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A study of the quality of life and cost-utility of renal transplantation

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A study of the quality of life and cost-utility of renal transplantation. The objective of this study was to assess the cost-utility of renal transplantation compared with dialysis. To accomplish this, a prospective cohort of pre-transplant patients were followed for up to two years after renal transplantation at three University-based Canadian hospitals. A total of 168 patients were followed for an average of 19.5 months after transplantation. Health-related quality of life was assessed using a hemodialysis questionnaire, a transplant questionnaire, the Sickness Impact Profile, and the Time Trade-Off Technique. Fully allocated costs were determined by prospectively recording resource use in all patients. A societal perspective was taken. By six months after transplantation, the mean health-related quality of life scores of almost all measures had improved compared to pre-transplantation, and they stayed improved throughout the two years of follow up. The mean time trade-off score was 0.57 pre-transplant and 0.70 two years after transplantation. The proportion of individuals employed increased from 30% before transplantation to 45% two years after transplantation. Employment prior to transplantation [relative risk (RR) = 23], graft function (RR 10) and age (RR 1.6 for every decrease in age by one decade), independently predicted employment status after transplantation. The cost of pre-transplant care ($66,782 Can 1994) and the cost of the first year after transplantation ($66,290) were similar. Transplantation was considerably less expensive during the second year after transplantation ($27,875). Over the two years, transplantation was both more effective and less costly than dialysis. This was true for all subgroups of patients examined, including patients older than 60 and diabetics. We conclude that renal transplantation was more effective and less costly than dialysis in all subgroups of patients examined.

Renal transplantation is generally believed to provide a considerable improvement in health-related quality of life when compared with dialysis, and is felt to be associated with a more favorable cost-effectiveness ratio. However, some of the studies upon which these assumptions have been made have compared different patient populations at varying intervals of treatment, sometimes without regard to co-morbidity or mortality. To avoid these important limitations, an economic evaluation of renal transplantation should ideally fulfill five criteria. It should: (a) include an unselected sample of patients followed from dialysis through transplantation, (b) measure health-related quality of life using a generic questionnaire that allows comparison with other interventions, (c) comprehensively record the resources used by patients and their families, (d) attach a monetary value to these resources using appropriate costs, and (e) combine the health outcomes and monetary values to obtain a cost-effectiveness ratio [1]. We have conducted a prospective cost-utility study of patients on the transplant waiting list of two Canadian university centres before and up to two years after transplantation, that attempts to follow these methodological criteria.

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Methods

Patients

Patients were recruited at University Hospital, London (University of Western Ontario - UWO) and the Vancouver Hospital and Health Science Centre and St. Paul's Hospitals, Vancouver (University of British Columbia - UBC). Clinically stable patients who had been on the transplant waiting list for at least three months were eligible for the study. Patients were excluded if they were 18 years of age or younger, did not speak or understand English, did not receive a transplant during the study period, and were not geographically accessible after transplantation.

Follow-up

Patients were routinely interviewed every six months prior to transplantation. If a major clinical event occurred (such as myocardial infarction) they were interviewed again one month later. After transplantation they were interviewed at 1, 3, 6, 12, 18 and 24 months. The interview consisted of health-related quality of life measures, and questions about employment and costs borne by the patients and their families. Patients who lost their graft were followed using the same schedule.

Health-related quality of life measures

Health-related quality of life measures were personally administered by a trained interviewer in identical order at each study visit.

Hemodialysis questionnaire. The Hemodialysis Questionnaire (also known as the Kidney Disease Questionnaire) is a 26 item

disease-specific questionnaire developed for patients on hemodialysis [2]. It has five dimensions: physical symptoms, fatigue, depression, relationships with others, and frustration. The physical symptoms dimension is patient-specific (patients identify up to 6 physical symptoms that are of most concern to them, and these items are used throughout the study). The reproducibility of the Hemodialysis Questionnaire dimensions in stable patients varies between 0.74 and 0.95. The instrument has been shown to be sensitive to change in patients with end-stage renal failure receiving erythropoietin [3].

Kidney Transplant Questionnaire. The Kidney Transplant Questionnaire is a 25 item disease-specific questionnaire developed for patients with a renal transplant [4]. It has five dimensions: physical symptoms, fatigue, uncertainty, appearance, and emotional dysfunction. The reproducibility of the KTQ in stable patients varies between 0.70 and 0.87. The responses to both the Hemodialysis and Kidney Transplant questionnaires were recorded on a seven point Likert Scale, with a higher score indicating a better quality of life. At follow-up visits, patients were informed of their previous responses when completing the questionnaire [5].

Sickness Impact Profile (SIP). The Sickness Impact Profile is a behaviorally-based generic health index that contains 136 items and 12 dimensions [6]. The dimensions can be aggregated to form psychosocial, physical and global summary scores. The range of scores in each dimension and summary score varies between 0 and 100, with a lower score being better.

Time-Trade Off. The Time-Trade Off is a preference measurement instrument that produces a score varying between 0 (a patient who is indifferent between life and death) and 1.0 (perfect health) [7]. In addition to rating their own state of health, patients were asked to rate four hypothetical scenarios chosen to represent patients who were doing well and poorly on both dialysis or transplantation.

Employment. The patient's employment status was determined at each visit. If they were unemployed the reason was ascertained.

Resource use and costs

Resource use and costs were divided into five categories: in-patient hospitalizations, outpatient visits (including dialysis, transplant clinic visits, medications, laboratory tests and physician fees), nephrectomy of the living related donor, the transplant program (including organ retrieval and cross-matching) and patient-borne costs (including transportation, accommodation, child care and time).

The resources used by patients at both UWO and UBC were recorded prospectively from a variety of sources including patient charts (for hospitalizations and outpatient visits in the study hospitals), provincial government billing systems (for physician fees and community diagnostic tests) and patient interview (for costs borne by patients and their families, and hospitalizations at other centers). The costs of hospitalization and outpatient visits at a study hospital were derived from a fully allocated costing model developed at the Vancouver Hospital and Health Sciences Centre (details from the authors on request). Province-specific charges were used for physician fees, per diem rates for non-study hospitals and medications. The time spent by all patients to receive care (including hospitalization, clinic visits, dialysis and travel time) was valued at the British Columbia industrial sector rate ($14.73/hr). Costs were collected in 1990 to 91 Canadian dollars and converted to 1994 Canadian dollars using the 5.61% increase in the Health & Personal Cost component of the Consumer Price Index that occurred between those two dates.

Cost-utility analyses

Costs, time trade-off scores and survival were combined to estimate the cost-utility of transplantation compared with dialysis, for two years after transplantation. The standard formula [cost(transplantation) − cost(dialysis)]/[QALY(transplantation) − QALY (dialysis)] was used, where QALY is quality adjusted life years. Complete costs and utilities were not available for all patients at all time points due to sickness, withdrawal or loss to follow-up. The methods of calculating costs, utilities and QALYs, are described in the following sections.

QALY transplantation

For the primary analysis, only the 139 patients who were on dialysis when they entered the study were included. Time trade-off values were available for 136 patients after transplantation, 76 of whom were followed for two years or until death. A value of zero was assigned at the time of death. Time trade-off values were not available for all patients at each visit. The reasons for missing data (and the method of estimating the time trade-off values) were: (1) study ended earlier than two years after transplantation (51 patients, the mean time trade-off value of all patients was imputed for subsequent visits), (2) patients no longer wished to participate or moved to another area for non-health related reasons (9 patients, the mean time trade-off value for all patients was imputed for subsequent visits), (3) patients missed an interview because they felt unwell (10 patients, a time trade-off value of 0.2 was assumed for that visit), and (4) a visit was missed for non-health reasons (40 patients, the average of the visits before and after was used). Altogether, 224 values were imputed out of 952 "potential visits."

Costs of transplantation

Costs were divided into four periods: (1) the pre-transplant period, (2) the first 90 days after transplantation, (3) 91 to 365 days after transplantation, and (4) the second year after transplantation. If a patient was only followed for part of a period, costs were extrapolated from the available data, provided at least 90 days of data were available (for example, if data were only available for 100 days on dialysis which cost $20,000, then the yearly cost of dialysis was estimated to be 365 × $20,000/100 = $73,000). When a patient died, costs were assigned a value of zero at the time of death.

QALY dialysis

To estimate the QALYs associated with dialysis, the pre-transplant time trade-off values from the 136 patients who were on dialysis at the time of transplantation were used. It was assumed they would have remained unchanged during two years of dialysis treatment. We assumed that the mortality rate on dialysis would have been the same as that after transplantation, but unlike transplantation, we assumed that it was constant. There were 13 deaths after transplantation. Therefore, when estimating QALYs on dialysis, we assumed that one death occurred every 56 days (730 days/13), that the same patients who died after transplantation would have died on dialysis, and that they would have died in the same order.

Table 1. Patient characteristics

	Transplanted	Not transplanted	*P*
UWO %	48	47	
UBC %	52	53	
Mean age *years*	42 ± 14	49 ± 14	< 0.001
% Male	62	66	
Time on dialysis *years*	2.0 ± 2.7	3.0 ± 3.5	< 0.011
Employment %			
Full-time	21	20	
Part-time	9	9	
Unemployed	70	71	
Renal disease %			
Glomerulonephritis	32	37	
Diabetic nephropathy	15	11	
Polycystic	13	9	
Hypertension/vascular	2	6	
Other	38	38	

Cost of dialysis

It was assumed that, on average, the cost of dialysis remained constant. Of the 100 patients with at least 90 days costing data from Period 1, there were nine deaths and they were assumed to have occurred every 81 days (730 days/9). Costs were assumed to become zero at the time of death.

Statistical analysis

Patient characteristics were compared between transplanted and non-transplanted patients using Student's *t*-test for continuous variables and the chi-square test for categorical variables. Overall patient and graft survival were estimated using the Kaplan-Meier product limit methods. The log-rank test was performed to compare the subgroups. Student's paired *t*-test was used to examine the change in quality of life from pre-transplant to the post-transplant follow-up visits. No adjustments for multiple comparisons were made. Multivariate stepwise logistic regression was applied to identify factors which were associated with employment status one year after transplantation. Descriptive summaries of costing and cost-utility data are presented, but no statistical tests were performed.

Results

Transplanted and non-transplanted patients

During the study period, 269 patients on the transplant waiting lists were evaluated. One hundred and seventy were transplanted but two were missed by the study interviewers after transplantation. This left 168 patients in the study. Reasons that patients were not transplanted were: entry into the study had ended (78), death (11), removal from the transplant waiting list because of their health (5), loss to follow-up (3), and personal choice (2). Of the patients who were transplanted, 4 refused follow up at any time after transplantation, 80 were followed for two years, and 62 were still being followed but were not yet two years after transplantation at the time of analysis. The average length of follow-up was 19.5 months after transplantation. Twenty-nine (17%) of the transplanted patients were not on dialysis at the time of their transplant. The patients who were transplanted were younger ($P < 0.001$) and had been on dialysis for a shorter period of time ($P = 0.011$) than those who were not transplanted (Table 1).

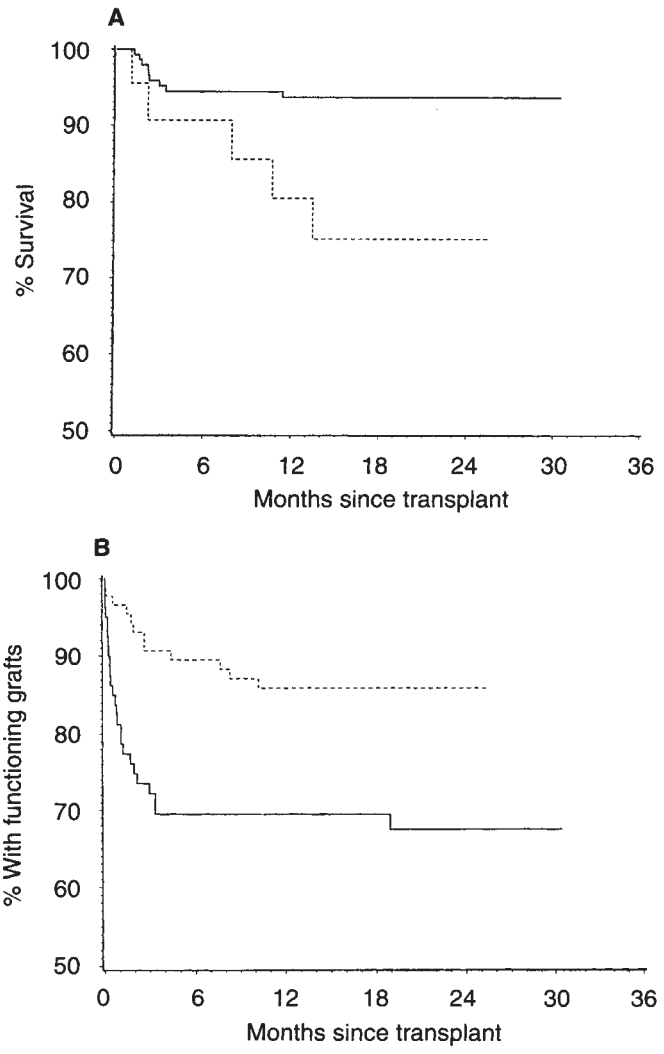

Fig. 1. A *Patient survival after transplantation in patients ≤ 60 years of age (—) and patients > 60 years of age (– – –).* **B.** Graft survival after transplantation in Center 1 (—) and Center 2 (– – –).

Patient and graft survival

At two years, overall patient survival was 91%; 94% in patients younger than 60 years, and 75% for those 60 years and older ($P = 0.007$; Fig. 1A). Time of death varied between 30 and 408 (median 66) days after transplantation. Causes of death were sepsis (7), cardiac (4), malignancy (2) and idiopathic pulmonary fibrosis (1). Overall the two-year graft survival rate was 77%; 86% at one center (C-1) and 68% at the other (C-2) ($P = 0.003$). Eleven patients at the second center lost their grafts due to thrombosis compared to two at the other, accounting for the difference between centers (Fig. 1B). The mean serum creatinine two years after transplantation in patients with a functioning graft was 143 ± 45 μmol/liter.

Quality of life

By six months after transplantation, the mean health-related quality of life scores of almost all measures had improved compared to pre-transplantation, and stayed improved throughout the two years of follow-up (Table 2). These improvements

Table 2. Quality of life before and after transplantation

	Pre-TX			1 Month		3 Months		6 Months		12 Months		18 Months		24 Months	
	N	Mean	SD	*N*	Mean	*N*	Mean	*N*	Mean	*N*	Mean	*N*	Mean	*N*	Mean
KTQ															
Fatigue	168	4.44	1.49	146	4.87[d]	132	5.25[a]	139	5.54[a]	134	5.71[a]	109	5.58[a]	77	5.70[a]
Uncertainty	168	4.25	1.66	146	4.76[b]	132	4.91[a]	139	5.21[a]	134	5.43[a]	109	5.37[a]	77	5.42[a]
Appearance	168	6.34	0.72	146	5.98[a]	132	5.84[a]	139	6.00[a]	134	6.07[b]	109	6.04[b]	77	6.24
Emotional	168	4.82	1.21	146	5.27[a]	132	5.32[a]	139	5.56[a]	134	5.65[a]	109	5.50[a]	77	5.56[a]
KDQ															
Physical	167	4.38	1.15	144	5.31[a]	131	5.51[a]	136	5.63[a]	132	5.66[a]	108	5.68[a]	77	5.60[a]
Fatigue	168	4.27	1.43	146	4.75[b]	132	5.15[a]	139	5.42[a]	134	5.57[a]	109	5.47[a]	77	5.58[a]
Depression	168	4.80	1.34	146	5.38[a]	132	5.43[a]	139	5.66[a]	134	5.72[a]	109	5.63[a]	77	5.68[a]
Relationships	168	5.00	1.14	146	4.87	132	5.37[b]	139	5.81[a]	134	5.92[a]	109	5.80[a]	77	5.93[a]
Frustration	168	4.63	1.53	146	5.34[a]	132	5.44[a]	139	5.56[a]	134	5.71[a]	109	5.59[a]	77	5.56[a]
SIP															
Sleep & rest	167	24.4	23.9	146	28.0	131	15.6[b]	139	12.0[a]	133	10.0[a]	109	12.8[a]	76	8.5[a]
Emot. behavior	167	12.8	16.8	146	9.9	131	7.4[a]	139	6.4[a]	133	5.7[a]	109	7.5[a]	76	5.3[a]
Body care and movement	167	4.6	8.4	146	7.0[d]	132	4.6	139	3.5	133	2.8[c]	109	3.9	76	2.6
Home management	167	15.7	17.0	146	35.9[a]	131	15.6	139	7.9[a]	133	7.9[a]	109	11.6	76	6.5[b]
Mobility	167	5.4	11.7	146	14.9[a]	132	6.6	139	2.7[b]	133	3.1[d]	109	4.4	76	1.8
Social interaction	167	14.4	14.9	146	14.8	132	9.3[a]	139	6.2[a]	133	5.7[a]	109	6.7[a]	76	4.3[a]
Ambulation	167	11.6	12.3	146	14.0	132	10.3	139	7.8[b]	133	6.5[a]	109	7.8[b]	76	6.5[d]
Alertness behavior	167	16.6	23.2	146	10.5[b]	132	9.1[a]	139	6.8[a]	133	6.7[a]	109	10.0[d]	76	6.8[d]
Communication	167	3.7	9.6	146	3.8	132	3.6	139	3.5	133	2.0	109	3.7	76	2.5
Work	167	40.4	31.9	146	54.8[a]	132	41.3	139	28.1[a]	133	28.1[b]	109	27.7[c]	76	19.4[a]
Recreation & pastimes	167	31.9	25.4	146	37.9[d]	132	19.6[a]	139	14.5[a]	133	10.6[a]	109	11.9[a]	76	9.0[a]
Eating	167	9.0	6.6	146	5.1[a]	132	3.1[a]	139	3.8[a]	133	3.3[a]	109	3.1[a]	76	2.9[a]
Total physical	167	6.4	8.7	146	10.3[b]	132	6.3	139	4.4[c]	133	3.7[a]	109	4.9	76	3.3
Total psychosocial	167	12.4	13.1	146	10.8	132	7.8[a]	139	5.8[a]	133	5.2[a]	109	7.0[a]	76	4.7[a]
Overall SIP	167	13.1	9.9	146	16.1[b]	131	10.1[b]	139	7.1[a]	133	6.4[a]	109	7.8[a]	76	5.3[a]
TTO															
Good dialysis	167	0.54	0.27	146	0.55	131	0.53	137	0.53	132	0.54	107	0.52	76	0.55
Bad dialysis	167	0.34	0.27	146	0.35	131	0.34	137	0.38	132	0.36	107	0.35	76	0.38
Good transplant	167	0.77	0.22	146	0.82[b]	131	0.81	137	0.78	132	0.79	108	0.73	76	0.78
Bad transplant	167	0.47	0.27	145	0.50	131	0.46	137	0.48	132	0.40	108	0.43	76	0.46
Patients themselves	167	0.57	0.29	145	0.68[a]	131	0.71[a]	137	0.75[a]	132	0.74[a]	108	0.70[a]	76	0.70[b]

P values compare pre- and post-transplant scores.
[a] $P < 0.001$
[b] $P < 0.005$
[c] $P < 0.01$
[d] $P < 0.05$

were seen in measures assessing psychosocial as well as physical well-being, in disease-specific and generic measures, and their magnitude was clinically important. However, the patterns of improvement among health-related quality of life measures differed. The Hemodialysis Questionnaire, Transplant Questionnaire and time trade-off scores were already better one month after transplantation (except for the appearance dimension of the Transplant Questionnaire). On the other hand, many of the items of the Sickness Impact Profile (sleep and rest, body care and movement, home management, mobility, work, recreation and pastimes, and the total physical score) worsened transiently during the first month.

Other than fatigue, the 10 physical symptoms identified most frequently pre-transplantation were muscle, bone and joint aches; sleep disturbances; itchy, dry skin; gastrointestinal complaints; trouble concentrating; cough and shortness of breath; headaches; decreased sexual function; cramps; and dizziness. These all improved markedly after transplantation, except for sexual function (Table 3). Three months after transplantation, patients were asked if they had any new physical symptoms. Some indicated problems with acne and rashes, excessive hair growth, increased appetite, tremors, and weight gain, all of which could be considered symptoms of the patients' immunosuppressive medications. However, all of these symptoms improved considerably between three months and two years after transplantation (Table 3).

The total Sickness Impact Profile, the fatigue dimension of the Transplant Questionnaire and the time trade-off scores prior to and one year after transplantation are shown in Table 4, according to patient characteristics (age, diabetes, living related donor, pre-emptive transplantation). It is striking that, except for patients whose grafts failed, all subgroups of patients had a marked improvement in health-related quality of life. It is particularly noteworthy that the health-related quality of life of diabetics was very good after transplantation. Because of the relatively small numbers of patients and the large number of comparisons, the changes in health-related quality of life were not compared statistically among groups.

Employment

The proportion of individuals employed increased from 30% before transplantation to 45% two years after transplantation (Table 5). More patients with functioning grafts two years after transplantation were working (51%) than those with failed grafts (21%). The main reasons for not working full-time prior to

Table 3. Physical symptoms identified before and after transplantation

	Pre-TX	1 Month	3 Months	6 Months	12 Months	18 Months	24 Months
Physical symptoms identified before transplantation							
Muscle/bone/joint ache	4.01 (1.53)	5.20[a]	5.15[a]	5.47[a]	5.54[a]	5.26[a]	5.66[a]
Sleep disturbance	3.97 (1.61)	4.64[d]	5.37[a]	5.28[a]	5.49[a]	5.42[a]	5.20[c]
Itchy, dry skin	4.05 (1.61)	6.21[a]	6.21[a]	6.29[a]	6.42[a]	6.34[a]	6.30[a]
GI complaints	4.38 (1.68)	5.50[a]	6.14[a]	5.68[a]	5.58[a]	5.62[a]	5.62[d]
Trouble concentrating	4.21 (1.24)	5.36[a]	5.68[a]	5.59[a]	5.35[b]	5.37[b]	5.08[d]
Cough & SOB	5.11 (1.12)	5.76[b]	5.79[b]	5.91[b]	6.09[a]	6.14[b]	5.91[d]
Headaches	4.65 (1.64)	5.97[b]	6.00[a]	5.82[a]	5.66[b]	5.80[d]	6.00[d]
Sexual function	3.58 (2.12)	3.83	3.71	4.17	4.00	4.41	4.33
Cramps	5.11 (1.22)	6.48[a]	6.11[c]	6.28[b]	6.22[b]	6.41[b]	6.50[b]
Dizziness	5.00 (1.32)	5.75	5.93[b]	5.92[c]	5.93[c]	5.70[d]	6.39[a]
New, possibly drug-related symptoms identified after transplantation							
Acne and rashes			4.11 (1.82)	4.75	5.42	5.74	5.92
Hair growth			3.14 (2.07)	4.15	5.14	5.77	6.00
Increased appetite			4.98 (1.71)	5.48	5.94	5.93	5.93
Tremors			3.93 (1.87)	4.44	4.72	4.73	4.57
Weight gain			3.46 (1.39)	3.75	4.07	4.67	5.63

P values compare pre- and post-transplant scores. All values are means, except those in parentheses, which are standard deviations.
[a] $P < 0.001$
[b] $P < 0.005$
[c] $P < 0.01$
[d] $P < 0.05$

Table 4. Mean quality of life after transplantation in different groups of patients

	Pre-transplant				12 Months after transplant			
	N	Total SIP	KTQ fatigue	TTO	*N*	Total SIP	KTQ fatigue	TTO
≤ 60 years	146	13.5	4.4	0.57	121	6.5	5.7	0.75
> 60 years	22	10.9	4.7	0.55	13	4.9	5.9	0.72
Non-diabetic	141	12.9	4.4	0.58	112	6.3	5.6	0.73
Diabetic	27	14.4	4.7	0.49	22	6.6	6.4	0.82
Living-related	20	14.9	3.6	0.62	15	5.8	5.8	0.74
Cadaveric	148	2.9	4.6	0.56	119	6.4	5.7	0.74
Pre-emptive	29	10.6	4.3	0.64	24	4.5	6.2	0.79
On Dialysis	139	13.6	4.5	0.55	110	6.8	5.6	0.66
Functioning grafts	168	13.1	4.4	0.57	108	4.9	5.9	0.77
Graft loss	37	11.4	4.9	0.61	26	12.7	4.9	0.62

transplantation were health limitations (51%), early retirement due to health (16%) and personal choice (15%). Among persons with functioning grafts two years after transplantation the main reasons for not working full-time were health limitations (36%), early retirement due to health (14%), and personal choice (28%).

The influence of the following factors upon employment status one year after transplantation was examined: age, gender, race, education, employment before transplantation, diabetes, overall SIP score and graft function. Employment prior to transplantation [relative risk (RR) 23; $P < 0.0001$], graft function (RR 10; $P = 0.002$) and age (RR 1.6 for every decrease in age by one decade; $P = 0.02$) independently predicted employment status after transplantation.

Costs of dialysis and transplantation

While on dialysis, patients spent an average of 8.5 days per year as in-patients. During the first year after transplantation they spent an average of 32.2 days in the hospital, compared with 6.1 days during the second year.

Table 5. Employment outcomes (all subjects, irrespective of graft function)

Employment status	Pre-transplant ($N = 168$)	1 Year post-transplant ($N = 134$)	2 Years post-transplant ($N = 77$)
Employed full time or part time			
All patients	50 (30%)	50 (37%)	35 (45%)
Successful grafts		46 (43%)	32 (51%)
Failed grafts		4 (15%)	3 (21%)
Unemployed	118 (70%)	84 (63%)	42 (55%)
Main reason not working full time			
Unable due to health	68 (51%)	38 (40%)	23 (47%)
Personal choice	20 (15%)	19 (20%)	10 (20%)
Retired			
• Early due to health	21 (16%)	18 (19%)	7 (14%)
• At usual time	9 (7%)	3 (3%)	2 (4%)
Looking for work	3 (2%)	9 (9%)	4 (8%)
Student	8 (6%)	8 (8%)	2 (4%)
Temporarily laid off	4 (3%)	0 (0%)	1 (2%)

Table 6. Average costs of pre-transplant care and transplantation (1994 Canadian dollars)

Types of costs	Pre-transplant	Transplantation (0–3 months)	(4–12 months)	(Year 2)
Transplant program	2,791	3,271	2,171	2,856
Patient-borne	14,761	4,992	4,175	4,421
In-patient	6,317	26,213	4,507	4,099
Out-patient	42,748	5,911	14,523	16,500
Living-related donor	165	528	—	—
Total	66,782	40,914	25,376	27,875

Table 7. Cost of pre-transplant care and transplantation in different groups of patients (1994 Canadian dollars)

	Pre-transplant	Transplantation Year 1	Year 2
Study hospital			
1	61,153	73,653	32,158
2	81,039	63,664	25,010
3	67,419	58,193	23,809
< 60 years	66,944	66,655	28,632
≥ 60 years	65,720	63,708	21,160
Nondiabetic	67,166	65,318	27,883
Diabetic	64,522	71,654	27,791
Living-related	62,804	74,151	34,141
Cadaveric	67,266	64,979	26,725
Pre-emptive	13,779	48,710	14,594
Dialysis	72,609	68,193	29,803
Functioning grafts	67,839	54,155	15,376
Graft loss	63,252	112,193	73,777

The costs of dialysis and the costs of the first two years after transplantation are shown in Table 6 divided into five categories: operation of the transplant program, patient-borne, in-patient, out-patient (which includes dialysis) and costs related to management of the living-related donor. The average annual cost of dialysis was $66,782. The major components were the costs of dialysis itself (50%), patient borne costs (22%) and physician fees (10%). The average costs of the first year after transplantation were almost identical ($66,290), although this varied from $27,903 to $237,523. However, there was an important shift in how the costs were incurred. Dialysis costs were reduced to 10% of total costs. The other major components were in-hospital costs (45%), patient borne costs (14%), medication costs (10%), and physician fees (10%). The second year costs of $27,875 were only about 40% of the costs of the first year after transplantation. The most dramatic decrease was in patient borne costs, which included health care contact time, transportation, accommodation, and child care.

Costs were assessed in different patient groups (Table 7). There was very little difference in costs between groups except for patients who lost their grafts, where costs during the first year after transplantation were twice those of patients with functioning grafts. During the second year after transplantation, the costs for patients whose graft had failed continued about $10,000 higher than they had been on dialysis.

Cost-utility of transplantation

Data from the TTO measures and costs were combined as described in the **Methods** section to yield an incremental cost-utility ratio for transplantation. Thus, the costs and health-related quality of life of patients whose grafts failed and of those who died were included, as were patients with successful transplants. For patients who were on dialysis prior to transplantation (that is, excluding the patients not on dialysis, for whom it was impossible to calculate the cost of dialysis) the Δ cost/Δ QALY on progressing from dialysis to transplantation was −$59,325 for the first year and −$394,500 for the second year (Table 8). Thus, transplantation was both substantially more effective and less expensive than dialysis.

Discussion

Similar to other studies [8–11], we have shown that renal transplantation improves the health-related quality of life of patients on dialysis. This is the case even if one includes patients with failed grafts in the transplant group. The effect was seen irrespective of whether the patients were diabetic, older than 60 years, or had received a cadaveric graft. Health-related quality of life appeared to remain stable between one and two years after transplantation. Patients with failed grafts reported their health-related quality of life one year after the transplant to be comparable to that prior to the procedure, but worse than in patients with functioning grafts. This is similar to what has been found by other researchers [9].

The improvement was seen in all aspects of the patients' well-being, including physical, emotional and social dimensions. Some aspects of quality of life requiring mobility actually worsened during the first month after transplantation (presumably due to the pain of surgery), but improved thereafter. The physical symptoms that the patients complained of while on dialysis improved markedly after transplantation. Patients did develop some new side-effects by three months after transplantation that were probably due to prednisone and cyclosporine (such as hirsutism, tremor, etc.), but these had improved markedly by one year.

The improvement in health status was important enough to be reflected in the two generic measures employed: the Sickness Impact Profile and time trade-off. The scores on dialysis seen with the Sickness Impact Profile were similar to those found by Hart and Evans in their cross-sectional study of patients with end-stage renal disease [12], and the improvement appeared greater than that seen in one study of erythropoietin therapy in hemodialysis patients [3], although another study found a very substantial improvement on quality of life with erythropoietin therapy [13]. Russell and colleagues administered the time trade-off to 27 patients with functioning grafts an average of 31 months after transplantation [9]. The time trade-off score increased from 0.41 on dialysis to 0.74 ($P < 0.001$). Although the time trade-off score after transplantation was similar to ours, the improvement from dialysis to transplantation appeared greater. This may be because their patients were sicker while on dialysis, and they excluded patients whose grafts had failed.

The benefit of transplantation in our study was particularly marked in diabetic patients, in whom the time trade-off score improved by 0.33. However, the small numbers of diabetic patients did not allow us to conclude that their improvement was significantly greater than non-diabetics.

Despite the marked improvement, transplant patients did not rate their quality of life as normal. The mean time trade-off score

Table 8. Cost effectiveness of transplantation compared with dialysis

	Cost		QALY		
	Transplantation	Pre-transplant	Transplantation	Pre-transplant	ΔCost/ΔQALY
Year 1	66,540	73,659	0.65	0.53	−59,325
Year 2	27,474	70,869	0.62	0.51	−394,500

of patients with a functioning graft was 0.77, and the responses to the other questionnaires indicated that the patients' quality of life was not normal. Normative data from a predominately white, American population found a mean time trade-off score of 0.94 for men and 0.90 for women between 45 and 54 years of age [14]. Presumably concern about losing the graft, side-effects from medications, chronic rejection, and concomitant diseases all adversely affected these patients' quality of life.

The cost of the first year of transplantation was similar to the annual cost of hemodialysis, but was much less during the second year after transplantation. The costs were not affected by the patients' age, whether they were diabetic, or whether they had received a cadaveric or living related graft. The cost of a failed graft was considerable; it was about twice the cost of patients with a successful transplant during the first year, and about $10,000 more than dialysis during the second year. This is similar to the results of Manninen et al who studied 22 patients with graft failures [15].

When costs and consequences were combined in a cost-utility analysis, renal transplantation was both more effective and less costly than dialysis. Relatively few new health care technologies are this attractive from a cost-effectiveness point of view [16, 17]. Since the costs of dialysis remain relatively constant and the majority of transplant costs tend to occur early after the procedure, the cost-effectiveness of transplantation would have appeared even more attractive had the study been extended to five or ten years. It should be remembered that the alternative to which transplantation is being compared (dialysis) is itself a costly technology, and this is part of the reason the cost-effectiveness of transplantation is so appealing. The results do suggest that both from a patient and health policy point of view, every effort should be made to maximize the number of patients receiving transplantation. This includes approaching the families of all potential cadaveric donors, encouraging living related transplantation, and considering donation from friends and distant relatives.

The strengths of this study include: (a) inclusion of all transplant recipients at both centers during the study period, (b) follow-up of failed grafts as well as successful transplant recipients, (c) prospective measurement of quality of life and resources used, and (d) use of a fully-allocated method of costing in-patient and out-patient visits. It is worthwhile considering its weaknesses.

The rate of graft loss in one center was higher than expected during the study, which reduced the apparent improvement in quality of life seen with transplantation. Because time trade-off data were not available on all patients, extrapolations were made for some values. We feel that the values used to substitute for missing data were reasonable. The choice of a score of 0.20 for patients who were too sick to answer the questionnaire was arbitrary, but we feel that this low score reflects their quality of life at that time.

Although outcomes were evaluated in two university centers and three hospitals, costs were largely derived from one hospital (Vancouver Hospital and Health Sciences Centre) because of the sophistication of its costing methodology. There is no commonly agreed upon standard for the calculation of hospital costs in a multi-center study [18]. However, we feel that since renal transplantation is usually performed in university based hospitals, the costs derived from the Vancouver Hospital and Health Sciences Centre are a reasonable estimate of the average costs. Since this study was conducted in Canada, Canadian costs were used to value the resources consumed. There is evidence that the costs of health-care interventions are not as generalizable across different countries as is efficacy [19–21]. A detailed description of the resources used by the patients in this study are available from the authors on request. The marked attractiveness of transplantation from a cost-effectiveness point of view makes it very unlikely that the "bottom line" would change considerably in other countries.

In order to compare the incremental cost-effectiveness of transplantation with dialysis, we had to estimate what the utilities and costs of the dialysis patients would have been, had they not been transplanted. We assumed that the quality of life on dialysis would have remained the same over two years, and that the mortality rate would have been similar to transplantation (but that the deaths would have occurred at a constant rate, rather than early as is the case with transplantation). Both of these assumptions favored dialysis, since there is evidence that the death rate on dialysis is higher than after transplantation even after adjustment for patient characteristics [22]. Similarly, one might have expected the average quality of life of patients on dialysis to deteriorate slightly over two years. The fact that these assumptions favored dialysis makes the case for the cost-effectiveness of transplantation even more compelling.

During this study we only followed patients for a maximum of two years. Therefore, we were not able to provide an overall estimate of the cost-utility of transplantation, although it would become more attractive from an economic point of view with longer follow-up.

The quality of life and cost data collected in this study are transparently displayed in the tables. Therefore, we have not performed arbitrary sensitivity analyses, but leave it to readers to adjust the data as seems appropriate for their particular circumstances.

In summary, renal transplantation was both more effective and less costly than dialysis in all subgroups of patients examined.

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