RENAL PERFUSION MODEL: OUTCOME PREDICTIONS

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ABSTRACT

The Banner University Medical Center's (BUMC) renal transplant program relies on the LifePort Kidney Transporter to optimize marginal kidney organs via hypothermic machine perfusion (HMP) prior to transplantation. Hemodynamic parameters produced by the device followed over the duration of support, combined with clinical experience, guide decisions in determining the acceptability of a donor kidney for implantation. Thus far, statistical evidence supporting ideal parameters remain undefined. The purpose of this study is to create a logistic model that will ascertain the post-implant sustainability of LifePort® supported kidneys and predict clinical outcomes. My hypothesis is that the statistical models constructed based on retrospective LifePort® parameters and clinical outcome data will successfully predict donor organ vascular health for transplantation and the optimal support duration. A successful model will contribute to increased efficiencies in the kidney transplant process as well as improved patient outcomes.

An overview of the institution's success was weighed using a survival analysis, with delayed graft function (DGF) as the endpoint. A logistic regression model and forecast model were built to predict the outcome for rejecting or accepting the organ for transplant, as well as to predict the hemodynamic parameters hours after the start of infusion.

Results concluded a flow greater than 80 mL/min had a 90% probability of transplantation. The forecast model was capable of predicting flow for up to five hours. The calculated flow was in a 10 mL/min range of the actual flow, when up to one hour parameters were entered into the model. The study concluded practicality in the clinical setting, in kidney transplantation.

INTRODUCTION

Approximately, over 118,000 people are listed on the UNOS – United Network for Organ Sharing – waiting list; of all the candidates listed for a specific organ, about 81% are waiting for a kidney (20). The recovery of organs is both crucial and essential, in order to contend with such high necessity. At Banner University Medical Center (BUMC) the renal transplant program relies on the LifePort Kidney Transporter to optimize marginal kidney organs via hypothermic machine perfusion (HMP). Perfusion supported organ recovery in kidney transplantation is the main focus of the donor procurement team, the perfusionist assistants at BUMC.

HMP via the LifePort®, is a fairly new method of preservation; Organ Recovery Systems introduced the ex vivo perfusion machine in 2003 (4). The few reports available are focused on benefits, whether clinically or cost effectiveness. Although there is general understanding of the LifePort® functions, guidelines are elusive and institutional based. Relying heavily on surgeon experience and popularized protocols to guide decision making, the exact LifePort® produced hemodynamic parameters are unknown.

The ex vivo perfusion system has the capacity to measure hemodynamic parameters, inclusive of flow, pressure – systolic and diastolic – and resistance, other measurements are time of perfusion and temperatures. The parameters are significant indicators of the renal organ's physiological health and vouch for the status of the organ, whether or not to implant the organ. The protocol at BUMC is an ideal flow of perfusion greater than 80 mL/min, a systolic pressure of 30 mmHg, and a resistance less than .3 mmHg/mL/min. Since, not all kidneys are similar, issues have arisen and exposed the weakness in having open ended guidelines. For instance, at

what parameter is a kidney considered unacceptable? Why is a kidney with a flow of 64 mL/min or a kidney with a resistance of .51 mmHg/mL/min acceptable? The parameters for those situations are unclear; the way in which a surgeon makes a decision is not an exact science either.

Purpose of the Study

Hemodynamic parameters produced by the device followed over the duration of support, combined with clinical experience, guide decisions in determining the acceptability of a donor kidney for implantation. Thus far, statistical evidence supporting ideal parameters remain unavailable. The purpose of the study is to construct models that will ascertain the post-implant sustainability of LifePort® supported donor kidneys and predict clinical outcomes. The hypothesis is that the statistical models created based on retrospective LifePort® parameters and clinical outcome data will successfully predict I) donor organ vascular health for transplantation and II) the optimal support duration. A successful model will contribute to increased efficiencies in the kidney transplant process.

The primary aim is to formulate a logistic regression model based on retrospective data collected from past donor procurements. The intended use of the statistical score produced is to deduce the renal organ's vascular health, for transplantation. The secondary objective is to forecast the optimal time point, to terminate HMP whereby the vasculature has likely reached the beneficial limits from the LifePort. Both models were tested and validated, also utilizing retrospective data.

BACKGROUND

Kidney Transplantation

To approach the matter at hand, the current process in kidney transplantation is explained. When a donor organ becomes available, the kidney is systematically allocated. Immediate transplantation is not always possible; multiple factors go into finding a recipient for the organ such as a combination of donor, and recipient medical aspects as well as respective geographical locations. More specifically, blood type, weight, height and factors unique to the individual kidney are taken into account. Two central components of individuality is the kidney donor profile index (KDPI) and estimated post-transplant survival (EPTS) number. KDPI is a percent number grading the kidney's longevity based on age, hypertension, diabetes, cause of death, creatinine levels and hepatic C status. The higher the KDPI percentage the lower the life span is on the organ, and lower percentage is indicative of long lasting kidneys. EPTS rankings the recipient rather than the donor kidney; this number also determines their placement on the waiting list. The number advocates for the recipient's survival rate post-surgery and is dependent upon age, diabetes, if they have received a prior transplant, and the diagnosis period of chronic kidney disease (CKD). Opposite to KDPI, a low EPTS number is expressed higher on the waiting list, having a greater urgency for a kidney. The matching of both KDPI and EPTS ensures the best kidney is placed with the most suited recipient (9). This avoids any future dilemma, where a recipient outlives their donor kidney and would need another down the road.

Once assigned, the organ is placed on ice and relocated. At BUMC the organ can either remain on ice until transplant or placed on the LifePort® machine. Both methods of preservation are meant to avoid ischemic injury. Hypothermic conditions slow down the metabolic rate of the organ. Some noted differences are the length in preservation allowed with each method. The renal organ can remain on ice for up to 30 hours, while the kidney can be allowed 72 hours of cold ischemia with HMP (7).

Moers et al, (2009) indicated HMP as the superior preservation method. Taking pairs of kidneys and splitting them into opposite preservation methods, three endpoints were chosen to identify which had the better outcomes. The outcome endpoints were delayed graft function (DGF), serum creatinine levels, and one year graft survival rate. For all three endpoint, HMP was statistically significant by better. Ice storage does not prevent all ischemic injury, whereas with ex vivo perfusion some injury is reversed and overall decreases risk of injury is possible, thus increasing the pool of renal organs available for transplant (12).

At the institution, the decision behind placing a kidney on the LifePort® pump is dependent on the risk of developing delayed graft function. DGF is defined as the requirement of dialysis within seven days after transplant. There is a higher incidence of acute rejection if DGF occurs (11). Donor kidneys can have a predisposition for DGF based on the donor. One factor that weighs on the predisposition is the kidney category as described below.

Deceased donor kidneys are subcategorized according to cause donor's of death. A standard criteria donor (SCD) is a healthy donor and with no significant medical issues. The cause of death is most commonly traumatic or self-inflicted. Donation after circulatory death donor (DCD) occurs after a patient is removed from life support, and whose heart and lung function has naturally ceased. Donation after brain death donors (DBD) are patients who are considered dead due to ceased brain activity. Expanded criteria donors (ECD) are kidneys coming from patients older than 60 years old, whose organs have more 'wear' (17). According to Hameed et. al, "There are higher rates of delayed graft function (DGF) for both DCD and ECD kidneys, and higher discard rates and by definition poorer survival in the ECD subset, when compared with standard criteria DBD kidneys" (5).

The more important risk factors for DGF are cold ischemic time (CIT), panel reactive antibody (PRA), age, and serum creatinine levels. CIT is defined as the time the renal organ is placed on ice to the point when the organ is removed in anticipation of implant. Ojo et. al, utilized data from the U.S. Renal Data System to gauge the effects cold ischemia had on DGF. "Cold ischemia time was strongly associated with DGF, with 23% increase in the risk of DGF for every 6 hr of cold ischemia ($P<.001$)" (13). Minimizing ischemic time is critical; in such an environment the organ's physiologically health is impacted. "Extended CIT can contribute to the intensity of the oxidative stress at reperfusion by increasing the accumulation of hypoxanthine, which has been shown to be the major source of oxygen free radical species" (11). The oxygen free radicals can cause harm to the tissue; the vascular endothelium is activated by the radicals promoting a pro-inflammatory response which can lead to acute rejection episodes (11).

PRA is routinely tested on organ recipients; the test measures the immune systems' reactivity, or predict one's sensitivity due to pre-existing antibodies. The higher the PRA score, (0-99%) the greater the likelihood of developing DGF. The mechanism behind this incidence involves HLA – human leukocyte antigen – antibodies. "Antibodies cause hyperacute rejection by initiating a cascade of events leading to coagulation and immediate circulation blockage" (23). The mechanism of the reaction is characterized as the Shwarzman reaction, a considerable amount of fibrin found, intravascular. Generating extensive occlusion of the glomerular capillaries, leading to abnormal organ function (20).

An older harvested kidney is also predisposed to DGF and other complications. Moreso et. al found "the relative risk for graft failure only increases after the fifth decade" (13). Donor age's affect on DGF is explained by chronic nephropathy; the decline in graft function is the combination of hypertension and proteinuria (13).

The donor's serum creatinine level prior to the retrieval of the kidney is revealing of the vascular network's functionality. Koning et. al's study was able to conclude that a serum creatinine level greater than 120 μmol/L is significantly associated with DGF. With a lower creatinine level, the incidence of DGF was minuscule. The group also noted that high levels of serum creatinine in the donor, would likely lead to high serum creatinine levels in the recipients as well (6).

There is relevance in knowing why a kidney is managed with HMP, versus letting the organ remain on ice. As is the awareness of the predisposition the organ may have and the likely outcomes. Following the procurement process, a donor kidney is recognized to have a predisposition for DGF, is always placed on the LifePort® at BUMC.

LifePort® Kidney Transporter

Both the pump machine and kidney are prepped for perfusion. The surgeon scrubs in to dissect the surrounding fat and the renal artery of the donor kidneys. To avoid any losses in flow or pressure, any open ended vessels are tied up with sutures. The renal artery is cannulated with specially made cannulas that attach to the machine for perfusion. Preparation of the LifePort® requires familiarization of the pump's component and disposables. The machine itself consists of a roller head, bubble sensor, bubble trap, pressure transducer, temperature sensor, and an ice trap. The ice trap is typically filled with sterile water and ice to provide the hypothermic environment. The monitor on the front side of the LifePort displays pressure, temperature, duration of perfusion, resistance, flow, and any patient information entered into software. The software carries the capability to record essential information. For example, the UNOS ID, laterality, cross clamp time, and more. The disposable cartridge is a sterile circuit that fits into the transporter

pump; the circuit connects to the roller head and transducer. The cartridge also comes with a cassette on which the surgeon will place the kidney and cover with a mesh sheet attached to the cassette. The mesh merely holds the kidney in place; the cannula is connected to a piece of tubing coming off the circuit. Before the kidney is attached to the circuit, the system is primed and set up. At BUMC, the preferred solution to prime with is Kidney Perfusion Solution – 1 (KPS-1), the solution is continuously perfusing through the renal organ.

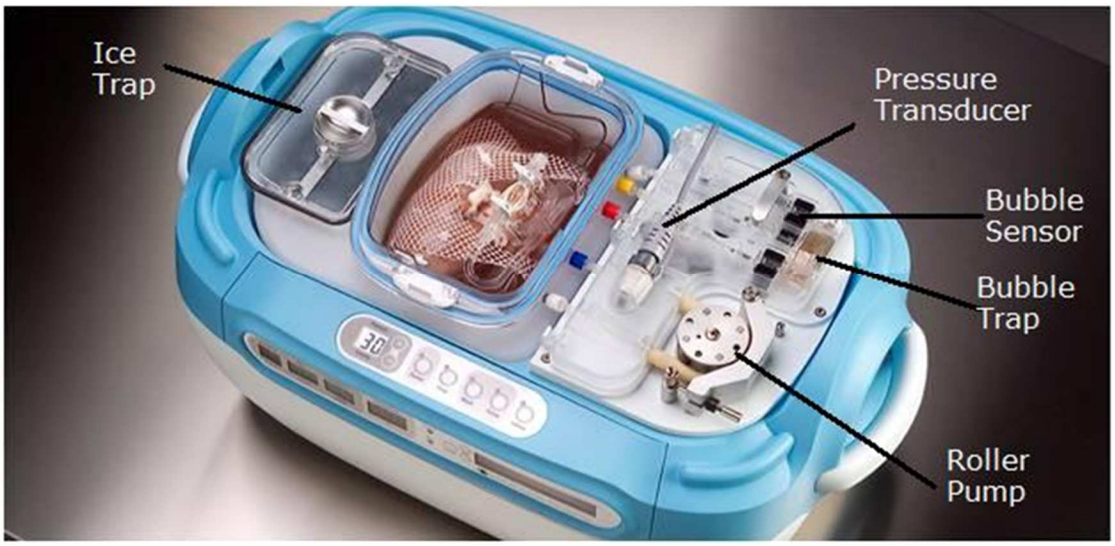

Figure 1. LifePort and its featured components. Cassette has a cannulated kidney.

KPS is provided by the same company that designed the LifePort, Organ Recovery Systems, Inc. Other solution options are University of Wisconsin Solution (UW), and EuroCollins Solution. KPS "is a clear, sterile, non-pyrogenic, non-toxic solution for the in-vitro flushing and temporary continuous perfusion preservation of explanted kidneys. This solution has an osmolality of 300 ± 15 mOsm/kg, a sodium concentration of 100mEq/L, a potassium concentration of 25 mEq/L and a pH of 7.4 ± 0.1" (15). All solutions must have a composition consistent with extracellular solution. The purpose of the solution is to diminish cell swelling brought upon by hypothermic conditions, minimize intracellular acidosis, avert interstitial space

expansion –edema – , inhibit oxygen free radicals injury during reperfusion, and supply supplemental substrates for reperfusion e.g. ATP, antioxidants (2).

The preservation solution runs continuously through the circuit into the renal artery and out the renal vein. To start the roller pump head and provide pulsatile flow through the renal organ's vasculature, the system is set to infusion. The machine will then occlude certain areas of the tubing to redirect the solution into the organ, instead of letting the prime re-circulate through the circuit. The pump flow will build up the pressure to the factory setting, 30 mmHg, and the system will measure the rest of the parameters – resistance and pressure. Once, adequate flow is reached and there are no leaking sites, the cassette is closed off with lids. Organ preservationists monitor the hemodynamic parameters throughout the duration of HMP.

The organ's ability to sustain the proper hemodynamic parameters can differentiate an acceptable kidney from an unacceptable one. Over the duration of HMP the perfusion flow rate will increase in response to decreases in resistance, and the pressure remains constant (10). At our institution the ideal parameters are a flow greater than 80 mL/min, a resistance less than .3 mmHg/mL/min, and a systolic pressure greater than 30 mmHg. The LifePort® cannot pump against a pressure setting greater than 45 mmHg. Before the LifePort®, hypothermic machine preservation has been a study of interest since the early 60's.

In 1972, the common practice was to discard any renal organ with a flow rate below 80 mL/min (3), and in 1974, Sterling et. al would discard those under 100 mL/min (21). Baxby et. al. considered the process of making decisions based on a set of parameters arbitrary (1). Others argue no statistically significant difference in clinical outcomes, between kidneys under 80 mL/min or above 100 mL/min (19). At BUMC flow, resistance, and patient's assessment weighs

in on the decision making. Cut off parameters are sometimes surgeon based; raising issues and lack of evidence on what is considered adequate or low flow. Frequently, kidneys flow at a rate that is borderline, where the flow is not low enough to reject, but not high enough to have considerable health.

Amongst other issues is the appropriate amount of time to wait for the vasculature to open and allow necessary flow. In relation to hospital resources, time is expensive. According to Patel et al., "Prognostic information of value for deceased donor transplantation can be obtained in the first 2 hours on machine perfusion" (17). The group studied 2, 4, and 6 hour time frames, the average flow was reached within 2 hours demonstrating statistically significant. The institution allows a minimum of four hours for preservation. The reasoning behind four hours is that kidneys not reaching the targeted flow have a chance to open up and are not prematurely rejected. The downside with the method is the time management; within the first 15 minutes of preservation perfusion, a picture is painted. Either there is no concern about the kidney's implantation status or there is, caused by a low flow rate or a borderline flow rate. Dependent on how low the flow is, the intervention to increase pressure is done immediately or postponed for some time. The common denominator is the inability to predict the effects the interventions. Will resistance fall enough to assume the ideal flow rate, if so, what is the required duration of support to reach that point? The reality of the matter is, no one knows and this results in wasted staff management and operating room (OR) availability. The parameters after two hours on HMP are reviewed. A surgeon will decide to increase the pressure once again, or continue perfusing as before. The hours that follow, no other interventions are possible; the only path is to continue to monitor and see if the vasculature has opened up and decreased the resistance. This is a common cycling pattern, repeated amongst different occasions. A consequence is keeping the OR

stagnant, thus wasting money. The same is said in keeping staff in-house; where the cycle ends is hard to say. Officially rejecting a renal organ can take anywhere from one hour to six hours. Hospital time consumption is not ideal and difficult when there are many uncontrolled elements. In the case, when increasing pressures does works different steps are taken.

As mentioned a form of intervention for reaching appropriate flow rates include raising the pressure. Only the surgeon can officially decide to change the pressure, throughout the duration of support the surgeon is kept updated and made aware of the hemodynamic parameters. Typically, the pressure setting is increased by 5 mmHg/mL/min; as noted earlier the LifePort® can only pressurize the organ to a certain point. Too high of a pressure will automatically stop the pump machine. Higher pressures, closer to a systolic of 60 mmHg/mL/min can add to post operation kidney dysfunction, due to shear stress and injury to endothelial cell in the graft (8). However, there is a well understanding that increasing the pressure will surpass the resistance in the vasculature, thus increasing the flow rate. Further investigation in increasing pressure by Patel et. al demonstrates, "using higher pressure setting to overcome an elevated resistance. The incidence of DGF function was not decreased by the increased pressure, and 1-year graft survival remains unchanged" (17). Therefore, even when there was not a significant improvement, the action of implantation is made possible. The organs are not wasted and discarded, increasing the overall pool of organs available for transplant.

The ultimate objective is to optimize the use of marginal organs, utilizing the LifePort® Kidney Transporter has demonstrated the rehabilitation of these donor kidneys. Even though this method of preservation is successful, and has increased the quantity of implantable organs (12), there are still some issues within the process. The purpose behind this study is to address those problems.

The Banner University Medical Center's renal transplant program relies on the LifePort Kidney Transporter to optimize marginal kidney organs via hypothermic machine perfusion (HMP) prior to transplantation. Hemodynamic parameters produced by the device followed over the duration of support, combined with clinical experience, guide decisions in determining the acceptability of a donor kidney for implantation. Thus far, statistical evidence supporting ideal parameters remain undefined. The purpose of this study is to create a linear model that will ascertain the post-implant sustainability of LifePort® supported donor kidneys and predict clinical outcomes. **My hypothesis is that the statistical models constructed based on retrospective LifePort® parameters and clinical outcome data will successfully predict I) donor organ vascular health for transplantation and II) the optimal support duration.** A successful model will contribute to increased efficiencies in the kidney transplant process as well as improved patient outcomes.

My primary objective is to construct a logistic regression equation, to produce a statistical score that will be predictive of a kidney's vasculature health, for transplantation. A model will be built by running a regression analysis and manipulating variables, which include indicator and artificial variables. My secondary objective is to forecast an optimal time point, to terminate hypothermic machine perfusion (HMP). A center moving average analysis will be utilized to create a timescale or forecast. A linear regression model will be constructed as a result of the analysis. This model will produce a time at which the vasculature has reached its beneficial limits from the LifePort®. My tertiary objective is retrospectively validate the model as a functional tool. The model will be adjusted as needed to be able to pinpoint the ideal parameters and modify for the variances, for the perfusion of kidneys. The validation will prove whether the hypothesis is valid or not.

METHODS

Data Collection

In the study the following research methods are based on data collected from donor procurement records archived within BUMC's Transplant Services. The sample from the population of donor kidneys, only includes those put under HMP via a LifePort®. A collective of 69 kidneys are used in the investigation; the information accumulated is kept on an Excel® workbook file. All analyses are ran on Stata 13 software, and Microsoft Excel (2013) software with Analysis Toolpak-VBA add in program.

The renal information was from procurements that ensued on, April 25, 2015 to January 30, 2017. The total amount of kidneys, 69, were divided into two categories, accepted and rejected. Meaning, kidneys implanted into the patient and ones discarded, not transplanted. There were 54 accepted kidneys and 15 rejected kidney. Some kidneys were removed from the total of each category, for the later conduction of validations on the logistic and forecast models. Leaving 47 accepted, 7 accepted for validation, 10 rejected, and 5 rejected for validation.

Specific information taken from Transplant Services records were mostly numerical data, they are the measurements of flow, pressure, resistance, and time points – hemodynamic parameters – throughout the time the kidney spent on the machine. The numerical values were used as continuous variables in all the analyses, if applicable. Nominal data on the recovery status of the kidneys post-implant was noted as – yes or no. Indicating, whether or not the patient had undergone hemodialysis within 7 days post operation.

DATE	PRESERVATION START TIME	TIME	PRESSURE (S) (mmHg)	PRESSURE (D) (mmHg)	FLOW (mL/min)	RESISTANCE (mmHg/mL/ min)	MAP	COMMENTS
4/18/2016	0329	0329	29	23	41	0.61	25.0	
		0348	30	23	72	0.36	25.3	
XC TIME		0400	30	24	75	0.34	26.0	
0258		0430	30	24	86	0.32	26.0	
		0500	30	23	89	0.29	25.3	
KIDNEY		0530	29	22	97	0.26	24.3	
Right		0600	30	22	98	0.26	24.7	
		0630	30	21	96	0.27	24.0	
DGF		0700	30	21	95	0.26	24.0	
Yes		0730	30	21	99	0.25	24.0	
		0800	29	20	98	0.25	23.0	
		0830	30	19	99	0.25	22.7	
		0900	29	19	99	0.25	22.3	
		0930	29	19	99	0.24	22.3	
		1000	30	19	98	0.25	22.7	
		1030	30	19	100	0.24	22.7	
		1100	30	19	97	0.24	22.7	
		1130	30	19	98	0.24	22.7	
		1158	29	20	105	0.23	23.0	End Pump
								Total Ischemic Time: 33 hr
		Average	29.7	20.9	91.6	0.3	23.8	MAP: 23.8 mmHg
								Pump Time: 8 hr 29 min

Table 1. Data Collection Sample. Not all information collected was used in the analyses. Yes under DGF is represented by 0; No is represented by 1.

Analyses

Before creating models, the first step was to develop an understanding of the institution's overall success. A survival analysis, is a method of studying the data while focusing attention on outcomes at certain events or times. In this case, delayed graft function is the outcome variable taken into consideration at the event of flow. Final flow is utilized as a variable for a concrete measurement of the effect or motive behind developing DGF. Only the accepted kidney data, 47, is employed in the analysis as the model's focus is specifically about the transplant outcome findings. In other words, DGF is the dependent variable of interest and is solely a valuation of implanted renal organs.

In order to run a survival analysis in Stata the data is set up and declared to the memory of the program using the command ***stset Flow, failure (dgf==0) scale(1)***. Flow is the time variable, 0 represents the occurrence of DGF, and is considered a failure outcome. The command will also produce 4 new variables, labeled _st, _t0, _t, _d. Once the initial setup is complete, the Kaplan-Meier survival estimate graph is produced with the command: ***sts graph***. For a better understanding and support for the graph the data is summarized and describe by commands: ***stsum*** and ***stdescribe*** (Table 3 & 4).

After gaining a better insight into the data, creating a logistic regression model is the next step in predicting renal vasculature health. This method allows the usage of dependent and independent variables, to predict an outcome. The regression model employs the same binary representation as DGF in the survival analysis – 0, 1. Running the analysis with 'accepted or rejected' as the DV, the former is represented by a 1 and the latter by a 0, the variable itself is called Status. With the combination of the DV and IV, last measurement of flow and resistance of 57 kidneys, the model will predict the status of the kidney. Targeted results of the analysis include an R^2 close to 90%, and a p-value less than .05 to show statistical significance. The logistic regression analysis in Stata is commanded by: ***logit Status Flow***.

The computed results supply coefficients to build an equation with and entered into the log-odds function. The model will assign a probability – a percent – of accepting the kidney for each data point.

$$Y = \beta_0 + (\beta_1 * X_1) + \varepsilon$$

$$\frac{e^{\beta 0+(\beta 1*X1)}}{1+\ e^{\beta 0+(\beta 1*X1)}} = \Pr(Status)$$

The variable X_1 is representative of kidney perfusion flow and the β coefficients remain the same, from the regression analysis. The statistical regression equation is then retrospectively validated, using the 12 kidneys that were randomly removed from the main data collection. The validation of the logistic regression is performed to justify the rationale behind choosing an exact Pr(Status) cutoff.

Forecasting

The purpose of constructing a forecast is to predict a flow at a given hour. In Excel, the data is set up in a matrix table; out of 47 transplanted organs, 39 are isolated and utilized. Setting up the data included determining how many hours of the HMP to analyze. At BUMC, the duration a kidney is kept on the LifePort ranged from a minimum of 4 hours to a maximum of 20 hours. The length the renal organs were perfused for varied; the average pump time was 5 hours. For the forecast only the organs with perfusion periods of 5 hours or greater were utilized. Under such criteria, data points for up to 5 hours were collected from only 38 out of 47 kidneys. The hemodynamic parameters gathered included flow, resistance, systolic, and diastolic pressure. Since the parameters were measured at every hour, each measurement is considered a variable. A total of 15 independent variables were employed in the forecast. Systolic and diastolic pressures were combined as one predictor variable, using the formula for MAP – mean arterial pressure.

In the matrix table, the column representing the dependent variable (*Y*) is filled 1 through 5 for every kidney, designating the hour. The row containing the 15 parameter variables (*X*) are also numbered. Not every cell is filled with data, to avoid running analyses with missing points zeros are inputted into those cells. Overall, there are a total of 2,660 data observations; every

hour is analyzed. The data is set in a matrix table system to run a linear regression and construct a model, different from the logistic regression produced earlier.

Kidney	F0	R0	P/R0	F60	R60	P/R60	F120	R120	P/R120	F180	R180	P/R180	F240	R240	P/R240
K1-0	89	0.29	93.1	0	0	0	0	0	0	0	0	0	0	0	0
K1-60	0	0	0	104	0.25	112	0	0	0	0	0	0	0	0	0
K1-120	0	0	0	0	0	0	103	0.25	112.0	0	0	0	0	0	0
K1-180	0	0	0	0	0	0	0	0	0	104	0.25	108.0	0	0	0
K1-240	0	0	0	0	0	0	0	0	0	0	0	0	104	0.25	110.7
k1-300	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
K2-0	182	0.12	200	0	0	0	0	0	0	0	0	0	0	0	0
K2-60	0	0	0	179	0.11	200.0	0	0	0	0	0	0	0	0	0
K2-120	0	0	0	0	0	0	169	0.13	179.5	0	0	0	0	0	0
K2-180	0	0	0	0	0	0	0	0	0	169	0.13	176.9	0	0	0
K2-240	0	0	0	0	0	0	0	0	0	0	0	0	176	0.12	194.4
k2-300	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
K3-0	77	0.33	82.8	0	0	0	0	0	0	0	0	0	0	0	0
K3-60	0	0	0	76	0.34	78.4	0	0	0	0	0	0	0	0	0

Table 2. Example of data setup in a matrix table system. N=38. The predictor variables go up to P/R300.

Excel's Analysis Toolpak-VBA is an add-in extension that allows users to run linear regression analyses. Each hour is analyzed to create 5 individual models; the setup for the first hour equation includes Flow in the 1st hour (F1) as the *Y* variable and the remaining 14 predictor variables as *X*. That is resistance in the 1st hour (R1), pressure per units of resistance in the 1st hour (P1/R1), flow in the 2nd hour (F2), and so forth until the last variable is included (P5/R5). The second hour linear regression equation is formed differently to accommodate for that hour's parameters. The dependent variable (*Y*) now is flow in the 2nd hour (F2), the predictor variables (X) are resistance in the 2nd hour (R2), pressure per units of resistance in the 2nd hour (P2/R2), flow in the 3rd hour (F3), and once again the pattern is repeated. The last independent variable is pressure per units of resistance in the 5th hour (P5/R5); there are a total of 11 predictor variables

used to construct the 2nd hour's equation. The rest of the three models are fashioned in the same way. As more models are created, the less number of *X* variables are accessible to incorporate into the analyses.

- **1st Hour Flow Model**

$$F1 = 11.9 + (2.2 * R1) + \left(.85 * \frac{P1}{R1}\right)$$

- **2nd Hour Flow Model**

$$F2 = .36 + (19.7 * R2) + \left(.92 * \frac{P2}{R2}\right)$$

- **3rd Hour Flow Model**

$$F3 = .16 + (15.4 * R3) + \left(.95 * \frac{P3}{R3}\right)$$

- **4th Hour Flow Model**

$$F4 = .15 + (22.5 * R4) + \left(.92 * \frac{P4}{R4}\right)$$

- **5th Hour Flow Model**

$$F5 = .08 + (18.5 * R5) + \left(.94 * \frac{P5}{R5}\right)$$

Figure 2. Linear Regression Models with Flow as the DV. F: Flow at the hour indicated; R: Resistance at the hour indicated; P: Pressure at the hour indicated.

Combining all five equations to create one model and to predict the flow at the 5 hour mark is not as simple. The flow predicted will not have any accuracy because the flow is dependent on the extent the vasculature opens up. The linear regression models do not take into consideration the rate at which dilation occurs. One way to solve the issue was to also construct linear models that could forecast resistance, with the use of different variables.

The setup for forecasting the resistance is similar to the former forecast; using a matrix table with resistance as the dependent variable (*Y*) and predictor variables (*X*) are flow and pressure per units of flow (P/F). The latter is considered an interaction variable since there is a relationship between both, flow and pressure. The connection is demonstrated by Ohm's Law in relation to fluid flow, *Resistance = Pressure/Flow.* In Excel, the linear regression analysis is

administered for every hour, producing 5 separate equations. Resistance in the 1st hour (R1) is Y, X variables include flow in the 1st hour (F1), pressure per units of flow in the 1st hour (P1/F1), resistance in the 2nd hour (R2) , and so forth ending with pressure per units of flow in the 5th hour (P5/F5), for a total of 14 predictor variables. The method is imitated another 4 times for the remaining hours; starting the second analysis with resistance in the 2nd hour (R2) as the dependent variable and independent variables, flow in the 2nd hour (F2), pressure per units of flow in the 2nd hour (P2/F2), flow in the 3rd hour (F3), continued to the last *X* variable. Once again the number of accessible *X* variables decreases as more equations are built.

- **1st Hour Resistance Model**

$$R1 = .013 + (-.0002 * F1) + \left(1.04 * \frac{P1}{F1}\right)$$

- **2nd Hour Resistance Model**

$$R2 = .0002 + (-.0002 * F2) + \left(1.06 * \frac{P2}{F2}\right)$$

- **3rd Hour Resistance Model**

$$R3 = .0001 + (-.0001 * F3) + \left(1.06 * \frac{P3}{F3}\right)$$

- **4th Hour Resistance Model**

$$R4 = .0002 + (-.0001 * F4) + \left(1.06 * \frac{P4}{F4}\right)$$

- **5th Hour Resistance Model**

$$R5 = .00005 + (-.0001 * F5) + \left(1.06 * \frac{P5}{F5}\right)$$

Figure 3. Linear Regression Model with Resistance as the DV.

The five equations constructed to forecast flow are joined together with the five equations predicting resistance. Taking any set of hemodynamic parameters from the group of 39 kidneys, the first hour flow is entered into the first hour flow equation, to calculate the flow. The calculated flow is inserted into the second hour resistance model; the predicted resistance is entered into the second hour flow equation. The pattern is continued until the fifth hour flow equation has predicted the last flow.

The equations are set up in Excel to make all the individuals models act in conjunction with one another, therefore producing one entire model. Excel also allows for pressure adjustment, if at any point the surgeon is considering altering the pressure, the pressure is keyed in and the entire model modifies. Thus, demonstrating whether or not, the change in pressure will produce the required flow for an acceptable kidney.

Using a couple of the seven accepted kidneys from the validation group to complete several runs through the model to predict flow. The model is then compared to rejected kidneys, from validation group of five. Assessing the models will verify practical insight of the renal vasculature health.

RESULTS

The purpose of the study was to build models that would ascertain the post-implant sustainability of HMP supported donor kidneys and predict clinical outcomes. There were targeted aims to test the hypothesis, which included the construction of a logistic regression model and a forecast model.

Survival Analysis

Delayed graft function is a marker of the donor kidney's vasculature health. BUMC's transplant program DGF results were overviewed in the survival analysis. Where the survival outcome was normal graft function, the patient did not develop DGF or need hemodialysis. Out of the 47 kidneys implanted, approximately 51% (24) of patients were dialyzed. The mean and median flow were similar; while the minimum flow of the set was 56 ml/min and the maximum flow was 185 mL/min.

```
. stdescribe

        failure _d:  dgf == 0
  analysis time _t:  Flow
```

Category	total	per subject: mean	min	median	max
no. of subjects	47				
no. of records	47	1	1	1	1
(first) entry time		0	0	0	0
(final) exit time		98.70213	56	97	185
subjects with gap	0				
time on gap if gap	0				
time at risk	4639	98.70213	56	97	185
failures	24	.5106383	0	1	1

Table 3. Description of the survival analysis data in Stata 13. More than half of the kidneys were hemodialyzed.

Survival analysis summary (Table 4) reveals the rate of survival, the recipient did not undergo hemodialysis. At flow of 185 mL/min there is a 75% probability DGF will not occur, therefore at such high flow in this group there is a 25% chance the of developing DGF. At a lower flow, 92 mL/min, the odds the patient will get dialysis is 75% since the expected survival is 25%.

```
. stsum

        failure _d:  dgf == 0
  analysis time _t:  Flow
```

	time at risk	incidence rate	no. of subjects	Survival time: 25%	50%	75%
total	4639	.0051735	47	92	105	185

Table 4. Stata 13 results of the survival analysis data summary. Survival time represents healthy graft function.

Overall, the survival analysis graph (Figure 4) demonstrates a visual outlook for the effect flow can have on graft function. As perfusion flow increased the odds of undergoing dialysis decreased. The analysis graph also demonstrated an expected 100% dialysis rate for a kidney flowing 55mL/min and under. However, even at higher flows a 0% likelihood of DGF does not materialize. A result of dialyzing some patient's with high flowing donor kidneys and not dialyzing others with lower flowing donor kidneys.

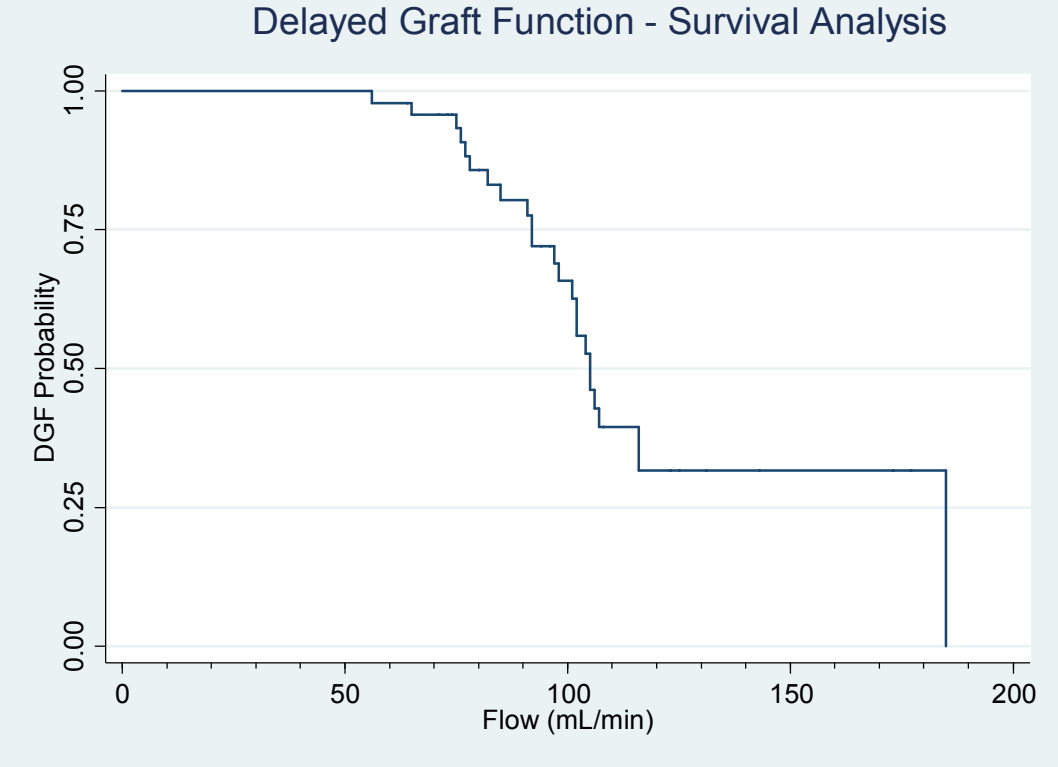

Figure 4. Survival analysis graph. Flow vs. Probability of delayed graft function. The lower the flow the higher the probability of needing dialysis.

Logistic Regression

The primary objective of the study is the construction of a logistic regression model. By logistically analyzing the data of 57 renal organs, both rejected and accepted, Stata 13 computes the following table.

```
. logit Status Flow

Iteration 0:   log likelihood = -26.471134
Iteration 1:   log likelihood = -15.774685
Iteration 2:   log likelihood = -9.3333685
Iteration 3:   log likelihood = -8.3610162
Iteration 4:   log likelihood = -8.3440572
Iteration 5:   log likelihood = -8.3440071
Iteration 6:   log likelihood = -8.3440071

Logistic regression                               Number of obs   =         57
                                                  LR chi2(1)      =      36.25
                                                  Prob > chi2     =     0.0000
Log likelihood = -8.3440071                       Pseudo R2       =     0.6848

------------------------------------------------------------------------------
      Status |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        Flow |   .2361625   .0846881     2.79   0.005     .0701768    .4021482
       _cons |  -14.80585   5.485725    -2.70   0.007    -25.55767   -4.054029
------------------------------------------------------------------------------
```

Table 5. Results of a logistic regression. DV is Status and the IV's are Flow.

The statistical regression (Table 5) establishes flow as a significant predictor for the status of a perfusing kidney, Prob > $chi^2 = 0.0$, thus the p-value is less than .05. The variable account for 68% of the explained variability in status. The results also illustrate a positive correlation between flow and status of the kidney. The logistic regression model is:

$$\text{Logistic Regression} = -14.80585 + (.2361625 * \text{Flow})$$

$$\frac{e^{-14.80585+(.2361625*Flow)}}{1+\ e^{-14.80585+(.2361625*Flow)}} = \Pr(Status)$$

The statistical equation was then graphically compared to the institution's probability rate of accepting donor kidneys. Of the 57 organs data was collected from, some deviation was seen. In Figure 4, the Probability of Accepting Kidneys Graph, a particular kidney perfusing at 72 mL/min was rejected; another organ was flowing at 56 mL/min and accepted. According to the transplant program's acceptance rate the rejected kidney had a 90% likelihood of implantation, and the accepted kidney had 85% chance of rejection.

Graphically in Figure 5, the curve was incredibly steep. There was a 45 point probability difference over a 10 point flow difference. This frame of area is considered a grey zone, where the status of the kidney is border line, for acceptance or rejection. A kidney flowing anywhere between 60 and 70 mL/min was on the edge of implantation or discarded, due to a drastic change in probability. The graph reveals such dilemma, where three kidneys very close in flow are not all transplanted. The two accepted had flows of 64 and 65 mL/min with a probability of 58% and 63% of implantation. On the other hand the rejected kidney had a probability of 45% and a flow of 62 mL/min. The flows are not radically different, but the difference in probability is greater. Flows greater or less than 60 – 70 mL/min have a more clear status.

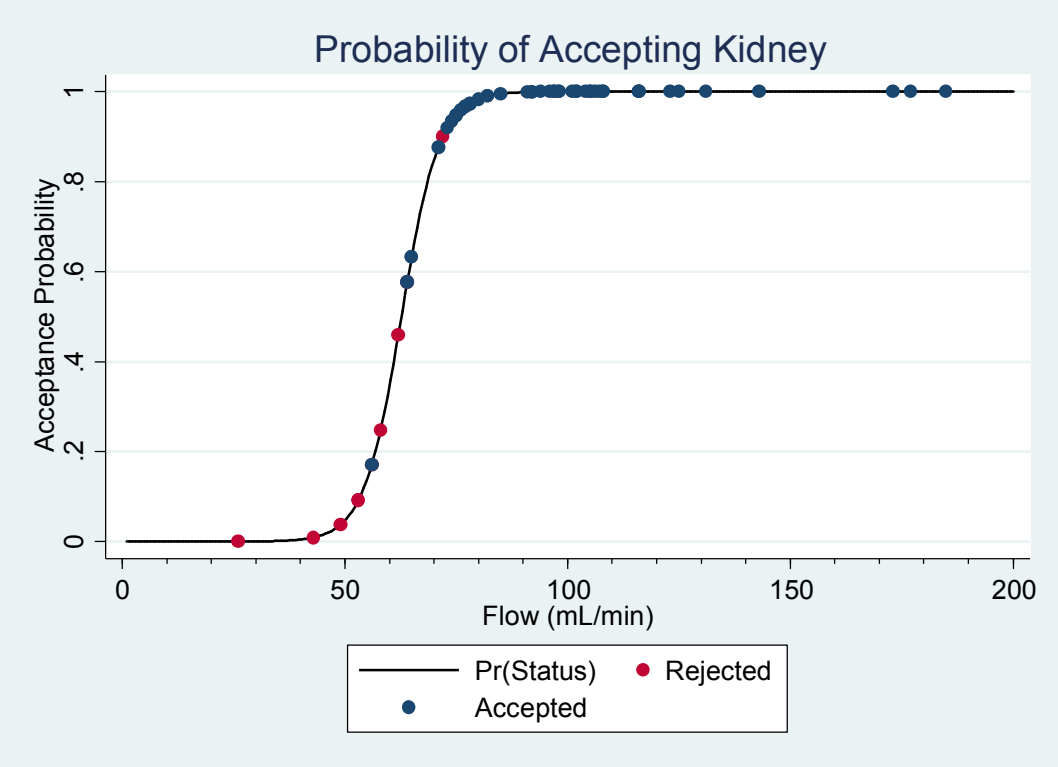

Figure 5. Predictive Logistic Curve Graph: The likelihood of rejecting a kidney increases the closer to 0 the probability is. Pr(Actual) is the rate at which BUMC accepts renal organs.

The logistic curve (Figure 5) of the predictive model lines up well with the institution's acceptance rate. The curve acknowledges the relationship, as flow increases the probability of acceptance rises. Additionally Figure 1 attests, at a certain flow or higher a 99% acceptability rate is constant. The logistic equation establishes a statistical score that is predictive and accurate of the organ's vascular health for implantation.

Proving the hypothesis, the equation was validated by assessing 12 kidneys not included in the model development. Seven out of the 12 kidneys were accepted and the rest rejected. Running the parameters through the logistic regression equation produced a statistical score in line with the clinical outcome.

	status	flow	predic~d	dgf
1.	1	106	.999964	NO
2.	1	110	.999986	YES
3.	1	114	.999995	YES
4.	1	70	.848839	YES
5.	1	114	.999995	YES
6.	1	98	.999761	YES
7.	1	62	.459148	YES
8.	0	57	.206757	
9.	0	52	.074097	
10.	0	32	.000711	
11.	0	36	.001826	
12.	0	68	.777853	

Table 6. Validation of Logistic Regression model. Predicted column is the calculated score. Status 1 represents accepted kidneys and 0 represents rejected kidneys.

However, there are two outliers present (Table 6 & Figure 5) in the grey zone mentioned earlier. The discarded kidney (no.12) had a flow of 68 mL/min and only a 23% probability of rejection. The accepted kidney (no.7) had a 46% probability of implantation and a flow of 62 mL/min. validating the regression equation, and the interpretation made from the model. At a certain flow or higher the probability rate holds constant with an acceptance probability of 99.9%, the higher the flow the higher the likelihood of transplantation. The validation model also proved the existence of a grey zone between flow rate of 60 – 70 mL/min, and that a definitive status of transplantation was only possible outside of that range.

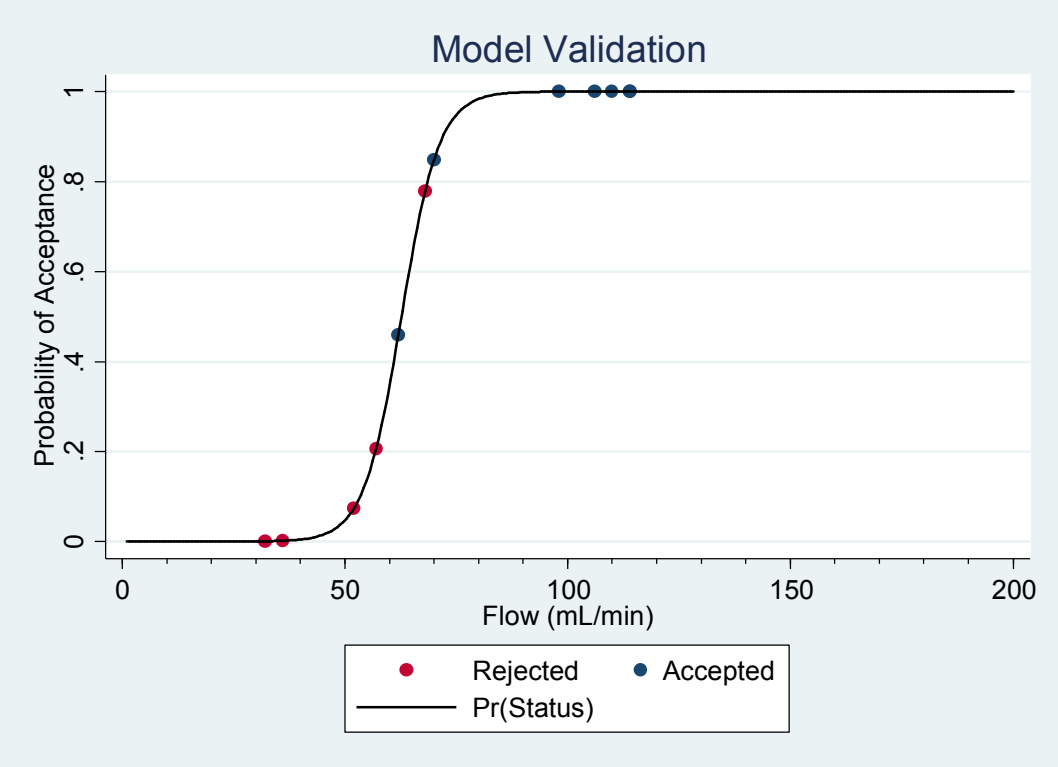

Figure 6. Validation of the Logistic Regression Model. Only 12 kidneys are used in the validation

Forecasting

In order to forecast the optimal support duration of the LifePort®, a model was constructed. With the combination of the 10 equations, the flow was predicted at every hour up to five hours. Implanted kidneys not utilized in the construction of the regression equations were used to validate the model's accuracy. In Figure 6, three parameters were inputted into Excel and the hourly flow was calculated. At the fifth hour, the projected flow did not match the actual flow rate in either instance. In the first case, the forecasted flow was 74 mL/min, opposed to the actual flow of 97 mL/min, a miscalculation by 23 mL/min. The error was due to the imprecision in the resistance regression models, the fluctuation or change was not constant in one direction.

Figure 6 has examples one of which the resistance was increasing and the other where the resistance was decreasing. Both kidneys developed clinical DGF, the patient's underwent hemodialysis within seven days post-implant.

LEGEND	Time	Pressure	Resistance	Flow	Actual Flow
User entered	**0**	30	0.45	60	*60*
Calculated	**60**	30	0.45	69.56	*87*
	120	30	0.43	70.83	*94*
	180	30	0.43	72.38	*96*
	240	30	0.42	73.73	*96*
	300	30	0.42	74.42	*97*

Time	Pressure	Resistance	Flow	Actual Flow
0	30	0.3	84	*84*
60	30	0.31	97.56	*95*
120	30	0.32	94.63	*92*
180	30	0.33	94.86	*102*
240	30	0.34	92.18	*103*
300	30	0.34	90.24	*102*

Figure 7. Examples of Forecast model (version 1) predicting flows at every hour. The top example has resistance decreasing and the bottom example has a rising resistance. The red box highlights the calculated fifth hour flow.

An alternative method to improve the forecast and produce a more precise flow was by including the one-hour parameters in the forecast model (version 2). The setup will provide the model with a better foundation; structurally, the model can perceive the rate at which the vasculature is dilating with more accuracy. For example (Figure 8), the two same kidneys were tested from the seven in the validation group. The results established were more prominent, the calculation for flow was enhanced. Of the two, the predict flow of the first is 91 mL/min, only 6 mL/min difference from the actual flow. While the other had a lower differentiation, 1 mL/min; the actual flow was 102 mL/min and the equation system predicted 101 mL/min. By far a more accurate system, than a model that only includes kidney parameters from the starting point.

Time	Pressure	Resistance	Flow	Actual Flow
0	30	0.45	60	*60*
60	30	0.31	87.00	*87*
120	30	0.31	95.50	*94*
180	30	0.32	95.74	*96*
240	30	0.33	92.94	*96*
300	30	0.34	90.91	*97*

Time	Pressure	Resistance	Flow	Actual Flow
0	30	0.3	84	*84*
60	30	0.27	95.00	*95*
120	30	0.27	107.90	*92*
180	30	0.28	108.64	*102*
240	30	0.29	104.38	*103*
300	30	0.30	101.31	*102*

Figure 8. Forecast model (version 2). Inputting one-hour parameters improves prediction accuracy. Outlined in red is the final flow at five hours.

Another practicality tested in the model was predicting abnormal vasculature change. In other words, situations when the flow of a kidney stays consistent and the vessel network does not open up appropriately. The model can account for such scenario, recognizing a kidney that was not viable. In Figure 9, rejected kidneys from the validation group were tested, calculating a flow of 71 mL/min and 65 mL/min, in comparison to flows of 51 mL/min and 34 mL/min. The hypothesis was validated, the forecast model can predict optimal duration of perfusion support. True for all five kidneys the parameters of a declined kidney produced a predicted flow greater than the actual flow. Notably, a rejected kidney was distinguishable based on the model. Since, the forecast model continues to predict an increased flow, when a kidney was flowing below the predict value the organ was considered unviable. Although clinically functional, a shortcoming of the regression system was the inability to forecast such outcome within the first hour of HMP.

Time	Pressure	Resistance	Flow	Actual Flow
0	30	0.5	52	*52*
60	30	0.51	52.00	*52*
120	30	0.48	64.52	*50*
180	30	0.47	66.91	*56*
240	30	0.45	69.59	*54*
300	30	0.44	71.04	*51*

Time	Pressure	Resistance	Flow	Actual Flow
0	30	0.84	32	*32*
60	30	0.79	39.00	*39*
120	30	0.62	50.86	*37*
180	30	0.56	55.96	*34*
240	30	0.51	61.85	*35*
300	30	0.48	64.98	*34*

Figure 9. Rejected kidneys keyed into the forecast model. Notable difference include a lower actual flow than predicted.

Overall, the forecast model reveals flow increasing over time and a larger increase in flow as pressure was adjusted. In both regression systems, resistance continued to increase over the course of HMP. However, when compared to a rejected kidney the resistance decreased as time goes long. In reality, as the vasculature of the renal organ opens up the resistance would decrease, and would increase or stay constant if the organ is unhealthy. Thus the inconsistent behavior of resistance, attested for decrease in flow over time and for some of the inaccuracy in calculating the final flow.

The forecast model proved to have clinical practicality and with some adjustments improved vastly. A rejected kidney was recognizable, and the calculated flow of an accepted kidney was within a significant range of the actual flow. After entering the first hour parameters the five hour forecast was substantially accurate.

DISCUSSION

Survival Analysis

Banner University Medical Center's renal transplant program has flourished over the past two years. Investigating the institution's advancements, allows support and better understanding of organ outcomes. The implemented survival analyses highlight features based on delayed graft function. Survival is indicative of a healthy patient that did not undergo dialysis because they retained normal graft function for seven days after surgery.

Derived from 47 kidneys, the resulting graph validated points already understood, and introduced new discoveries. In particular, anticipating the probability of developing DGF according to the rate of flow the kidney is perfused. As follows, certain decision making can alter, such as aiming to maintain a flow higher than 55 mL/min to avoid a 100% probability of dialysis. However, as opposed to a 100% likelihood of developing DGF, a 0% chance of DGF does not exist.

A possible reason for never reaching a 0% likelihood of DGF, statistically the data collected included high flow kidneys that were dialyzed and low flow kidneys that were not, emanating high flows with the probability of dialysis, no lower than 25%. Largely, the reason behind the improbability of 0% DGF is due to the fact that every kidney placed on ex vivo perfusion is predisposed for DGF. The inclination is contingent on donor health and ischemic time.

Logistic Regression

In accomplishing the primary aim of the study, a logistic regression equation was constructed to implant or discard the kidney. Built on 47 accepted kidneys and 10 rejected the analysis managed to prove, the variables in the equation accounted for 68% of the variation in

status. Following the model provides significant, statistical evidence behind the decision to transplant a kidney based on perfusion rate. Each range of flows has an assigned probability of acceptance, most of the institution's accepted kidneys have an 85% or greater probability of acceptance and the rejected have 30% or less probability of acceptance.

Within both percentages, the choice between accepting and rejecting the organ is not very clear. Also referred to as the grey zone, a flow rate between 60 – 70 mL/min has a wide area of probability, 25 – 80% chance of implantation. Since the range in flow is only a differential of 10, determining the kidney's future is difficult. Suggesting to avoid the zone altogether and only consider implantation for the kidneys that perfuse higher than 70mL/min.

To anticipate proper vascular health for transplantation, ideally the cutoff flow for implantation is 90 mL/min. Due to the fact, flows greater than 90 mL/min have a constant rate of 99% probability of acceptance, completely avoiding the grey zone. Consequently, as mentioned earlier the demand for donor kidneys is very high and following the ideal parameters will indefinitely decrease the amount of kidneys transplanted. Additionally, at 90 mL/min the probability of developing DGF is 77%. Although still a large chance of needing dialysis, fortunately DGF is not the end for the organ.

After treatments of dialysis, the kidney can regain full graft clearance, and become an entirely functional renal organ. Making possible, the acceptance of kidneys with lower perfusion rates. In actuality with such allowance, the cutoff parameter for flow is 80 mL/min. increasing the quantity of kidneys available for transplant. At this rate the probability of acceptance is 90%, likewise a high acceptance rate. The probability of DGF is 85%, but as indicated earlier receiving dialysis post operation is tolerable.

Achieving an adequate prediction for donor organ vascular health. Since the logistic model was validated, real life trials are feasible. Inputting flow and taking into consideration the probability calculated. At an acceptance of kidneys with flows equal or higher than 80 mL/min has a very high probability of implantation and is not subjected to the ambiguous definition of the kidney status.

Forecast

The secondary objective, to discover the optimal duration for ex vivo perfusion, was retrospectively solved with a forecast model. A forecast was created by assembling multiple regression equations to fashion a model system. In the first run through of testing the model, the model had the capability of producing a higher flow then what was original keyed in. There was a drastic increase between the starting flow and the second hour flow. Defectively, after the second hour prediction the flow would continuous drop, yet not below the starting flow. This is a byproduct of the abnormal increasing of resistance; rationally the 38 kidneys used to build the models are not a sufficient amount. Some of the kidneys had resistance increase by a hundredth, possibly affecting the resulting models. Generally, the model predicted unreliable flow rates at the end of five hours.

To correct the regression system, one hour parameters were also entered into the model. Ultimately improving the forecast model; the calculated flow was not the exact flow measured at the five hour mark, but more accurate than before. Despite a great improvement, the problems with the model are similar to the ones with the prior system. Resistance continues to increase over time; using a much higher quantity of kidneys to construct the linear regressions can not only enhance the prediction accuracy, but also correct the resistance trend. Overall when the

forecast takes the one hour parameters into account, the prediction of flow for every hour afterwards is closer to actual flow. Due to the model gaining a better idea of the rate at which the network of vessels is opening up. In the few kidneys tested, the difference between predicted and actual flow at five hours was no greater than 9 mL/min.

The forecast model is also seen as a useful tool in terms of rejected kidneys; when entering parameters of a declined organ the actual flow falls short of the calculated flow. Characterizing a major difference between the models when running an accepted kidney versus a rejected kidney. The model cannot recognize a vasculature network that does not open up, therefore assuming the kidney is healthy the system will act in conjunction and produce an increased flow. Realistically the flow only increases slightly and is far below the forecasted flow. However, identifying a rejected kidney is not forecasting, but validating. In other words, after inputting the one hour parameters the flow is loosely reliable in classifying the kidney as rejected. Comparing the second hour flow to the actual flow will cannot completely determine the fate of the kidney. When comparing the final flow, in this case the fifth hour flow, of both calculated and actual the decision to reject is validated because the actual flow is much lower than the predicted.

Considering the objective, the forecast model is limited in identifying the optimal duration of HMP. The model only allows the prediction of up to five hours of flow, however the equation system grants telling insight within those five hours. The system is setup in way that pressure can change by choice of the user. For instance, if the surgeon is contemplating an increase in pressure because of inadequate perfusion. The surgeon is made aware of the effects on flow the increase in pressure will have. The calculated parameters are close to the actual flow

measured, and can validate a rejected kidney. Addressing the issues with the forecast model, consist of more data collection, possibly improving the forecast accuracy.

Future Work

Taking into account the hypothesis of the study and the objectives set for testing, there is room for improvement. In all three statistical analysis flow is a concrete variable; a significant factor in running the analyses. Foremost to improve the study in general, a greater amount of data collection is recommended. Both the logistic regression model and the forecast model could have enhance the accuracies in predicting the status or flow of the renal organ. Also to the point, where the forecast model would only need the starting parameters to produce accurate flow prediction. As things go sequential kidneys were included in the data collection and treated as single kidneys. The main issue is, those kidneys have lower flows than usual used for implantation. Affecting the logistic regression model more so since the probability is absorbing in the analysis, accepted kidneys with low flow rates.

Another key improvement can be made with the addition of other variables, outside of the parameters. Unfortunately, this would mean starting the data collection from scratch. One example, is using the weight of the kidney as a variable. The weight would attest for any developments of edema while on ice. There are a vast number of variable options to create or use apart from the scope of the LifePort®.

To conclusively validate the models besides running more validations with a larger quantity of kidney, is testing the models in real clinical settings. Comparison of the models to actual events, and identify the significance in any variance, evaluating how well the model does. Furthermore, an extension to the study would include investigating the one year graft survival

rate. How the flow rates compare or effect the one year survival rate? The one year survival rate is indicative of a truly successful implant. Gathering information on that front can conceptualize the benefits the models could have if implemented into BUMC's renal transplant program.

CONCLUSION

Banner University Medical Center's abdominal transplant program continues to evolve and adapt. Over the past two years, the volume of donor kidneys made available to the program has increased. The institution's ability to optimize kidneys of all health, is the main agenda due to the high urgency. To maintain their functionality and ensure a quality organ is transplanted the preferred method of preservation is the LifePort, the renal perfusion machine pump. HMP is a more recent development in the abdominal transplant world. There is a lack of statistical evidence behind operation of the LifePort®.

The purpose of this study is to ascertain post-transplant sustainability of HMP kidneys and predict the clinical outcome. My hypothesis that models constructed based on retrospective LifePort® parameters and clinical outcome data will successfully predict donor organ vascular health and optimal support duration, is correct, but limited. With the support of statistical evidence, the models are headed in the right direction. For the most part they are successful, but with some inaccuracy have room for improvement.

The survival analyses discerns BUMC's outcomes, in relation to DGF or requiring dialysis. In the process, revealing a source of outlooks; at a given flow the odds of developing DGF is established. Such discovery could have clinical application. The logistic regression model is capable of calculating the kidneys probability of acceptance or transplantation. The advocated perfusion flow rate for implantation is 80 mL/min or greater. For the forecast model,

the prediction of flow is only allowed for up to five hours, due to limited resources. Entering the starting and one hour parameters in the system, the model will predict the fifth hour flow within a range of 10 mL/min. An added benefit of the model included accurately predicting rejected kidneys.

The models can make a difference in the way parameters are monitored. A decision on whether to transplant or reject the kidney is obtained quicker, by the first hour of perfusion support. Instead of waiting to recognize a point the kidney will not improve, the model will distinguish a flow pattern to eliminate guessing. Removing one factor from the process, can lead to salvation of hospital resources such as staff management, operating room scheduling, and cost. The time a surgery can begin or is scheduled to start is anticipated by the forecast model, since an optimal duration is recognized.

Results and findings are most likely related to the study's design and size. Replicating the methodology with many more kidneys would make a compelling difference. The study is unrestricted and can move into different directions or expanded upon. Formulating the equations have proven forthcoming in the right direction and practicality in the clinical sense. Promoting advancement in the institution's procurement progress.

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