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Association of lower costs of pulsatile machine perfusion in renal transplantation from expanded criteria donors

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Abstract

Pulsatile machine perfusion (PMP) has been shown to reduce delayed graft function (DGF) in expanded criteria donor (ECD) kidneys. Here, we investigate whether there is a cost benefit associated with PMP utilization in ECD kidney transplants. We analyzed United States Renal Data System (USRDS) data describing Medicare-insured ECD kidney transplant recipients in 1995–2004 (N=5,840). We examined total Medicare payments for transplant hospitalization and annually for three years post-transplant according to PMP utilization. After adjusting for other recipient, donor and transplant factors, PMP utilization was associated with a \$2,131 reduction ($p = 0.007$) in hospitalization costs. PMP utilization was also associated with lower DGF risk ($p < 0.0001$). PMP utilization did not predict differences in rejection, graft survival, patient survival, or costs at one, two and three years post transplant. PMP utilization is correlated with lower costs for the transplant hospitalization, which is likely due to the associated reduction in DGF among recipients of PMP kidneys. However, there is no difference in long-term Medicare costs for ECD recipients by PMP utilization. A prospective trial is necessary as it will help determine if the associations seen here are due to PMP utilization and not differences in the population studied.

Keywords

kidney transplantation; expanded criteria donors; pulsatile machine perfusion; delayed graft function; Medicare; cost benefits

Introduction

Transplantation is the optimal treatment for patients with end-stage renal failure (1,2). Transplantation provides the best clinical outcomes, optimal quality of life and cost-savings when compared with other modalities of renal replacement therapy (2,3). Despite these advantages of transplantation, maximization of these benefits cannot be obtained due to the severe shortage of donated kidneys. The number of patients being placed on the waiting list for a renal transplant increased by 61% between 1996 and 2005 (4). In 2005 there were 46,351 patients on the active wait-list with 29,135 being added in 2005 as new wait-list registrants (4). For those receiving deceased donor kidneys the median wait time for a transplant in 2002 was 1,136 days (4). The wait time and growing waiting list has led to the

more frequent use of sub-optimal kidneys known as expanded criteria donor (ECD) kidneys. In 2005, 1,609 ECD transplants were performed, a 17% increase from 2004 (1,378 transplants) (4).

In order to maximize the number and benefit of donated kidneys it is essential to have effective organ preservation. Over the past 30 years two methods of kidney preservation have been developed. With cold storage (CS), the kidney is flushed once it is removed from the donor and placed in an ice-cooled container with preservation solution (5,6). With the use of pulsatile machine perfusion (PMP), the kidney is connected to a machine which pumps a cold solution containing oxygen and nutrients through the kidney (5,6). This process allows for metabolism to continue in the kidney with end products being removed from the kidney (5,6). While the kidney is receiving PMP, the machine measures filtration flow and resistance, which can aid in deciding whether the organ could be utilized for transplantation (5,6).

To date, there is a lack of evidence supporting the benefits of PMP. Previous studies have shown that PMP reduces delayed graft function (DGF), specifically in ECD recipients (7-9). Others have concluded that there are no long-term benefits of PMP utilization, with equal or small graft survival differences between recipients of PMP and CS kidneys (7,10-12). Despite the lack of long-term benefits, PMP has become more common as the transplant community attempts to utilize more ECD organs while minimizing risk of reperfusion injury and DGF (7,9,13-15).

No previous study of PMP has focused on preservation-related costs among ECD recipients. Typically, DGF incurs increased costs in transplant recipients when compared to those who do not experience DGF (16,17). It is also believed that DGF increases the risk of graft failure and death, which can add substantial cost (7,13,18). Reducing DGF in ECD recipients can in turn reduce the cost of care for the recipients. In this study, we examined whether the utilization of PMP in renal transplants from ECDs is cost-saving. Secondary analysis included examining differences in DGF, length of stay for transplant hospitalization, rejection, graft failure, and mortality for ECD recipients by PMP utilization as these are outcomes likely associated with additional costs.

Methods

Study design, population, inclusion and exclusion criteria

This is a retrospective study of data from the United States Renal Data System (USRDS) (19). The USRDS contains descriptive and clinical data on all renal transplants performed in the United States, as collected by the Organ Procurement and Transplantation network (OPTN), along with linked Health Care Financing Administration (HCFA) billing claims for the Medicare-insured renal transplant recipients. The cost data for this study were derived from Medicare claims and the clinical data were derived from the OPTN registry.

Our study population included all adult (age ≥ 18 year old) ECD renal transplant recipients in the USRDS registry from 1995 to 2004 with Medicare as their primary payer. Patients with multiple organ transplants or previous transplants were excluded. Kidney transplants were categorized as those in which PMP was utilized and those in which PMP was not utilized.

Definitions and assumptions

We defined ECD transplants according to OPTN criteria as allografts from deceased donors greater than 60 years of age and those from donors aged 50 to 59 years old with at least two

of the following: history of hypertension, serum creatinine greater than 1.5 mg/dL, or cerebrovascular cause of death (20).

Recipients were considered to have Medicare as their primary payer if the total cost for the initial transplant hospitalization exceeded \$15,000 and HCFA indicated Medicare as the primary payer for that transplant.

The cost estimates were made by selecting all Medicare claims post transplant for each recipient. These claims were the payments made to the recipients' dialysis center, health providers, and hospitals. Claims were included from the date of transplant until the earliest of date of death or three years post transplant (the time when Medicare coverage after transplant ends in the absence of age >65 or disability). Any claim dated after the patient date of death was set to zero dollars. Transplant hospitalization costs included any claims with a Diagnosis-related group (DRG) code of 302, which indicates hospitalization for a kidney transplant. One, two, and three year post transplant costs were computed as the sum of the patient's claims from transplant hospitalization to the indicated follow-up time. In the case where the time between a patient's transplant and end of study date (December 31, 2004) was less than the indicated follow-up time the corresponding post transplant cost was set to missing. Follow-up outcome information was censored at three years post transplant.

The primary outcome examined was cost as defined above. Secondary outcomes examined were DGF (defined as the need for dialysis within the first week post-transplant), length of transplant hospitalization stay, creatinine at transplant discharge, rejection (within 3 years post transplant), death-censored graft failure and mortality. The rejection outcome included OPTN reporting of acute or chronic rejection, rejection as a cause of graft failure, or administration of anti-rejection immunosuppression. Covariate characteristics examined in analyses included recipient gender, race, ethnicity, age at transplant, body mass index (BMI), primary cause of end stage renal disease (ESRD), pre-transplant dialysis duration, donor gender, race, ethnicity, age, BMI, stroke cause of death, terminal creatinine greater or equal to 1.5 mg/dL, history of hypertension, diabetes, cytomegalovirus (CMV) status, peak panel reactive antibody (PRA) percent, types and number of ABDR mismatches, number of HLA mismatches, CMV sero-pairing, delayed graft function, year of transplant, cold-time, and warm-time.

Statistical Analysis

Recipient, donor, and transplant characteristic differences between those who received a PMP kidney and those who did not were examined using chi-square and t-tests. In order to determine the characteristics associated with PMP utilization, propensity analysis was performed by multivariable logistic regression, entering characteristics known at the time when the decision to utilize PMP is made. These include all recipient and donor characteristics listed above as well as the following transplant characteristics; peak PRA percent, number of HLA mismatches, CMV sero-pairing, year of transplant, and cold ischemic time. A missing indication of PMP utilization was considered a non-PMP. Missing data on the characteristics examined fell into a category of not present, other, missing, or unknown depending on the frequency of missing data for the characteristic.

The unadjusted mean cost of transplant hospitalization, and costs incurred in one, two, and three years post-transplant were compared for both groups using the non-parametric Wilcoxon rank-sum test. Regression analysis was then performed on the cost of transplant hospitalization and the post transplant costs adjusting for recipient, donor, and transplant characteristics. Kaplan-Meier curves were drawn depicting the three year patient and graft survival differences of those who received a PMP kidney versus those who did not. The log-rank test was used to determine if there was a significant difference in the curves. We used

Cox Proportional Hazard analyses to examine the impact of PMP on graft and patient survival, adjusting for key covariates. An alpha level of 0.05 was used for all significance tests. Analyses were performed using SAS v.9.1 (SAS Institute, Cary, NC).

Results

There were 9,733 ECD recipients in the USRDS database during the period of study who did not receive multiple organs or a previous kidney transplant. Of these recipients 5,840 (60%) had Medicare as their primary payer, of which 1,114 (19.1%) received an allograft that use PMP (PMP group). The remaining 4,726 (80.9%) Medicare patients had only CS, without PMP utilization (no PMP group). The remaining 3,893 (40%) of the ECD recipients did not have Medicare as their primary payer and were not included in the study (~16.4% of these non-Medicare patients received a PMP kidney). The characteristics of the Medicare study subjects are shown in Table 1. Recipients of kidneys which received PMP were more likely to be African American, over 45 years of age, obese, been on dialysis for more than five years or had a pre-emptive transplant, have an African American donor, have a donor over the age of 60, have an obese donor, be transplanted in more recent years, have shorter cold (and longer warm) times, and have a lower creatinine at discharge. They were less likely to be Hispanic and have a Hispanic donor, have no HLA mismatches, and have a PRA between 0 and 10 %.

The average cost for patients who did not receive a PMP kidney was higher than those who did receive a PMP kidney for all time points of interest (Table 2). However, the difference was only significant for the transplant hospitalization cost which was \$34,849 for those who did not receive a PMP kidney versus \$31,134 for those who did, a difference of \$3,715 ($p < 0.0001$). Considering the number of possible confounders, seen in table 1, a multiple regression analysis was conducted to adjust for the potential confounders. As seen in Table 3, PMP utilization was only significant in the transplant hospitalization cost after adjusting for characteristics known at the time the decision to utilize PMP is made. Utilization of PMP is associated with a decrease in the cost of the transplant hospitalization by \$2,131. At one, two, and three years post transplant the utilization on PMP does not add to or decrease the total cost of treating a kidney transplant recipients. We also found that Non-white, old recipients who have been on dialysis for the longest and carry risk factors for cardiovascular disease (diabetes and hypertension) would be more likely to be associated with a high cost at the admission and in the long term. Donor characteristics (age > 60, Creatinine > 1.5, and a history of hypertension) and transplant factors such as degree of sensitization and HLA mismatch also contribute directly the short and long term cost of renal transplantation.

Differences in outcomes between PMP and non-PMP kidneys can be seen in table 4 as well as figures 1 and 2. There was no difference in length of transplant hospitalization stay or rejection within three years post transplant. There was no difference in the number of rejections occurring within one year, one to two years, and two to three years post transplant (results not shown). There was, however, a difference in DGF rate (27% of PMP and 38% of non-PMP $p < 0.0001$). There was also a difference in mean creatinine at discharge with PMP kidneys having a significantly lower level than those that did not receive PMP ($p < 0.0001$).

As seen in figure 1 three year graft survival was no different for those who received a PMP kidney compared to those who did not receive a PMP kidney (log-rank p -value = 0.26). Figure 2 shows that there was no difference in patient survival between the two groups (log-rank p -value = 0.60).

After adjusting for recipient, donor, and transplant characteristics in multivariable Cox regression, PMP utilization neither increases nor decreases graft or patient survival (HR =

0.97, 95% CI 0.86-1.08 and 0.99, 95% CI 0.87-1.13 respectively). According to the Cox model delayed graft function, ethnicity, being older than 60 years, having a female donor, African American donor, a donor with history of hypertension, donor terminal creatinine greater or equal to 1.5 ml/dL, a peak PRA greater than 10 percent, more than one HLA mismatch, and being transplanted in an earlier year all increase the risk of graft failure. The most important factor for patient survival is age. Recipients who are 60 years old or older are more than 3 times as likely to die as those 18 to 30 years old (HR = 3.7, 95% CI = 2.5-5.4, $p = <0.0001$). Recipients who are 31-44 years old have a 75% higher risk of dying than those 18-30 (HR = 1.7, 95% CI = 1.2-2.6, $p = 0.01$).

Table 5 shows the propensity of receiving a PMP kidney among ECD transplant recipients. Given the factors known at the time a decision of PMP utilization is made donor and transplant characteristics play a stronger role determining if PMP is used. If the donor is 60 years old or older the kidney is 40 percent more likely to receive PMP than donors 50-59 years old (OR = 1.4, 95% CI = 1.2 - 1.7). Stroke as the cause of the donor's death and a terminal creatinine greater or equal to 1.5 ml/dL also increase the likelihood that a kidney received PMP (OR = 1.3 95% CI = 1.1 - 1.6 and OR = 1.3, 95% CI = 1.1 - 1.5 respectively). Having 2 or more HLA mismatches almost doubles the utilization of PMP with ORs ranging from 2.0 to 2.9. PMP was more likely to be used in 2004 than in any of the previous nine years (ORs of 0.2 to 0.6).

Discussion

In order to increase the pool of available kidneys for donation UNOS implemented a policy to utilize the kidneys of older donors with certain risk factors (20). These ECD kidneys come with an increased risk of DGF and graft failure compared to SCD kidneys (12,21-23). Matsuoka et al have shown that PMP is associated with reduced DGF in ECD recipients, but it is not related to an increased graft survival (9). While the long term benefits and immediate outcomes of PMP utilization on ECD kidneys has been defined, to date there has been no studies investigating the cost benefits of PMP utilization in ECD kidneys.

The major finding of our study is the association of lower cost with PMP utilization during the transplant hospitalization, but not at the annual follow-up time points. These results support the idea that the increased cost of the non-PMP kidneys is associated with the increased risk of DGF in these kidneys. Despite of the incremental organ acquisition cost associated with the use of pulsatile machine, PMP still produces savings by lowering the DGF rate and the creatinine at discharge. Importantly there is no difference in the rate of acute cellular rejection or in the late term costs and outcomes. Similar outcomes between the recipients of PMP kidneys and non-PMP kidneys have also been found in prior studies (8,9,24).

Another interesting finding of our study was the identification of donor, recipient and transplant factors that drive the economics of renal transplantation. Non-white, old recipients who have been on dialysis for the longest and carry risk factors for cardiovascular disease (diabetes and hypertension) are more likely to be associated with a high cost. Older donors with abnormal kidney function were also found to have a major impact. Degree of sensitization and HLA mismatch also contributed directly to the short and long term cost of renal transplantation. We also demonstrated that similar factors contributed to a higher hazard ratio of graft and patient failure, as previously shown (25). Being a non-white, older recipient not only contributes to additional cost, it comes with an additional risk of both graft failure and death. Similarly, a longer pre-transplant dialysis time increased the risk of death. Donor and transplant factors that were related to costs were also related to increased risk of graft failure and sometime death. Our propensity analysis also showed that the

majority of these same donor and transplant factors (older donor, higher terminal creatinine, and HLA mismatches) were associated with an increased probability of receiving PMP. Finally, the relative cost savings of PMP in the long term may be underestimated because individual transplant characteristics found to be associated with increased cost were also shown to significantly predict PMP use. Moreover, there was no association with PMP and early death.

Sung et al determined that the overall discard rate of ECD kidneys was 41%, while PMP ECD kidneys were discarded at a rate of 29.7% and non-PMP ECD kidneys were discarded at a rate of 43.6% (25). The discard rate for PMP kidneys in Sung's study was consistent with the rate found by Mozes et al, which was 23.5%(26). Not only are PMP ECD kidneys utilized more often, they can save Medicare over \$3,700 per kidney in transplant hospitalization costs compared to non-PMP kidneys. Using the rate of discard estimated by Sung et al. and the number of non-PMP kidneys in our study, an estimated 2,142 additional kidneys would have been transplanted if all of the non-PMP kidneys received PMP. Furthermore, if all of the ECD kidneys in our study received PMP instead of CS the over \$17.5 million could have been saved (4,726 non-PMP times \$3,715 savings from PMP utilization). Due to the additional costs of African American recipients and recipients 60 years old or older these recipients might particularly benefit by receiving a kidney that received PMP.

Although not unanimously accepted, the reduction in DGF may be due to conservative selection in deciding which kidneys to transplant and which to discard after analyzing the kidney function parameters obtained from the perfusion machine (27). Both Sung et al. and Mozes et al determined that higher resistance values in PMP ECD kidneys were associated with a higher rate of discharge (25,26). In our study recipients of a PMP kidney had a lower creatinine at discharge which may indicate less desirable kidneys that received PMP have been discarded instead of transplanted. Our results also indicate that it could be the "healthier" kidneys that are more likely to receive PMP as Sung suggested (25). In addition, it is possible that PMP can actually provide benefits to a kidney such that it might perform better than those at CS. Possibly, continuous perfusion can target key intracellular molecules or different biochemical pathways that could lead to lower rate of apoptosis therefore generating less DGF (7).

Another point to be highlighted is the relationship of the utilization of PMP and the cold ischemic time. While PMP utilization can increase cold ischemic time we included it as a possible predictor of PMP utilization. This is due to the fact that at the time of making the decision to utilize PMP surgeons may consider the amount of cold ischemic time that has already passed. The way cold ischemic time is recorded in the USRDS it is impossible to tell how much time passed before the decision to utilize PMP was made and how much time passed after the kidney was placed on PMP. To account for this limitation we analyzed the propensity to used PMP in two models, one including cold ischemic time and another excluding this factor (results not shown). The significant factors that can be used to predict the decision to utilize PMP were the same in both models indicating that cold ischemic time did not impact any other factors that may lead to the decision of PMP utilization. Ischemic times impacted the cost of renal transplantation directly, without any long term impact on patient and graft survival.

Our results were subject to limitations. First, our study design was a retrospective registry analysis. Thus, we could not control who received a PMP kidney and who did not. We attempted to address this concern by conducting multivariate analysis, including factors that we knew were different between PMP and non-PMP recipients. However, there may have been some characteristics that we did not have the data available to include in our models. A

prospective study is needed to determine if the cost associations we found are due to PMP and not the characteristics of the population. Second, if patients had claims with a private insurance as well as Medicare we were unable to include the private claims in the study. To limit the impact of this possible scenario we limited the patients to those in which Medicare was the primary payer. To ensure this restriction we required that Medicare paid for their transplant, that is Medicare paid at least \$15,000 for the initial transplant hospitalization.

While we have shown the cost benefits associated with PMP utilization in Medicare ECD recipients for the transplant hospitalization, future studies will be needed to determine if the same results hold for ECD recipients covered with private insurance. Results from those studies could help our society develop stronger policies and practices in providing optimal care and organs to those in need of a renal transplant. Further studies will also have to be done to see if there is a cost benefit for recipients of standard criteria donor and donation after cardiac death donor kidneys.

In summary, we found that while PMP may not be beneficial to long term outcomes, it provides an immediate cost benefit for the transplant hospitalization. PMP allows for the selection of higher functioning kidneys as seen through a lower creatinine level at time of discharge. Being able to discard poorer kidneys prior to transplant is more desirable, especially with ECD kidneys as this reduces the rate of DGF and in turn reduces the cost of care.

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Abbreviations

BMI	body mass index
CMV	cytomegalovirus
CS	cold storage
DGF	delayed graft function
DRG	diagnosis related group
ECD	expanded criteria donor
ESRD	end stage renal disease
HCFA	Health Care Financing Administration
PMP	pulsatile machine perfusion
PRA	panel reactive antibody
SCD	standard criteria donor
UNOS	United Network for Organ Sharing
USRDS	United States Renal Data System

Figure 1.
Graft Survival of Medicare ECD recipients in the USRDS 1995-2004 by PMP utilization.

Figure 2.
Patient survival for Medicare ECD recipients in the USRDS 1995-2004 by PMP utilization.

Table 1

Characteristics of Medicare-insured ECD recipients transplanted in 1995-2006 according to PMP utilization

	No PMP N = 4726	PMP N = 1114	
	n (%)	n (%)	p-value*
Recipient Characteristics			
Female	1823 (38.6)	433 (38.9)	0.86
Race			0.002
African American	1554 (32.9)	414 (37.2)	
White	2802 (59.3)	640 (57.5)	
Other	370 (7.8)	60 (5.4)	
Ethnicity			
Hispanic	495 (10.5)	93 (8.4)	0.03
Age (years)			0.001
18-30	189 (4.0)	26 (2.3)	
31-44	779 (16.4)	145 (13.0)	
45-59	1743 (36.9)	436 (39.1)	
≥ 60	2015 (42.6)	507 (45.5)	
BMI category (kg/m²)			0.04
BMI < 10 or Missing	1262 (26.7)	258 (23.2)	
BMI ≥10 to <25	1376 (29.1)	319 (28.6)	
BMI ≥ 25 to <30	1217 (25.8)	303 (27.2)	
BMI ≥ 30	871 (18.4)	234 (21.0)	
Primary cause of ESRD			0.18
Diabetes mellitus	1161 (24.6)	254 (22.8)	
Hypertension	1288 (27.3)	303 (27.2)	
Glomerulonephritis	757 (16.0)	159 (14.3)	
Other	596 (12.6)	162 (14.5)	
Unknown	582 (12.3)	141 (12.7)	
Pre-Transplant Dialysis Duration			<0.0001
None (pre-emptive)	359 (7.6)	109 (9.8)	
0-12 months	337 (7.1)	50 (4.5)	
13-24 months	670 (14.2)	157 (14.1)	
25-60 months	2341 (49.5)	513 (46.1)	
More than 60 months	1019 (21.6)	285 (25.6)	
Donor Characteristics			
Female	2536 (53.7)	585 (52.5)	0.49
Ethnicity			
Hispanic	495 (10.5)	93 (8.4)	0.03
Race			0.003
African American	434 (9.2)	139 (12.5)	
White	4092 (86.6)	934 (83.8)	
Other	200 (4.2)	41 (3.7)	

	No PMP N = 4726	PMP N = 1114	
	n (%)	n (%)	p-value*
Age (years)			0.0001
50-59	1913 (40.5)	382 (34.3)	
≥ 60	2813 (59.5)	732 (65.7)	
BMI category (kg/m²)			0.001
BMI < 10 or Missing	174 (3.7)	15 (1.4)	
BMI ≥ 10 to <25	1699 (36.0)	398 (35.7)	
BMI ≥ 25 to <30	1667 (35.3)	396 (35.6)	
BMI ≥ 30	1186 (25.1)	305 (27.4)	
Death due to stroke	3997 (84.6)	956 (85.8)	0.30
Terminal Creatinine ≥ 1.5	928 (19.6)	246 (22.1)	0.07
Hypertension history	3050 (64.5)	689 (61.9)	0.09
Diabetes	453 (9.6)	118 (10.6)	0.31
CMV sero-positive	3406 (72.5)	820 (73.8)	0.30
Transplant Factors			
Peak PRA %			<0.0001
0-10%	3312 (70.1)	732 (65.7)	
11-30%	503 (10.6)	115 (10.3)	
>30%	572 (12.1)	132 (11.9)	
Unknown	339 (7.2)	135 (12.1)	
Mismatches			<0.0001
0 ABDR mismatches	312 (6.6)	30 (2.7)	
0 DR mismatches	898 (19.0)	211 (18.9)	
> 0 DR mismatches	3382 (71.6)	847 (76.0)	
Unknown	134 (2.8)	26 (2.3)	
HLA Mismatches			<0.0001
0 HLA mismatches	312 (6.6)	30 (2.7)	
1 HLA mismatches	233 (4.9)	31 (2.8)	
2 HLA mismatches	487 (10.3)	124 (11.1)	
3 HLA mismatches	1002 (21.2)	229 (20.6)	
4 HLA mismatches	1236 (26.2)	347 (31.2)	
5 HLA mismatches	940 (19.9)	227 (20.4)	
6 HLA mismatches	382 (8.1)	100 (9.0)	
Unknown	134 (2.8)	26 (2.3)	
CMV sero-pairing			0.24
Donor - / Recipient -	361 (7.6)	71 (6.4)	
Donor - / Recipient +	842 (9.4)	223 (20.0)	
Donor + / Recipient -	808 (17.1)	199 (17.9)	
Donor + / Recipient +	2270 (48.0)	526 (47.9)	
Unknown	445 (9.4)	95 (8.5)	
Year			<0.0001

	No PMP N = 4726	PMP N = 1114	
	n (%)	n (%)	p-value*
1995	457 (9.7)	49 (4.4)	
1996	439 (9.3)	83 (7.5)	
1997	529 (11.2)	99 (8.9)	
1998	525 (11.1)	73 (6.6)	
1999	497 (10.5)	72 (6.5)	
2000	404 (8.6)	76 (6.8)	
2001	423 (9.0)	85 (7.6)	
2002	486 (10.3)	135 (12.1)	
2003	506 (10.7)	188 (16.9)	
2004	460 (9.7)	254 (22.8)	
	mean (std)	Mean (std)	
Cold-time	20.9 (8.7)	19.9 (8.3)	0.001
Warm-time	32.8 (28.7)	38.8 (25.8)	<0.0001

* P value for the difference in trait distribution according to PMP utilization was computed by the Chi-square test for categorical variables and the t-test for continuous variables.

Table 2

Average costs for transplant hospitalization and care over 1, 2, and 3 years post transplant among Medicare-insured ECD recipients from 1995-2004 according to PMP utilization in US dollars.

Time	PMP Use	n	Mean (std)	p-value *
Transplant hospitalization	No	4726	34,849 (24,828)	<0.0001
	Yes	1114	31,134 (19,766)	
One year post transplant	No	4294	88,823 (64,505)	0.08
	Yes	872	84,978 (58,131)	
Two years post transplant	No	3860	117,150 (87,348)	0.25
	Yes	712	111,898 (79,934)	
Three years post transplant	No	3274	141,882 (102,282)	0.62
	Yes	537	137,995 (98,227)	

* P value for the difference in cost distribution according to PMP utilization was computed by the Wilcoxon rank-sum test for continuous variables.

Table 3

Estimated contribution to total accumulated Medicare cost (in dollars) at transplant hospitalization cost and one, two, and three year post transplant costs for ECD recipients in the USRDS 1995-2004. Coefficient Estimates (95% CI).

Variable	Transplant hospitalization	One year post transplant	Two years post transplant	Three years post transplant
Base Cost	15,296 (8,145 - 22,446) *	28,755 (8,789 - 48,722) *	33,603 (5,189 - 62,018) *	33,214 (-2,149 - 68,577)
PMP use	-2,130 (-3,676 - -585) *	-3,173 (-7,774 - 1,429)	-5,536 (-12,417 - 1,344)	-5,800 (-15,074 - 3,473)
Recipient characteristics				
Female	-590 (-1,839 - 660)	761 (-2,823 - 4,345)	-971 (-6,164 - 4,221)	-2,596 (-9,337 - 4,146)
Race				
African American	3,568 (2,103 - 5,033) *	3,769 (-471 - 8,009)	5,614 (-554 - 11,782)	4,536 (-3,507 - 12,580)
White	Reference	Reference	Reference	Reference
Other	-716 (-3,127 - 1,696)	-7,373 (-14,550 - -196) *	-9,768 (-20,168 - 632)	-13,757 (-27,303 - -211) *
Hispanic	2,631 (554 - 4,707) *	4,581 (-1,109 - 10,272)	7,708 (-433 - 15,849)	13,178 (2,868 - 23,488) *
Age (years)				
18-30	Reference	Reference	Reference	Reference
31-44	3,354 (-82 - 6,791)	13,263 (3,737 - 22,789) *	20,014 (6,686 - 33,342) *	16,797 (316 - 33,278) *
45-59	3,063 (-232 - 6,357)	13,428 (4,294 - 22,562) *	16,252 (3,500 - 29,003) *	9,138 (-6,648 - 24,925)
≥ 60	4,643 (1,325 - 7,960) *	18,481 (9,255 - 27,707) *	23,926 (11,012 - 36,840) *	18,747 (2,703 - 34,790) *
BMI category (kg/m²)				
< 10 or Missing	-403 (-2,051 - 1,246)	-838 (-5,508 - 3,832)	1,625 (-5,068 - 8,317)	5,629 (-2,856 - 14,115)
≥ 10 to <25	Reference	Reference	Reference	Reference
≥ 25 to <30	309 (-1,301 - 1,919)	2,399 (-2,232 - 7,030)	3,266 (-3,520 - 10,052)	4,886 (-4,091 - 13,864)
≥ 30	-116 (-1,892 - 1,660)	4,860 (-292 - 10,012)	5,126 (-2,404 - 12,657)	8,861 (-1,107 - 18,828)
Primary cause of ESRD				
Diabetes mellitus	1,531 (-600 - 3,661)	7,884 (1,560 - 14,208) *	16,137 (6,932 - 25,341) *	23,282 (11,320 - 35,244) *
Hypertension	3,062 (973 - 5,152) *	4,604 (-1,744 - 10,951)	6,458 (-2,791 - 15,707)	7,571 (-4,428 - 19,570)
Glomerulonephritis	947 (-1,300 - 3,194)	-4,569 (-11,230 - 2,092)	-4,447 (-14,050 - 5,157)	-7,165 (-19,436 - 5,106)
PKD	1,149 (-1,613 - 3,910)	-7,757 (-15,844 - 330)	-10,968 (-22,678 - 742)	-10,240 (-25,302 - 4,822)
Other	Reference	Reference	Reference	Reference
Unknown	2,718 (329 - 5,107) *	2,948 (-4,112 - 10,008)	3,278 (-6,979 - 13,534)	2,440 (-10,836 - 15,716)

Variable	Transplant hospitalization	One year post transplant	Two years post transplant	Three years post transplant
PVD	-136 (-3,010 - 2,738)	2,070 (-6,132 - 10,271)	5,126 (-6,546 - 16,797)	1,657 (-13,262 - 16,577)
Pre-Transplant Dialysis				
None (pre-emptive)				
0-12 months	1,066 (-2,135 - 4,266)	12,028 (2,795 - 21,261)*	11,087 (-2,284 - 24,458)	10,922 (-6,327 - 28,170)
13-24 months	-640 (-3,106 - 1,826)	2,506 (-4,450 - 9,463)	2,096 (-7,889 - 12,081)	2,843 (-9,618 - 15,303)
25-60 months	1,082 (-1,611 - 3,774)	10,834 (3,200 - 18,468)*	13,609 (2,594 - 24,624)*	18,647 (4,760 - 32,533)*
More than 60 months				
Donor Characteristics				
Gender				
Female	-295 (-1,535 - 944)	532 (-3,026 - 4,090)	1,225 (-3,940 - 6,390)	3,214 (-3,495 - 9,923)
Race				
African American	-695 (-2,756 - 1,367)	6,451 (474 - 12,428)*	10,203 (1,318 - 19,087)*	10,056 (-1,776 - 21,889)
White	-640 (-3,106 - 1,826)	2,506 (-4,450 - 9,463)	2,096 (-7,889 - 12,081)	2,843 (-9,618 - 15,303)
Other	361 (-2,705 - 3,427)	-2,182 (-11,997 - 7,633)	-2,266 (-16,421 - 11,889)	1,944 (-16,847 - 20,736)
Age (years)				
50-59		Reference	Reference	Reference
≥ 60	2,548 (1,143 - 3,953)*	8,897 (4,867 - 12,926)*	12,426 (6,589 - 18,264)*	14,319 (6,761 - 21,878)*
BMI category (kg/m²)				
< 10 or Missing	2,065 (-1,588 - 5,718)	1,268 (-8,609 - 11,146)	5,550 (-7,988 - 19,088)	4,440 (-11,755 - 20,635)
≥ 10 to <25		Reference	Reference	Reference
≥ 25 to <30	051 (-1,367 - 1,470)	2,017 (-2,040 - 6,073)	3,781 (-2,109 - 9,672)	4,093 (-3,480 - 11,667)
≥ 30	-296 (-1,880 - 1,288)	364 (-4,204 - 4,933)	-3,562 (-10,231 - 3,108)	-7,450 (-16,179 - 1,278)
Death due to stroke				
Terminal Creatinine ≥ 1.5	1,610 (-991 - 3,310)	1,747 (-3,162 - 6,657)	3,233 (-3,970 - 10,436)	5,993 (-3,487 - 15,472)
Hypertension history				
Diabetes	3,323 (1,734 - 4,913)*	5,396 (844 - 9,949)*	9,145 (2,611 - 15,679)*	12,908 (4,429 - 21,386)*
	2,412 (1,022 - 3,801)*	6,424 (2,444 - 10,404)*	9,561 (3,797 - 15,325)*	13,221 (5,791 - 20,652)*
	1,279 (-744 - 3,302)	1,423 (-4,380 - 7,227)	-573 (-9,087 - 7,940)	3,532 (-7,945 - 15,010)
Transplant Factors				
Peak PRA %				
0-10%	Reference	Reference	Reference	Reference
11-30%	1,837 (-129 - 3,803)	9,779 (4,255 - 15,303)*	11,511 (3,582 - 19,439)*	6,799 (-3,277 - 16,874)

Variable	Transplant hospitalization	One year post transplant	Two years post transplant	Three years post transplant
>30%	3,252 (1,313 - 5,190) *	8,382 (2,891 - 13,872) *	14,535 (6,671 - 22,399) *	18,563 (8,493 - 28,633) *
Unknown	6,543 (3,857 - 9,228) *	20,400 (9,424 - 31,375) *	13,315 (-3,499 - 30,129)	27,329 (4,456 - 50,203) *
HLA Mismatches				
0 HLA mismatches	Reference	Reference	Reference	Reference
1 HLA mismatches	3,553 (-148 - 7,254)	7,474 (-2,713 - 17,660)	8,686 (-5,680 - 23,053)	11,358 (-6,677 - 29,392)
2 HLA mismatches	2,054 (-1,032 - 5,139)	3,237 (-5,347 - 11,820)	3,511 (-8,667 - 15,689)	4,257 (-10,977 - 19,491)
3 HLA mismatches	1,300 (-1,501 - 4,101)	6,560 (-1,245 - 14,365)	9,938 (-1,207 - 21,084)	11,792 (-2,201 - 25,784)
4 HLA mismatches	1,468 (-1,290 - 4,225)	7,159 (-562 - 14,880)	8,425 (-2,637 - 19,488)	13,342 (-616 - 27,299)
5 HLA mismatches	1,371 (-1,486 - 4,227)	7,467 (-582 - 15,515)	7,904 (-3,732 - 19,540)	10,739 (-4,059 - 25,538)
6 HLA mismatches	3,389 (115 - 6,664) *	10,969 (1,638 - 20,299) *	13,949 (241 - 27,657) *	11,117 (-6,534 - 28,769)
Unknown	3,845 (-565 - 8,256)	9,313 (-2,902 - 21,527)	20,804 (3,582 - 38,027) *	17,683 (-3,577 - 38,943)
CMV sero-pairing				
Donor - / Recipient -	Reference	Reference	Reference	Reference
Donor - / Recipient +	-297 (-2,925 - 2,332)	-1,772 (-9,318 - 5,775)	-4,814 (-15,832 - 6,203)	-999 (-15,190 - 13,193)
Donor + / Recipient -	1,165 (-1,421 - 3,752)	7,101 (-268 - 14,469)	7,055 (-3,660 - 17,769)	10,898 (-2,814 - 24,610)
Donor + / Recipient +	1,543 (-837 - 3,922)	3,636 (-3,166 - 10,437)	4,280 (-5,615 - 14,174)	8,299 (-4,406 - 21,004)
Unknown	265 (-2,711 - 3,240)	3,940 (-4,620 - 12,500)	9,028 (-3,322 - 21,377)	13,231 (-2,478 - 28,940)
Year				
1995	Reference	Reference	Reference	Reference
1996	1,835 (-1,077 - 4,747)	5,183 (-2,672 - 13,038)	5,308 (-5,428 - 16,044)	10,127 (-1,083 - 21,337)
1997	-1,851 (-4,597 - 894)	-1,033 (-8,446 - 6,381)	-4,966 (-15,110 - 5,178)	-2,399 (-12,736 - 7,939)
1998	-3,121 (-5,885 - -356) *	-5,248 (-12,711 - -2,214)	-8,744 (-18,951 - 1,463)	-6,622 (-17,018 - 3,774)
1999	-2,440 (-5,226 - 347)	-10,408 (-17,932 - -2,884) *	-7,718 (-18,010 - 2,573)	-2,778 (-13,173 - 7,616)
2000	-1,954 (-4,883 - 974)	-7,336 (-15,252 - 581)	-1,194 (-12,039 - 9,650)	6,049 (-4,966 - 17,064)
2001	-4,328 (-7,217 - -1,439) *	-5,520 (-13,328 - 2,287)	-7,862 (-18,559 - 2,835)	-
2002	-6,485 (-9,272 - -3,699) *	-14,212 (-21,755 - -6,669) *	-16,992 (-27,345 - -6,638) *	-
2003	-8,123 (-10,880 - -5,366) *	-19,757 (-27,237 - -12,278) *	-7,875 (-26,522 - 10,773)	-
2004	-14,315 (-17,367 - -11,263) *	-24,763 (-45,377 - -4,149) *	-49,808 (-78,135 - -21,481) *	-
Cold-time				
0 - 14 hours	Reference	Reference	Reference	Reference

Variable	Transplant hospitalization	One year post transplant	Two years post transplant	Three years post transplant
15 - 19 hours	461 (-1,269 - 2,191)	2,640 (-2,357 - 7,638)	1,569 (-5,738 - 8,876)	1,710 (-7,887 - 11,307)
20 - 25 hours	2,673 (917 - 4,428) *	4,734 (-307 - 9,775)	5,318 (-2,023 - 12,658)	1,290 (-8,187 - 10,766)
26+ hours	11,963 (10,178 - 13,748) *	21,482 (16,372 - 26,591) *	20,303 (12,888 - 27,719) *	14,954 (5,342 - 24,565) *
Unknown	6,042 (3,830 - 8,253) *	14,122 (7,666 - 20,577) *	11,672 (2,033 - 21,310) *	10,379 (-2,829 - 23,587)

* P-value < 0.05.

Table 4

Outcomes of renal transplantations in the USRDS 1995-2004 by PMP utilization

	No PMP N = 4726	PMP N = 1114	
	n (%)	n (%)	p-value *
Delayed graft function	1795 (38.0)	300 (26.9)	<0.0001
Rejection	98 (9.0)	451 (9.8)	0.41
	mean (std)	mean (std)	
Creatinine at Discharge	4.4 (3.1)	3.5 (2.7)	<0.0001
Length of stay	14.1 (84.7)	12.2 (41.5)	.37

* P value for the difference in trait distribution according to PMP utilization was computed by the Chi-square test for categorical variables and the t-test for continuous variables.

Table 5

Propensity of PMP in Medicare-financed ECD kidney transplants in 1995-2004

Variable	Odds Ratio	95% CI	P-value *
Recipient characteristics			
Race			
African American	1.12	(0.95 – 1.32)	0.17
White	Reference		
Other	0.67	(0.49 – 0.91)	0.01
Pre-Transplant Dialysis			
Duration			
None (pre-emptive)	1.61	(1.09 – 2.37)	0.02
0-12 months	Reference		
13-24 months	1.55	(1.08 – 2.20)	0.02
25-60 months	1.30	(0.94 – 1.79)	0.11
More than 60 months	1.54	(1.09 – 2.17)	0.01
Donor Characteristics			
Race			
African American	1.27	(1.02 – 1.59)	0.03
White	Reference		
Other	0.77	(0.53 – 1.11)	0.16
Age (years)			
50-59	Reference		
≥ 60	1.42	(1.21 – 1.67)	<.0001
Death due to stroke	1.33	(1.09 – 1.63)	0.005
Terminal Creatinine ≥ 1.5	1.27	(1.06 – 1.52)	0.01
BMI category (kg/m²)			
BMI < 10 or Missing	0.43	(0.24 – 0.75)	0.003
BMI ≥ 10 to <25	Reference		
BMI ≥ 25 to <30	0.96	(0.82 – 1.13)	0.62
BMI ≥ 30	0.99	(0.83 – 1.19)	0.95
Transplant Factors			
HLA Mismatches			
0 HLA mismatches	Reference		
1 HLA mismatches	1.52	(0.88 – 2.60)	0.13
2 HLA mismatches	2.85	(1.85 – 4.41)	<.0001
3 HLA mismatches	2.31	(1.53 – 3.49)	<.0001
4 HLA mismatches	2.44	(1.63 – 3.66)	<.0001
5 HLA mismatches	1.96	(1.29 – 2.97)	0.002
6 HLA mismatches	2.15	(1.37 – 3.38)	0.001
Unknown	2.24	(1.25 – 4)	0.01
Year			
1995	0.17	(0.12 – 0.25)	<.0001

Variable	Odds Ratio	95% CI	P-value *
1996	0.34	(0.25 – 0.47)	<.0001
1997	0.32	(0.24 – 0.44)	<.0001
1998	0.23	(0.16 – 0.32)	<.0001
1999	0.24	(0.17 – 0.33)	<.0001
2000	0.31	(0.22 – 0.42)	<.0001
2001	0.31	(0.23 – 0.43)	<.0001
2002	0.44	(0.33 – 0.58)	<.0001
2003	0.61	(0.47 – 0.80)	0.0002
2004	Reference		

* Adjusted for all variables in table along with those where $p \geq 0.05$ [recipient gender, recipient age, recipient ethnicity, recipient BMI, cause of ESRD (diabetes mellitus, hypertension, glomerulonephritis, other, and unknown), PKD, donor gender, hypertension history, donor diabetes, peak PRA%, CMV sero-pairing, and cold ischemic time].