictors.

Table 8. Factors Associated with Vigorous Activity on Accelerometer

Variable	Pearson Correlation		Spearman's Rho	
	Correlation	p value	Correlation	p value
Blood Pressure (Systolic)	-0.425	0.062	-0.425	0.062
Blood Pressure (Diastolic)	-0.370	0.109	-0.415	0.069
Heart Rate	0.051	0.832	-0.135	0.572
Serum Creatinine	-0.197	0.404	-0.031	0.896
Blood Urea Nitrogen	0.072	0.763	-0.015	0.951

Table 9. Minutes of Moderate Activity on Accelerometer Modeling

(Complex Method)

Model	R	R^2	Adj. R^2	ANOVA	
				F value	Sig. of F Value
Predict "Minutes of Moderate activity on accelerometer"	.539	.290	.207	3.473	0.54
Variables	**Unstand. B**		**SE B**	***t* value**	**p value**
(Constant)	-324		359	-0.9	0.379
Serum Creatinine*	890		371	2.403	0.028
Blood Urea Nitrogen*	-9.79		15.7	-0.624	0.541
Variables not in Equation	**Beta**			***t* value**	**p value**
Age Group	-0.435			-1.969	0.061
Gender	0.173			0.767	0.454
Blood Pressure (Systolic)	0.003			0.013	0.990
Blood Pressure (Diastolic)	-0.076			-0.315	0.757
Heart Rate	-0.108			-0.462	0.651

* Placed using the Enter method in the first block

3.3 Secondary Outcomes

A secondary outcome for this study was to find if the amount of activity recorded on the digital accelerometer were reflected in the IPAQ surveys given to the subjects. The results of the correlations are reflected in Table 10. The association is shown in Figures 6 and 7.

Table 10. Correlation of IPAQ and Accelerometer Results

Variable	Test	Minutes of moderate activity (3.0 to 5.9 METS) per accelerometer	Minutes of vigorous activity (6.0 or more METS) per accelerometer	Minutes of moderate activity (3.0 to 5.9 METS) per IPAQ	Minutes of vigorous activity (6.0 or more METS) per IPAQ
Minutes of moderate activity (3.0 to 5.9 METS) per accelerometer	Pearson Correlation Sig. (2-tailed) Spearman's rho Sig. (2-tailed) N		0.209 p = 0.377 0.211 p = 0.372 N = 20	0.336 p = 0.173 0.195 p = 0.438 N=18	0.362 p = 0.140 0.253 p = 0.310 N = 18
Minutes of vigorous activity (6.0 or more METS) per accelerometer	Pearson Correlation Sig. (2-tailed) Spearman's rho Sig. (2-tailed) N	0.209 p = 0.377 0.211 p = 0.372 N = 20		0.661 p = 0.003 0.714 p = 0.001 N = 18	0.003 p = 0.991 0.495 p = 0.037 N = 18
Minutes of moderate activity (3.0 to 5.9 METS) per IPAQ	Pearson Correlation Sig. (2-tailed) Spearman's rho Sig. (2-tailed) N	0.336 p = 0.173 0.195 p = 0.438 N=18	0.661 p = 0.003 0.714 p = 0.001 N = 18		0.606 p = 0.008 0.685 P = 0.002 N = 18
Minutes of vigorous activity (6.0 or more METS) per IPAQ	Pearson Correlation Sig. (2-tailed) Spearman's rho Sig. (2-tailed) N	0.362 p = 0.140 0.253 p = 0.310 N = 18	0.003 p = 0.991 0.495 p = 0.037 N = 18	0.606 p = 0.008 0.685 P = 0.002 N = 18	

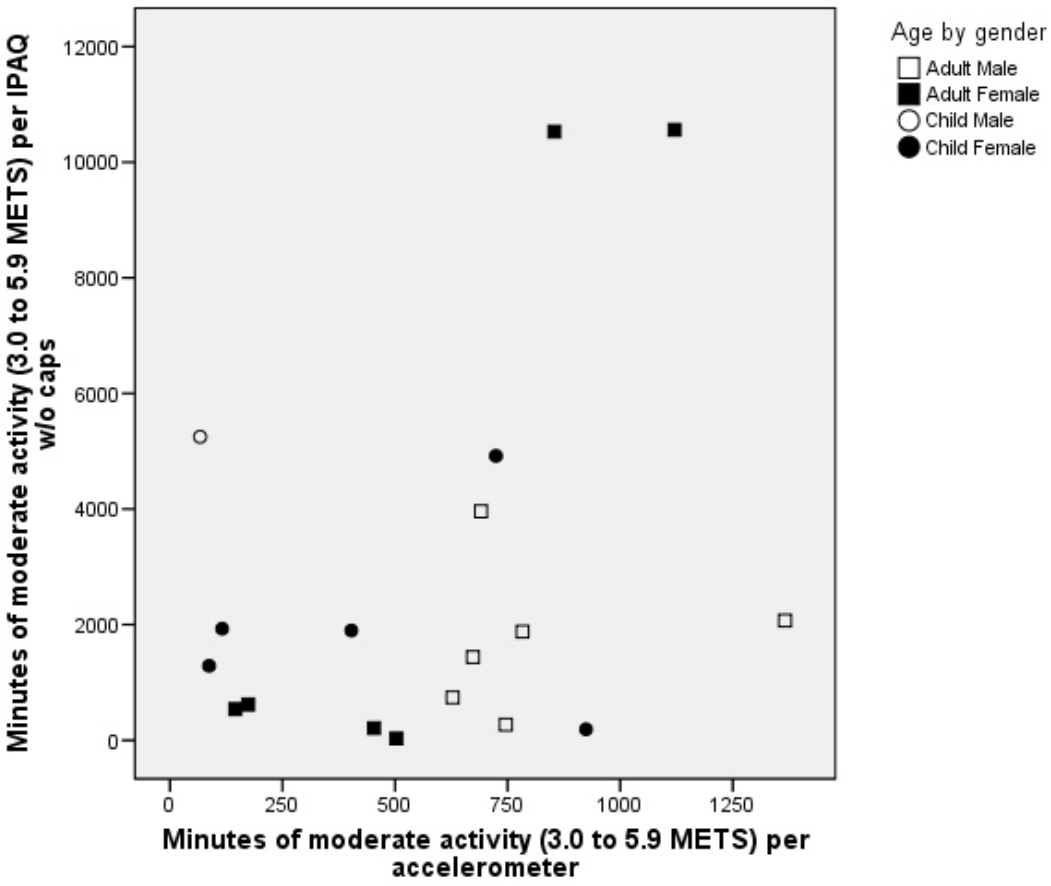

Figure 6. Minutes of Moderate Activity by Accelerometer compared to Minutes of Moderate Activity by IPAQ

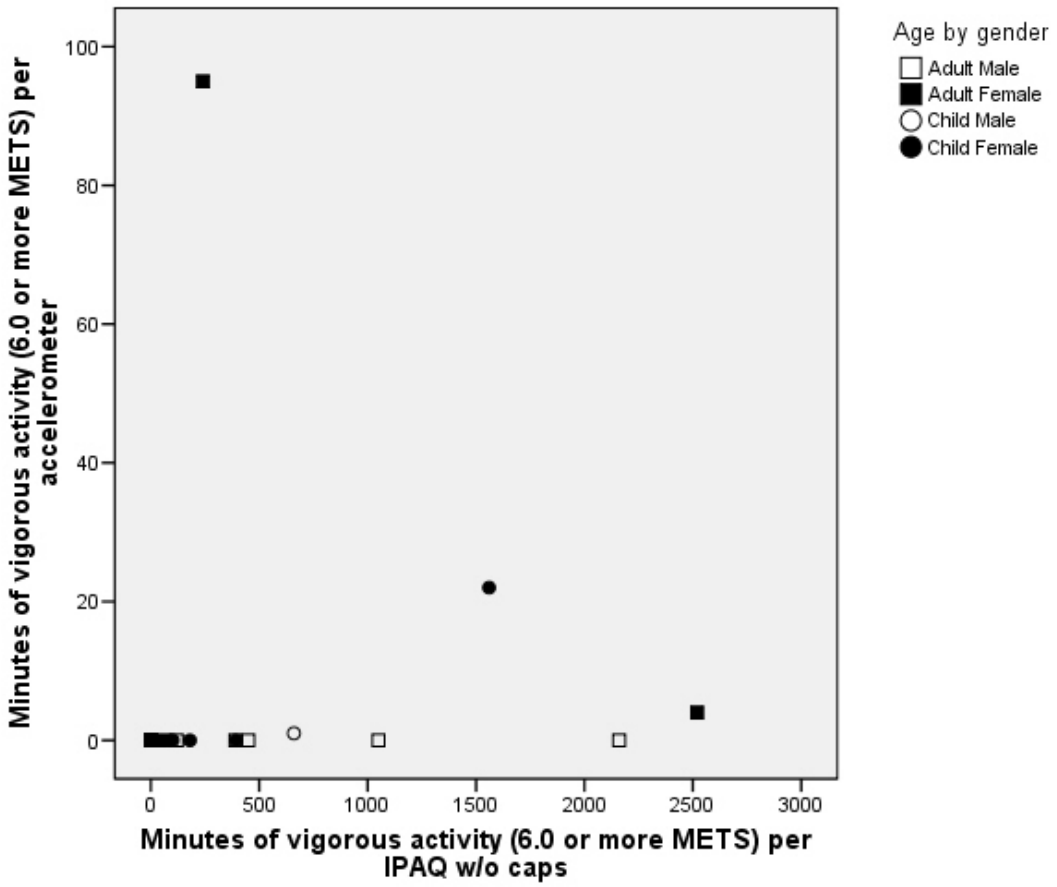

Figure 7. Minutes of Vigorous Activity by Accelerometer compared to Minutes of Vigorous Activity by IPAQ

During encoding of the data, a trend was noticed. Instead of encoding by CDC standards, each subject was given a new variable of longest time of moderate activity. Since subjects were not instructed to force themselves into activity, this variable was created as a cross section of the sample population. Like the modeling proposal in the protocol, kidney function would be used to predict physical activity level. Figure 8 shows the relationship between longest period of moderate activity and blood urea

nitrogen. Figure 9 shows the relationship between longest period of moderate activity and serum creatinine.

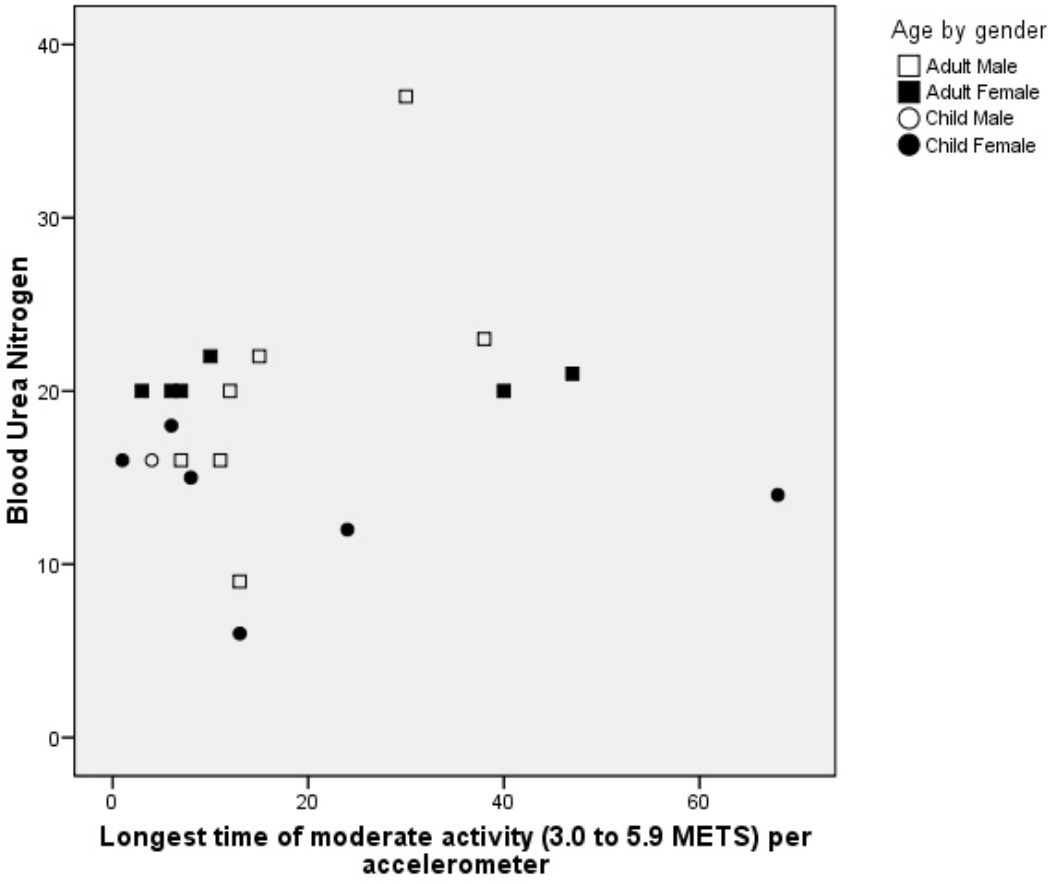

Figure 8. Blood Urea Nitrogen compared to Longest Period of Moderate (accelerometer)

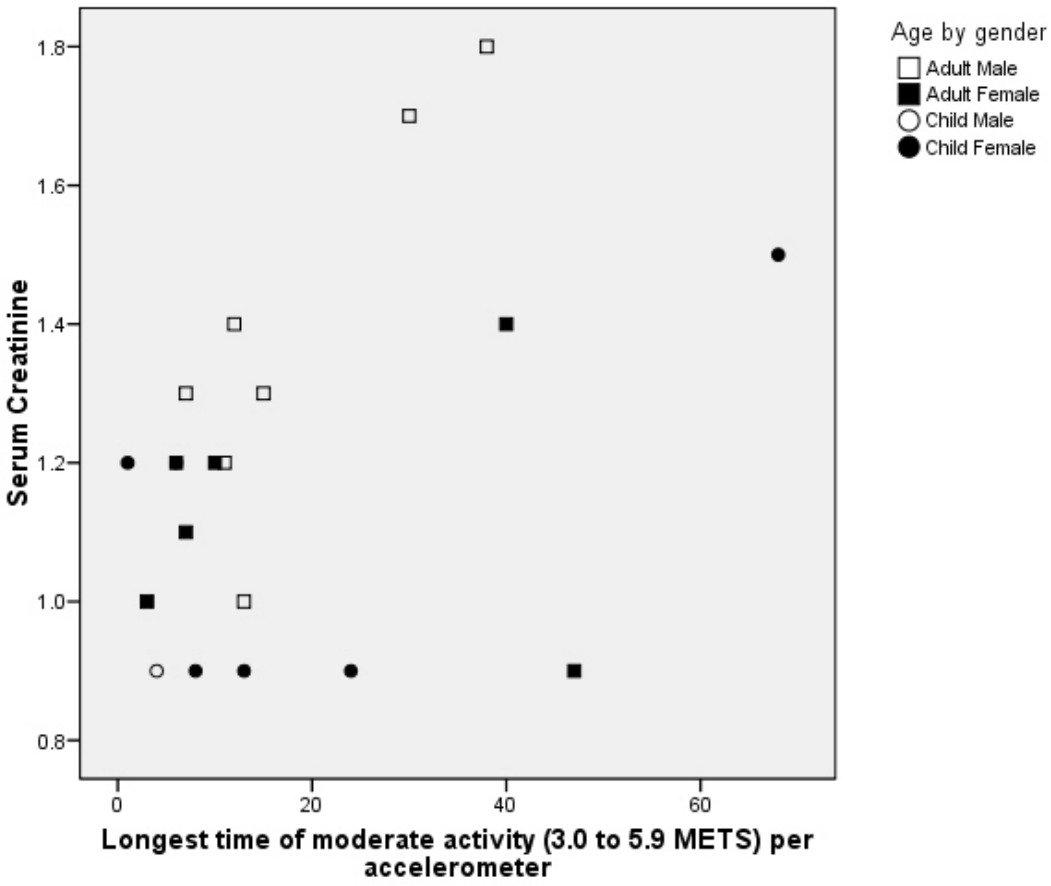

Figure 9. Serum Creatinine compared to Longest Period of Moderate Activity (accelerometer)

An Enter method of regression analysis was done to find the relationship between kidney function, being a minor, gender, blood pressure and heart rate has on longest period of moderate activity. This was followed by a stepwise regression model to predict minutes of moderate activity by the same predictors. Results are shown in Tables 11 and 12.

Table 11. Longest Period of Moderate Activity Modeling (Enter Method)

Model	R	R^2	Adj. R^2	ANOVA	
				F value	Sig. of F Value
Predict "Longest Period of Moderate Activity"	.730	.533	.261	1.960	0.146
Variables		**Unstand. B**		***t* value**	**p value**
(Constant)		158.5		2.139	0.054
Age Group		-11.1		-1.096	0.295
Gender		1.815		0.182	0.859
Blood Pressure (Systolic)		-0.526		-1.383	0.192
Blood Pressure (Diastolic)		-0.861		-1.225	0.244
Heart Rate		-0.550		-1.220	0.246
Serum Creatinine		49.9		2.264	0.043
Blood Urea Nitrogen		-1.489		-1.620	0.131

Table 12. Longest Period of Moderate Activity Model (Stepwise Method)

Model	R	R^2	Adj. R^2	ANOVA	
				F value	Sig. of F Value
Predict "Longest Period of Moderate Activity"	.502	.252	.211	6.607	0.024
Variables in Equation		**Unstand. B**		***t* value**	**p value**
(Constant)		86.5		3.093	0.006
Heart Rate		-0.868		-2.463	0.024
Variables not in Equation		**Beta**		***t* value**	**p value**
Age Group		-0.088		-0.419	0.681
Gender		-0.001		-0.003	0.998
Blood Pressure (Systolic)		-0.205		-1.005	0.329
Blood Pressure (Diastolic)		-0.060		-0.280	0.783
Serum Creatinine		0.258		1.151	0.266
Blood Urea Nitrogen		-0.023		-0.103	0.919

4. DISCUSSION

4.1 Primary Outcome (Study Aim)

For this study, the assumption was that a kidney function, as reflected by blood urea nitrogen (BUN) and serum creatinine (Cr), was associated with the amount of activity recorded on the digital accelerometer. Kidney function as well as demographic information was placed into a number of models that created some results that supported this hypothesis. The original modeling plan was to use logistic regression to find what factors were associated with meeting the CDC criteria for being physically active. If a subject met either the CDC criteria for moderate or vigorously active, they were considered an active person. Since only one person of the twenty met this criterion, this

type of modeling could not be used. Instead linear regression models were used to predict the number of minutes of activity.

Before the modeling was started, the amount of activity itself was examined. The average amount of moderate physical activity (METS of 3.0 to 5.9 per minutes) for this study was 567.2 minutes, or a little less than 9 and half hours (9.45 hours). The range of moderate activity was between 18 to 1,366 minutes for the twenty subjects for the study. The average amount of vigorous physical activity for the week was 6.1 minutes. The range of vigorous activity (METS 6.0 or more per minutes) was between 0 to 95 minutes for the twenty subjects for the study. This initial evaluation of the activity highlights a number of points. Under CDC guidelines, to be considered moderately active, a person needs to have five or more periods of physical activity in a week. Each period needs to last at least 30 minutes and be between 3.0 and 5.9 METS of activity (35). Based on the mean and range of moderate activity, it appears that it is possible for some subjects to meet these guidelines. To meet the guidelines, a person would have a minimum of 150 minutes of moderate activity (thirty minutes per period multiplied by five periods). Since some of these subjects have over this amount, it may be possible that the study does have people who meet the moderate guidelines. Under the CDC vigorous guidelines, a person needs to have three periods or more of vigorous activity in a week. Each period needs to be twenty minutes or more in length and at 6.0 or more METS per minute (35).

Considering the average number of minutes of vigorous activity was just over 6 minutes, it appears unlikely that very many of the subjects meet this criterion. It would require at least 60 minutes of vigorous activity to meet this criteria (three periods multiplied by twenty minutes).

Since weight is related to activity level, it was factored into the regression models. Body mass index (BMI) was used since it is a standardized form of measurement. The average BMI was 27.4 with a range of 18.8 to 37.7. The Centers for Disease Control (CDC) breakdown Body Mass Index into four categories (as shown on Table 14). Based on these results, this means the typical person in this study was clinically overweight. It should be noted that BMI was calculated for children in this study using the adult formula. While the BMI number itself is the same, how the BMI is interpreted for children differ from that of adults (36). This means the average for BMI would be in the "Overweight" category.

Table 13. Centers for Disease Control Body Mass Index Categories

Body Mass Index	Weight Status
Below 18.5	Underweight
18.5 – 24.9	Normal
25.0 – 29.9	Overweight
30.0 and Above	Obese

While the average BMI was higher than expected, the heart rate and blood pressure were close to average. The average blood pressure was 122.7 (systolic score) over 72.1 (diastolic score). This places the subjects close to normal blood pressure, but it should be noted that subjects were on medications that could modify this result. Heart rate, which has been traditionally associated with its ability to predict physical activity,

was on average 78.7 beats per minute with a range of 57 to 94 beats per minute. It should be noted that some subjects were on medications that could modify resting heart rate. In the aspect of time after transplant, subjects were between 86 days to 505 days after transplant with an average of 267 days. This creates a wide cross section of post-transplant subjects entered.

While these descriptive results describe the general health of the subjects, it is the modeling that showed results that supported the hypothesis. When taking into account confounders blood urea nitrogen did have a negative relationship against minutes of moderate activity ($p = 0.048$), but serum creatinine had a positive relationship ($p = 0.017$). When selecting the best predictors, serum creatinine was the only predictor of minutes of moderate activity ($p = 0.018$). Because of these mixed results, the BUN to serum ratio was tested, but yielded no useful results. The positive relationship between serum creatinine and activity could be due to muscle mass. Logically, children have a lower amount of muscle tissue than adults. Children did show a lower level than adults, but difference was not considered statistically significant ($p = 0.083$). But research in creatine supplementation has shown that elevating serum creatinine did not increase muscle creatine levels (40), therefore the muscle mass association is not an issue.

4.2 Secondary Outcomes

One of the secondary outcomes was if there was an association between the results of the digital accelerometer and the International Physical Activity Questionnaire (IPAQ). As seen in Table 10, moderate activity on the IPAQ survey did not correlate with moderate activity on the accelerometer (Pearson's $p = 0.173$, Spearman's Rho $p =$

0.438). In addition, vigorous activity on the survey had mixed correlation results with vigorous activity on the accelerometer (Pearson's p = 0.991, Spearman's Rho p = 0.037). While the correlation by rank method is significant, correlation by value was not. This could mean a non-linear aspect in correlation. In other words, when a subject does vigorous activity and attempts are made to estimate it, over estimation is likely. The more vigorous the activity, the greater the over estimation. This suggests recall bias. Since neither type of activity correlated using the Pearson's correlation, subjects were not recalling the exact amount of activity.

While encoding the data, the trend of longest time spent doing a moderate activity was encoded. This variable was created after the database was created. For the study, the variable "longest period of moderate activity" was encoded. This was defined as "the longest period of time a subject spent maintaining 3.0 METS or more". This new variable could be called "endurance" since it shows how long someone can be active before stopping. The modeling methods used was the same used in previous studies. Under the Enter method, a weak model was created (p = 0.146) with only serum creatinine acting as a positive predictor (p = 0.043). Since this matched the results of some of the previous models, it raises the issue of serum creatinine may be related to physical activity but not in a negative relationship. Under the Stepwise method, the model was strong (p = 0.024) with the only predictor being heart rate. This is interesting since resting heart rate has been known to be associated with being physically active due to improved cardiovascular health (36-39). It should be noted that this is not a method of monitoring activity that is used in this study.

5. LIMITATIONS

5.1 Sample Size

One of the primary limitations for this study was the sample size. The original protocol suggested between fifty to one hundred subjects should be enrolled in the study. The protocol involved identifying potential subjects before they arrived in clinic and approaching them after their clinic visit. Out of the approximately ninety potentials identified, only thirteen were recruited from the adult clinic. Roughly half of the subjects identified as possibilities simply did not show up to clinic that day. The other reasons for not qualifying included illness and lacking the ability to ambulate. This creates a sample bias. Medical staff in the adult clinic noted that patients tended not to show up to their appointments if they felt "okay". Those who did come to their scheduled visit tended to come for a particular reason such as feeling ill. This scenario likely led to selection bias.

While potential subject turn out was an issue, the criteria of having subjects be three to eighteen months may have also created selection bias. During the first 18 months after transplantation, subjects are more likely to have good kidney function. During this time subjects are heavily monitored regarding their kidney function while being on higher doses of medications to prevent rejection. This level of monitoring will facilitate early treatment of acute rejection and therefore promote preservation of good kidney function in the first 18 months, as demonstrated by the data collected for this study. This means subjects with moderate or severe kidney impairment were unintentionally excluded from this study.

5.2 Diet

Another limitation besides sample size is the diet of the subject. Studies have shown that people with healthy diets tend to be more physically active (38-39). Considering that this group already has diet requirements given to them by their physicians, it would have been a simple confounder to adjust for within the models. The main issue with adjusting for diet would have been how to capture this data and how to encode it. Future studies will need to solve these two issues in ways that would have external validity. An established food quality survey could be the best way to represent dietary habits in this group.

5.3 Medication

While medications were encoded into the SPSS database for the study, it was not used in this study analysis. The database was encoded for medications but was not utilized due to the small sample size. In addition, a wide variety of medications were being taken by the subjects, which made grouping or clustering of medication impractical. If the number of subjects was larger, analysis would have been done to find if medication has impact on physical activity. Medications would have also been analyzed as a confounder in logistical regression models.

5.4 Pre-transplant activity

While this study reviews post transplant activity, the amount of pre-transplant activity was not measured. It can be assumed that the amount of post transplant activity

has some relation to pre transplant activity. Meaning, someone who was not physically active before their transplant will not likely be highly active after transplant. Because of this dependence, this factor should be measured in future studies to find the impact of pre transplant activity on post-transplant activity and how the change in activity may be associated with other factors such as medication, vitals, and medical history.

5.5 Creatinine Clearance

While serum creatinine and blood urea nitrogen were used as surrogate markers to predict kidney function, in this study, creatinine clearance is a more accurate method to measure kidney function. The two most used formulas are Cockcroft and Gault formula for adults and the Shwartz formula for children. During the analysis phase of this study, the creatinine clearance for all subjects was explored in modeling, but no significant results were observed. Future studies in activity post kidney transplantation may need to use more accurate markers to measure kidney function instead of serum creatinine or creatinine clearance.

6. SUMMARY and CONCLUSIONS

The Hypotheses for this study was that "There is a relationship between the physical activity levels and renal function in post kidney transplant patients." The final results of a positive association of serum creatinine and negative blood urea nitrogen with physical activity in the main model did support the hypothesis. This was after adjusting for other factors such as age group, gender, heart rate, and blood pressure. The nature of this association needs to be explored. Further studies will need to add the factor of medications, which were not used in analysis. Medications should be assumed to have impact on activity, heart rate, and on diet, therefore they become an important confounding factor.

A secondary finding was the IPAQ survey; a commonly utilized activity survey did not correlate well with direct measurement of physical activity recorded on a digital accelerometer. Surveys are easy to implement and are widely used; but with such a poor correlation with actual activity, their reliability and validity comes into question. This issue, too, needs exploring since not only does it have impact on studying physical activity in post renal transplants, but it may call into question the results of the numerous studies done around the world using the IPAQ.

This study also found a new way to measure physical activity. The "endurance" factor as related by the longest period of moderate activity in the monitored week was associated with heart rate. This factor appears to be a good predictor of physical activity requiring further research.

Overall, this study shows that there appears to be an association between kidney function and physical activity. While one association, between high blood urea nitrogen

and low activity, was expected; the positive association between serum creatinine and activity was not expected. This fact, along with the poor correlation between physical activity determined by a self-reported survey and actual physical activity, highlights the need for further research in evaluating physical activity in post transplants patients.

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Appendix A

Study Protocol

eIRB #3174
Revised: 03/05/2007

GENERAL CLINICAL RESEARCH CENTER
Oregon Health & Science University
RESEARCH PROTOCOL

Protocol Title: Assessment of Physical Activity in Post Renal Transplant Patients Using Mini-Mitter Accelerometers

(Short Title: PA in Post Transplant Patients)

Principal Investigator: Amira Al-Uzri, M.D.

Co- Investigator: Paul Lees, M.S.

Sub- Investigators: Atif Zaman, M.D.; Tomi Mori, PhD.; Anuja Mittalhenkle, M.D.
Tamala LaBeck, RN.

Structured Scientific Abstract:
Background: Recent research has shown that there is a possible link between increased physical activity (and exercise) to improved health in post renal transplant recipients. While this research shows that there may be a positive association overall with increased activity, little research has been done in finding what may limit a patients ability to do exercise or be physically active.
Objective: To assess the physical activity level of post renal transplant patients and determine what factors are associated with inactivity in this at- risk population. This study will be used as a pilot study to secure funding for a larger study using the same methodology. This future study will attempt to find if the increased likelihood of inactivity is due to factors associated with kidney transplantation such as immunosuppression therapy, or if subjects who are active tend to have a better recovery and outcome after transplant.
Design: Cross Sectional observational study in addition to using a survey
Setting and Subjects: 50 Post renal transplant recipients from ages of 13 to 60 who had their transplants less than 18 months before date of consent. (Expect to consent up to 75 subjects due to the possibility of screen failures.) Subjects will be recruited from current OHSU and Doernbecher Children's Hospital patients.
Intervention: none
Measurements: Daily Active Energy Expenditure and Total Daily Energy Expenditure over a course of 7 days using the Actical accelerometer. Lab values from screening/baseline visit will be recorded, along with medical history. International Physical Activity Questionnaire (IPAQ) will be given to compare this sample group to sample similar groups from other studies.
Analysis: Logistic regression modeling will be used to find relationship between activity level to serum creatinine (Cr) and blood urea nitrogen (BUN after adjusting for time after transplant to BMI, gender, age, medical history and current medications. Physical activity level will be define will be defined as the subject being "active" or "inactive" per CDC guidelines.

a. Specific Hypothesis and Study Aims:

Primary Aims and Hypotheses:

Hypotheses: As renal function worsens, the Physical Activity levels will decrease in post renal transplant patients.

Primary Aim: To determine the association between BUN and Cr with physical activity levels as determined by digital accelerometers in post renal transplant patients"

b. Background and Significance:

There were 2004, there were 16,885 kidney transplants performed in the United States in 2004 with another 63,092 patients waiting as of August 2005 [1]. The median waiting time for a kidney transplant can be as long three years, depending on the transplant center [2]. During this time these potential transplant patients are in declining health which increases their amount of physical inactivity. This physical inactivity accompanied by decrease in kidney function, and dialysis therapy, the majority of patients will develop hyperlipidemia, worsening hypertension, and weight gain. The National Kidney Foundation recommends that those waiting for a kidney transplant be physically active and exercise whenever possible. After transplant, patients are advised to remain inactive for one to three months after surgery, then slowly become more physically active over time [3 & 4]. It is the amount of time after transplant and the level of physical activity that is currently debated.

While the National Kidney Foundation recommends that transplant recipients start off with mild exercise 10 to 15 minutes a day and progress to strenuous exercise 30 to 60 minutes a day, most days of the week; they do not recommend when to start exercise. They do emphasize that exercise will reduce some complications like increased body weight, increased likelihood of heart disease, high blood pressure, and an increase in cholesterol [5]. Some transplant centers, like the Mount Sinai Medical Center and USC Transplant Program, recommend that physical activity and exercise be limited and increased slowly under a doctor's supervision [6 & 7], other centers like The Cleveland Clinic ask that their patients attempt move to the level of exercising 20 to 30 minutes at a time, at least three days a week at their own pace [8]. These varied recommendations for exercise after renal transplant seem to have been created due to a lack of scientific evidence in the area. There have been few published studies that have researched exercise and physical activity levels after renal transplant.

In an attempt to learn more about the impact of exercise and physical activity post transplant, some studies monitored exercise levels after transplant. One of the first studies by JR Poortmans, et al… found that there was no decrease in renal function in post renal transplants after exercising, which supported the concept that the exercise was not harmful. This study only monitored subjects at nine months post transplant and dealt only with exercise as measured on a treadmill test [9]. These findings have been verified by other studies. The most recent was done by the University of California at San Francisco which evaluated children (ages 10 to 18) who were three months or more after transplant. This study used the FITNESSGRAM field tests for physical fitness. These series of tests are used across the United States in schools to evaluate the fitness levels of students. The authors looked at the field tests in 25 patients, 3 months or more after kidney transplantation and found no correlation time after transplant and being on prednisone therapy to the field tests scores. Overall, these patients did not score as high as their peers. It was also noted that the kidney transplant subjects were very inactive in their spare time with and average of only 1.8 METs in after school activity with an average peak of only 4 METs. (A MET of 1.0 is the energy required just sit at

rest). The low level of physical activity and low scores on the exercise field tests were correlated [10]. This same group of researchers have encouraged their patients to exercise, after a study in 2002 which showed that kidney transplant patients who maintained a regular exercise plan for a year had less need for anti-rejection drugs, lower body mass index (BMI) scores, less body fat, and better scores on tread mill testing than those who were on "standard of care" treatment. It also found no difference between the two groups in measurements of renal function. This research did not adjust for other variables, but instead just reported the differences in measures between the exercise and standard of care group [11]. This creates an issue for the need to find if there is an impact on amount of physical activity (and exercise) on a patient based on their reduced kidney function.

c. Preliminary Studies / Progress Report:

A preliminary study was carried out at OHSU (eIRB #1601) between the summer of 2005 and summer of 2006. This study used the International Physical Assessment Questionnaire (IPAQ) to assess the physical activity level of 103 patients who were between 3 months and 30 years post renal transplant (median= 4 yrs., mean = 6 yrs. S.D.= 5.7 years). The results of this survey showed that of the 103 patients surveyed; 11.7% were in the low/no activity group, 30.1% were in the moderate activity group, and 58.3% were in the high activity group. Furthermore, the study showed some association between inactivity and poor health in this group as measured by reduced kidney function. These results were presented in a poster at the World Transplant Congress in Boston in July of 2006. Presently, close to 39.1% of Oregonians were defined as physically inactive according to the Physical Activity and Nutrition Program of the State of Oregon. Considering that post transplant patients were taking a variety of medications, had a similar BMI as most Oregonians (57.3% of transplants were overweight or obese versus 59.2% of Oregonians), and a number of patients had decreased kidney function; there should have been a higher percentage of patients who did not meet physical activity standards than the state average rather than the opposite. The difference in these results may be attributed to the different definition used by the State of Oregon to define inactivity using the Centers for Disease Control (CDC) criteria of inactivity, while the IPAQ uses a METS assessment; the two do have similar standards for the definition of inactivity. (See Table 1 below for CDC and IPAQ definitions). We therefore conclude that, the IPAQ is a poor instrument to assess physical activity in this group and can not be used to link inactivity to health issues (in this at-risk group) such as BMI, medications, blood pressure, or lab values such as serum creatinine (Cr) and blood urea nitrogen (BUN).

To overcome this problem, a better method was researched. After a review of the literature, using digital accelerometers was found be the best method for assessment of physical activity for this group. These instruments allowed for the precise and reliable measure of activity that the IPAQ lacked. In addition, they gather the precise level of activity that is required to create models in physical assessment using a small sample size.

	Inactivity	Moderate	Vigorous
CDC definition	Not meeting the requirements for either Moderate or Vigorous	Attaining a MET level of 3 to 6 per minute for 30 or more minutes day, 5 or times a week	Attaining a MET level of over 6 per minute for 20 or more minutes day, 3 or times a week
IPAQ definition	Not meeting the requirements for either Moderate or Vigorous	Three or more activities considered "Vigorous" at 20 minutes or more in a week; Five or more activities considered "Moderate" at 30 minutes or more in a week; or 5 or more activities that achieve an minimum of 600 MET-minutes per week	Three or more activities considered "Vigorous" and at least 1500 MET-minutes per week; or 7 or more activities per week for a minimum total of 3000 MET -minutes

Table 1. CDC definition of Physical Activity and a comparison to IPAQ

d. Research Design and Methods

1. Experimental Design:

Description of subjects

Subjects who have had a transplant within 18 months on consent dates will be recruited from OHSU adult and pediatric transplant clinics.

Inclusion criteria:

- Be from 13 to 60 years of age
- Be able to ambulate (not in wheel chair or walking with assistance0
- Had a renal transplant within 18 months from enrollment
- Ability to speak and read English

Exclusion Criteria:

- Heart and/or lung disease
- Unable to wear the physical activity monitor
- Refuse to return the physical activity monitor
- Currently have a fever

Description of study procedures

Screening/Baseline Visit

Potential subjects will be first approached by their nephrologists for participation in the study. If the potential subject would like to join the study, a member of the research team will explain the study to them and obtain their consent. Those who do consent will be briefed on the use of the physical activity monitor, the IPAQ survey, and the requirements for returning the monitor. The subjects will also fill out a short questionnaire on their current health and background. They will be instructed to wear the monitor for exactly seven days. At the end of those seven days, they are to remove the monitor and to take the IPAQ survey. If the subject is planning on returning to OHSU the following week, he/she will be asked to return the survey and monitor at their next visit. Those not planning on returning the following week will be given a prepaid overnight shipping box to return the

monitor with the survey. This prepaid box will include instructions on how to return the device and survey, along with report slip for the subject to note the time they took off the device. The only visit that will occur for this study is the one immediately after consent. If the subject is planning on returning the monitor and survey to OHSU in person, they will just need to drop it off at their follow up visit with their nephrologist.

Figure #1: The Actical Digital Accelerometer
By Mini-Mitter

Physical activity will be monitored using an Actical accelerometer (Mini Mitter Co., Inc, Bend, Oregon.) The Actical activity monitoring device utilizes an multidirectional accelerometer to monitor the occurrence and intensity of motion. The Actical device measures 28 mm by 27 mm by 10mm, weighs 17.0 grams, and is securely attached to a waistband and placed around the waist (see picture above). The device can be worn and collect data for 44 days. For this study the subject will be required to wear the monitor for only 7 days. Data will be uploaded and downloaded using an ActiReader. This data includes Daily Active Energy Expenditure and Total Daily Energy Expenditure. Actical's activity count data is converted into minute-by-minute energy expenditure (Figure 2). This is used to calculate daily caloric expenditure. Using software that is provided with the ActiReader, the data can be analyzed to find if the subject met CDC standards of healthy physical activity for the week or not.

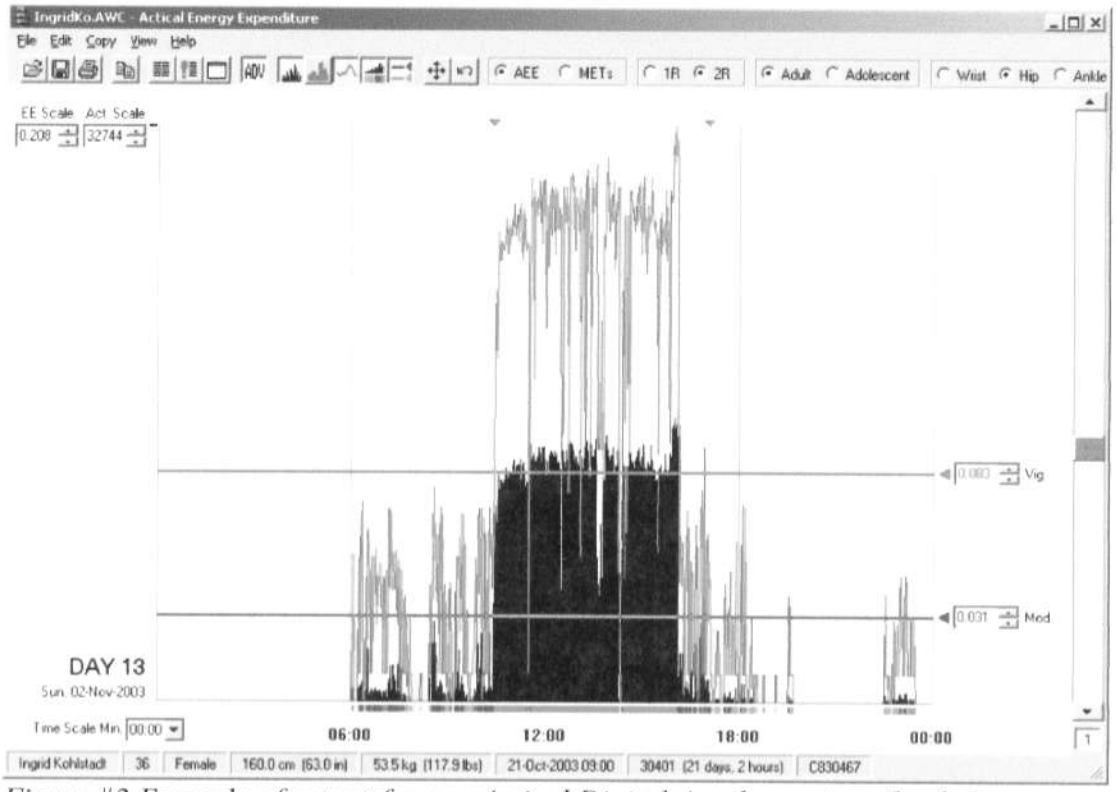

Figure #2 Example of output from a, Actical Digital Accelerometer after being accessed by a ActiReader. In this example, someone who ran the 2003 New York City Marathon. Note the adjustable activity thresholds.

Additional information for the subjects participating in the study will be collected from their medical records such as demographic data, blood pressure measurements, heart rate, height, weight, serum creatinine (Cr), BUN levels, cause of renal failure and medical history and a list of current medications. No additional labs or visits will be required for this study. This data, as well as the results from the IPAQ survey done at the end of the study week, and the data from the physical activity monitor (as "active" or "inactive") will be stored in the study database. Once 50 subjects have completed the study, the data will be analyzed to find possible predictors for physical inactivity as defined by the Centers for Disease Control (CDC).

2. Statistical considerations:

In October 2005, the "Oregon Overweight, Obesity, Physical Activity, and Nutrition Facts" booklet [12] reported that 60.2% of all adults in the state were meeting CDC requirements of minimum healthy activity. This figure was created by using a random digit dialing of 2900 people. Assuming that 60% of the patients are inactive at the mean Cr level, the sample size of 50 patients will provide 92% power to detect a difference of 60% (at the mean Cr level) vs. 80% (at the one standard deviation above the mean) with 5% significance level. This corresponds to a detectable odds ratio of 2.67. The sample size and power analysis were performed based on the logistic regression model with a continuous normally distributed covariate.

The variables that will be collected for model will be:

Predictor/Confounder	Reason
Age	Confounder
BMI	Confounder
Cr level	Predictor
BUN level	Predictor
Reason for transplant (categorical)	Confounder
Gender (categorical)	Confounder
CDC defined Activity level (categorical)	Outcome
Medication (categorical)	Confounder
Time since transplant	Confounder
Blood pressure*	Confounder

*note: may be turned into a categorical variable in analysis

The statistical analysis plan for this study will start with descriptive statistics for all variables. This includes mean, median, mode and variance for all continuous variables, as well as frequencies for categorical variables. This level analysis will be followed with chi-square testing between categorical variables in order to find possible associations. Continuous variables will be compared to each other using correlation and regression analysis. Categorical and continuous will be analyzed using t-tests and regression analysis using dummy coding. The final step of the analysis will be modeling using logistic regression to predict activity level using the predictors and confounders noted above. Results from the previous levels on analysis will be used to help determine the best logistic regression model for this sample size. The results of this analysis will be reported using odds ratios to show the level of association between Cr level and BUN level to physical inactivity after adjusting for other factors.

3. Human Subjects Considerations:

3.1 Potential Risks, Protection from Risks, and Risk/Benefit Discussion

Subjects will be wearing the Actical accelerometer for 7 days. There are no known risks or discomforts from wearing this device. Subjects will have their privacy protected under OHSU privacy policies as determined by the HIPAA rules (OSHU IRB. Their activity levels will not be placed in their medical record, nor will the principal investigator or the subject's primary physician will know the results. The database will be stored in a password protected file on the OHSU system. This system will require a log-on and electronic permission to access specific directories. The data will be stored on a directory specific to principal investigator and the co-investigator.

3.2 Rational for inclusion and protection of vulnerable populations

Patients between the ages of 13 to 17 will be included since this group is currently defined at risk of being physically inactive. The additional risk factor of being a post renal transplant needs to be studied to find if it creates a greater impact on being inactive on their general health than if the subject was an adult and being a post renal transplant patient.

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Appendix B

OHSU IRB Approval Memo

IRB only: IRB#3174

PPQ#_____

PROPOSED PROJECT QUESTIONNAIRE (PPQ) – PLEASE TYPE

Oregon Health & Science University Research Development and Administration (RDA)

This form must accompany all grant/contract applications and new protocols submitted for review by IRB or IACUC.

GENERAL INFORMATION

Principal Investigator (Last name, First name, Degrees)	Telephone Number	Mail Code	Email Address	NIH Commons UserID
Al-Uzri, Amira, M.D.	503-494-6956	CDRCP	aluzria@ohsu.edu	

Contact for questions during proposal review process (Last name, First name)	Telephone Number	Mail Code	Email Address
Amendolara, Cylia	x4-7171	CDRC-P	amendola@ohsu.edu

School/Unit: Medicine **Department:** Pediatrics **Division:** Nephrology

Award Owning Org Name (Name of the org that the Award will be assigned to and that will receive F&A credit unless otherwise specified below):
Please see the OHSU Project-Owning Org Finder Tool.
65714 SM. Peds Neph

Will F&A be shared by more than one department or unit? * If yes, indicate agreement by having each department/unit head and each internal project PI sign this PPQ. Also include an internal budget showing the distribution of funds requested. ☐ Yes* ☒ No

Project Title (240 characters maximum. Same as project title listed in grant or contract.)
Assessment of Physical Activity in Post Renal Transplant Patients Using Mini-Mitter Accelerometers

Project Dates			
	Initial Budget Period (Next if Non-Competing)	From: 3/12/2007	Thru: 03/12/2008
(N/A for industry contracts)	Entire Proposed Project Period	From: **3/12/2007**	Thru: 03/12/2008

Keywords (Please provide 3-5 keywords): Renal Transplant Physical Activity ____

Applicant Organization
☒ OHSU ☐ Other*
*If Other, please specify pass-through organization that will issue a subcontract to OHSU: ____

Sponsor: OHSU Division of Nephrology
(Example: NIH, American Heart Association, Acme Co.)

Sponsor Deadline: ____

Clinical Research Organization (CRO) (If applicable for an industry sponsored clinical drug / device investigation): ____
See Clinical Research Organization definition.

Funding Opportunity Number, Request for Proposal (RFP) #, Request for Application (RFA) #, Program Announcement (PA) #, or URL address for special instructions, if applicable: ____

ACTIVITY AND F&A RATE INFORMATION

Does the funding agency have a published policy requiring the use of an F&A rate that differs from OHSU's federally negotiated rate (See OHSU's F&A Cost Rates)? * If yes, please attach the published rate and policy of the funding agency. This does not apply to industry sponsors. ☐ Yes* ☒ No

Funding Agency Rate * ____

Primary location (Building Name) where the work is being performed (See the OHSU Building List): CSB 620

% of work performed at this location: 60%

Indicate 'Off-Campus' if the work is being performed at a non-OHSU facility.

Is the research primarily Basic or Applied? See Basic/Applied Research Definitions. Please select one: ☐ Basic ☒ Applied

TYPE OF FUNDING INFORMATION

Funding Mechanism *Other* * * If Other, please specify: Internal
If a Program Development Account (PDA) is funding this project, please specify the PDA account number: ____

Grant/Contract Type *Check all that apply*

☒ New – new project not previously funded by this sponsor

☐ Resubmission – revised or amended version of application not funded

☐ Competing Renewal – competitive application for funded project Sponsor Grant# ____

☐ Amendment/Supplement – request for additional funds Sponsor Grant# ____ *(if applicable)*

☐ Non-Competing Renewal * – renewal of a funded project (i.e., NIH progress report) Sponsor Grant# ____

** If this project involves humans and/or animals, please indicate applicable IRB Protocol #(s) ____ or IACUC Protocol #(s) ____*

☐ NIH eSNAP *

** If this project involves humans and/or animals, please indicate applicable IRB Protocol #(s) ____ or IACUC Protocol #(s) ____*

PPQ#_____

COMPLIANCE QUESTIONS	
1. **Will human subjects/tissues/data be used in the project?** a. From the start of the award? (If no, see Preaward Process for Proposals Involving Human Subjects at a Future Time.) b. Will the award fund core research or educational resources to be used by multiple independent human research projects (i.e., GCRC, OCI infrastructure, etc.)? All projects involving human subjects/tissues/data must be submitted to and approved by the IRB prior to beginning work on new projects or modifications to existing protocols.	☒ Yes ☐ No ☒ Yes ☐ No ☐ Yes ☒ No
2. **Will animals be used in the project?** a. * If yes, will non-human primates be used in the project? All projects involving animals must be submitted to and approved by the IACUC prior to beginning work on new projects or modifications to existing protocols.	☐ Yes* ☒ No ☐ Yes ☐ No
3. **If this study involves humans or animals, did OHSU personnel design/develop the study protocol?** The answer to this question will help determine how to handle the intellectual property terms of the proposal, determine appropriate IRB fees for the study, and allow tracking of this information for reporting and management purposes.	☒ Yes ☐ No ☐ N/A
4. **Will this project involve the use of non-recombinant infectious agents or certain biologically-derived toxins (including select agents and infectious proteins, cells, viruses, bacteria, etc.)?** See Definition. * If yes, complete the Infectious Agent/Toxin Questionnaire and submit it with this PPQ. **-OR-** Approved IBC registration #: _____	☐ Yes* ☒ No
5. **Will this project involve the use of recombinant DNA (rDNA, includes all recombinant plasmids/vectors/viruses)?** * If yes, complete the Initial rDNA Research Classification Form and submit it with this PPQ. **-OR-** Approved IBC registration # is: _____ -OR- This project was previously determined to be exempt and no changes are proposed that will affect the exempt status ☐	☐ Yes* ☒ No

ADMINISTRATIVE QUESTIONS	
6. **Does this application or proposal include committed cost-sharing/matching (i.e., is effort being committed without requesting that sponsor support salary at the same level? Are other resources, like new equipment or supplies, being committed without a budget request to support them?)** *Does not apply to industry sponsors.* See the OHSU Cost Sharing Procedure. * If yes, see the Department Award Checklist (DAC) provided by RGC for instructions for awards containing cost-sharing. If the cost sharing is from multiple departments, please complete a Cost-Sharing Agreement Form for each Department committing resources and submit with PPQ. If the cost sharing is with the VA, the Cost Sharing Agreement Form should be signed by the appropriate VA clinical service chief and submitted with the PPQ. *(Does not apply to internally funded projects; e.g., Bio-Science Innovation.)*	☐ Yes* ☒ No ☐ N/A
7. **Do any of the personnel listed on this project who have paid or unpaid appointments at OHSU also have paid VA appointments?** * If yes, please provide the most recent copy of the memorandum of understanding (MOU), dated within one year. The MOU is not required if the project is industry-sponsored. Note that if this project is funded, an updated MOU that accounts for effort on this project will be required at time of award. If any persons listed on this project have unpaid OHSU appointments and paid VA appointments, please be sure to complete the VA cost-sharing requirements referenced in Question 6 above.	☐ Yes* ☒ No
8. **Does this project involve Portland Veterans Affairs Medical Center (PVAMC) resources?** * If yes, please have this PPQ signed by the VA ACOS/R&D (Associate Chief of Staff for Research & Development) and prepare a VA PPQ for submission with the OHSU PPQ. In certain cases, the Research Service at the PVAMC will need to obtain the approval of the VA clinical service chief prior to VA signature on the OHSU PPQ. If this proposal includes research related expenses that will be incurred by the VA, you will need to complete a VA Administrative Review prior to VA signature of the OHSU PPQ. Non-competing renewals do NOT require a VA PPQ or VA Administrative Review. Please check all the following VA resources that apply: ☐ VA Space If checked, please indicate the VA Building Name: *Click Here to Select Building* ☐ VA Equipment ☐ VA patients seen at PVAMC	☐ Yes* ☒ No
9. **Is OHSU to subcontract part of the work?** * If yes, please include approved administrative materials for all proposed subcontractor institutions. Subcontract materials must be signed off in advance by authorized officials of the subcontract organizations. See the List of Required Subcontract Administrative Materials. *(Does not apply if sponsor is industry.)*	☐ Yes* ☒ No

PPQ#_____

APPROVALS & CERTIFICATIONS

All signatures below are required prior to institutional approval of the proposal.

As the PI of this project, I certify that the information submitted within the application is true, complete, and accurate to the best of my knowledge. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. I agree to accept responsibility for the scientific conduct of the project and, if a grant or contract is awarded as a result of this proposal, to comply with the terms and conditions of the award, including providing required progress reports. I understand that I am responsible for ensuring that the project is conducted in full observance of the financial, compliance, and administrative requirements described in the OHSU Roles and Responsibilities in Research document.

PI / Project Director, Date
Name: Amira Al-Uzri

The signatures of the Division Head, Department Chair and Unit Dean/Director indicate that:

- the proposed scientific work is appropriate;
- space and/or resources are, or will be, available;
- budgeted salaries and effort levels are appropriate for the personnel named in the application;
- the budget proposed is sufficient to cover the costs incurred in the study,
- and that roles and responsibilities assigned to the Division Head, Department Chair and Unit Dean/Director as described in the OHSU Roles and Responsibilities in Research document will be carried out or appropriately delegated.
- If the project involves resources (faculty, staff, equipment, space) from more than one OHSU Department/School/Unit, each Department Chair/Dean/Director should review the proposal and approve it by signing below.

The signature of the VA Research Service does not represent institutional approval. It simply indicates that the VA Research Service is aware of the proposal and the VA review process has commenced. The work cannot begin at the PVAMC without the approval of the R&D Committee.

Note: All staff with direct involvement in the design and/or conduct of the project (including, but not limited to, the principal investigator, co-investigators, research assistants/coordinators, and collaborators) must:

- Complete OHSU's Responsible Conduct of Research (RCR) Education
- Have a current OHSU Conflict of Interest in Research Disclosure form on file
- See Requirements for Investigators Outside OHSU

Division Head, Date 7/13/07 Name:	Department Chair, Date 3/14/07 Name:	Dean / Director, Date 3/16/07 Name: for Mark Richards
Division Head, Date Name: *(if appropriate)*	Department Chair, Date Name: *(if appropriate)*	Dean / Director, Date Name: *(if appropriate)*
VA ACOS/R&D, Date Name:	SON Advisor, Date Name: (*if PI is SON student*)	*Other:*

OREGON HEALTH & SCIENCE UNIVERSITY
Research Integrity Office, L106-RI
2525 SW First Avenue, Portland, OR 97201
Phone: (503) 494-7887

MEMO

Date: March 23, 2007

To: Amira Al-Uzri, MD

From: Susan B. Bankowski, MS, JD, Chair, Institutional Review Board, L106-RI
Gary T. Chiodo, DMD, FACD, Director, OHSU Research Integrity Office, L106-RI
Charlotte Shupert, Ph.D., Associate Director, Research Integrity Office, L106-RI
Kara Manning Drolet, Ph.D., IRB Co-Chair, Institutional Review Board, L106-RI
Susan Hickman, Ph.D., IRB Co-Chair, Institutional Review Board, L106-RI
Katie McClure, M.D., IRB Co-Chair, Institutional Review Board, L106-RI

Subject: IRB00003174, Assessment of Physical Activity in Post renal Transplant Patients Using Accelerometers

Initial Study Review
Protocol/Consent Form Approval

This memo also serves as confirmation that the OHSU IRB (FWA00000161) is in compliance with ICH-GCP codes 3.1-3.4 which outline: Responsibilities, Composition, Functions, and Operations, Procedures, and Records of the IRB.

This study is approved for 75 subjects.

Your protocol is approved for one year effective 03/26/2007 .

Your combined consent/authorization form is approved by the IRB effective 03/26/2007 .
You may use only copies of the approved consent/authorization form for the informed consent process.

Your child assent form is approved by the IRB effective 03/26/2007 .
You may use only copies of the approved child assent form for the informed consent process. The approved child assent form can be found by logging on to the eIRB system and going to your study. Next, click on the Study Documents tab and locate your approved child assent form under the Approved Documents heading.

Other items reviewed and administratively approved by the IRB include:

- **Lay Language Protocol Summary**
- **Data Sheet on Subjects**
- **IPAQ Physical Activity Survey**
- **IPAQ Physical Activity Survey Scoring Sheet**
- **Packing Slip**
- **Subject Instructions**

Other items reviewed and noted by the IRB include:

- **Cover Letter**
- **Studies in Children Using this Accelerometer**
- **Adult Studies Using this Accelerometer**
- **510K Clearance (parts 1 and 2)**
- **Accelerometer Description**
- **Accelerometer Tech Sheet**

This study met the criteria for EXPEDITED IRB review based on Categories #4, 5, and 7:

> (4) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing.
>
> (5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).
>
> (7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

- *Subjects must receive a copy of OHSU's Notice of Privacy Practices.*

Accounting for disclosures is not needed because all subjects will sign a consent form and HIPAA Authorization.

This approval may be revoked if the investigators fail to conduct the research in accordance with the guidelines found in the Roles and Responsibilities document (http://www.ohsu.edu/research/rda/rgc/randr.pdf). Please note that any proposed changes in key personnel must be submitted to the IRB via a Modification Request and approved prior to initiating the change. If you plan to discontinue your role as PI on this study or leave OHSU, you must arrange either (a) to terminate the study by so notifying the IRB and your department head, or (b) propose to transfer the responsibility of the PI to a new faculty member using a Modification Request.

Investigators must provide subjects with a copy of the consent form, keep a copy of the signed consent form with the research records, and place a signed copy in the patient's hospital/clinical medical record (if applicable).

This approval may be revoked if the investigators fail to conduct the research in accordance with the guidelines found in the Roles and Responsibilities document (). Please note that any proposed changes in key personnel must be submitted to the IRB via a Modification Request and approved prior to initiating the change. If you plan to discontinue your role as PI on this study or leave

OHSU, you must arrange either (a) to terminate the study by so notifying the IRB and your department head, or (b) propose to transfer the responsibility of the PI to a new faculty member using a Modification Request.

Appendix C

Variable List

Variable #	Name	Label
1	ID	ID #
2	S_date	Start Date
3	E_date	End Date
4	Act_lvl	CDC Activity Level (per accelerometer)
5	Act_cdc	Meets CDC guidelines for actvity? (per accelerometer)
6	age	Age at time of testing
7	Minor	Age group
8	gender	Gender
9	Hght	Height (in inches)
10	Wght	Weight (in pounds)
11	BP_s	Blood pressure (Systolic)
12	BP_d	Blood pressure (Diastolic)
13	HR	Heart Rate
14	Trans_rea	Reason for transplant
15	Cr_lvl	Serum Creatinine
16	BUN_lvl	Blood Urea Nitrogen
17	min_mod	Minutes of moderate activity (3.0 to 5.9 METS) per accelerometer
18	min_vig	Minutes of vigorous activity (6.0 or more METS) per accelerometer
19	time	Minutes on accounted for on accelerometers
20	IPAQ_mod	Minutes of moderate activity (3.0 to 5.9 METS) per IPAQ w/o caps
21	IPAQ_Vig	Minutes of vigorous activity (6.0 or more METS) per IPAQ w/o caps
22	IPAQ_cat	IPAQ Activity Level
23	time_mod	Longest time of moderate activity (3.0 to 5.9 METS) per accelerometer
24	mod_per	periods of CDC recognized of moderate activity
25	notes	Notes
26	BMI	BMI
27	Trans_days	Days since transplant
28	Tacrolimus	Tacrolimus, Prograf
29	MMF	mycophenolate mofetil / MMF / CellCept
30	Pred	Prednisone
31	Hydrocl	hydrochlorothiazide, Carozide, Diaqua, Esidrix, Ezide, Hydro Par, HydroDIURIL, Loqua, Microzide, Oretic
32	Levo	Levothroid Levothyroxine, Eltroxin, Euthyrox, Levo-T, Levotabs, Levothroid, Levoxyl, Synthroid, Unithroid
33	Meto	Metoprolol, Lopressor, Toprol-XL
34	Cycloben	Cyclobenzaprine, Flexeril
35	Omeprazole	Omeprazole, Prilosec, Zegerid
36	Oxycodon	Oxycodone, M-Oxy, OxyContin, Oxyir, Percolone, Roxicodone
37	MultiV	Multi-Vitamin

Variable #	Name	Label
38	Docusate	Docusate, Aqualax, Calube, Colace, Colace Micro-Enema, Correctol Softgel Extra Gentle, DC-240, Dialose, Diocto, Dioctocal, Dioctosoftez, Dioctyn, Dionex, Doc-Q-Lace, Docu Soft, Docucal, Doculax, Docusoft S, DOK, DOS, Doss-Relief, DSS, Ex-Lax Stool Softene
39	Potass	Potassium citrate, Urocit-K
40	Vit_d	Vitamin D
41	Tums	Tums
42	Mag	Magnesium
43	Asp	Aspirin
44	Vit_B12	Vitamin B12
45	Mag_ox	Magnesium Oxide
46	Myfortic	Mycophenolic acid, Myfortic
47	Folic	Folic Acid
48	K_Phos	potassium phosphate and sodium phosphate, K-Phos M.F., K-Phos Neutral, K-Phos No. 2, Neutra-Phos, Uro-KP-Neutral
49	Cinca	Cinacalcet, Sensipar
50	Warafin	Warfarin, Coumadin
51	Calc_car	Calcium Carbonate
52	Lanso	Lansoprazole, Prevacid, Prevacid I.V., Prevacid SoluTab
53	Prozac	Fluoxetine, Prozac, Prozac Weekly, Sarafem
54	Cipro	Ciprofloxacin, Cipro, Cipro XR
55	Acyclov	Acyclovir, Zovirax
56	Florinef	Fludrocortisone, Florinef Acetate
57	Zantac	Ranitidine, Zantac, Zantac 150, Zantac 300, Zantac 300 GELdose, Zantac 75, Zantac EFFERdose, Zantac GELdose
58	Norvasc	Amlodipine, Norvasc
59	Iron	Ferrous Sulphate
60	Liptor	Atorvastatin, Lipitor
61	Flovent	Fluticasone inhalation, Flovent, Flovent HFA, Flovent Rotadisk
62	Diovan	Valsartan, Diovan
63	Avandia	Rosiglitazone, Avandia
64	Well	Bupropion, Wellbutrin, Wellbutrin SR, Wellbutrin XL, Zyban SR
65	Valcyte	Valganciclovir, Valcyte
66	Nifedipine	Nifedipine, Adalat CC, Procardia, Procardia XL
67	Labetalol	Labetalol, Normodyne, Trandate
68	Calcitriol	Calcitriol, Rocaltrol
69	Bactrium	Sulfamethoxazole and trimethoprim, Bactrim, Bactrim DS, Bactrim Pediatric, Bethaprim, Bethaprim Pediatric, Cotrim, Cotrim DS, Cotrim Pediatric, Septra, Septra DS, Sulfatrim, Sulfatrim Pediatric, Sulfatrim Suspension, Uroplus, Uroplus DS
70	Clotrimzole	Clotrimazole, Mycelex Troche
71	Co_trim	Co-trimoxazole, sulfamethoxazole and trimethoprim
72	Ditropan	Oxybutynin, Ditropan, Ditropan XL, Oxytrol, Urotrol
73	Clonidine	Clonidine, Catapres
74	Acyclovir	Acyclovir, Zovirax
75	Gabepentin	Gabapentin, Neurontin
76	EPO	Epoetin alfa, Epogen, Procrit
77	Codeine	Codeine