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The Cost and Utility of Renal Transplantation in Malaysia

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on behalf of the Collaborative Kidney Transplant Economic Study Group

Background. Kidney transplantation is the optimal therapy for the majority of patients with end-stage renal disease. However, the cost and health outcomes of transplantation have not been assessed in a middle-income nation with a low volume of transplantation, such as Malaysia. **Aim and Methods.** This study used microcosting methods to determine the cost and health outcomes of living and deceased donor kidney transplantation in adult and pediatric recipients. The perspective used was from the Ministry of Health Malaysia. Cost-effectiveness measures were cost per life year (LY) and cost per quality-adjusted LYs. The time horizon was the lifetime of the transplant recipient from transplant to death. **Results.** Records of 206 KT recipients (118 adults and 88 children) were obtained for microcosting. In adults, discounted cost per LY was US $8609(Malaysian Ringgit [RM]29 482) and US $13 209(RM45 234) for living-donor kidney transplant (LKT) and deceased donor kidney transplant (DKT), respectively, whereas in children, it was US $10 485(RM35 905) and US $14 985(RM51 317), respectively. Cost per quality-adjusted LY in adults was US $8826 (RM30 224) for LKT and US $13 592(RM46 546) for DKT. Total lifetime discounted costs of adult transplants were US $119 702 (RM409 921) for LKT, US $147 152 (RM503 922) for DKT. Total costs for pediatric transplants were US $154 841(RM530 252) and US $159 313(RM545 566) for the 2 categories respectively. **Conclusions.** Both LKT and DKT are economically favorable for Malaysian adult and pediatric patients with ESRD and result in improvement in quality of life.

(*Transplantation* 2015;1: e45; doi: 10.1097/TXD.0000000000000553. Published online 20 November 2015.)

Malaysia is a middle-income country with a population of 27.9 million and a gross domestic product per capita of US $6913(RM23 674) in 2009.[1] The number of patients on renal replacement therapy (RRT) increased from 7965 in year 2000 to 23 346 in 2009.[2] In 2009, the rate of end-stage renal disease (ESRD) was 837 per million population (pmp) which was comparable to treatment rates in developed nations with higher gross domestic product per capita, such as Australia(850 pmp) and New Zealand(863 pmp).[3]

In 2009, 92% of the patients on RRT in Malaysia were on dialysis—only 8% received a kidney transplant. This is despite transplantation being available in Malaysia for more than 3 decades. The first living-donor kidney transplant (LKT) was performed in 1975, followed a year later by the first deceased donor kidney transplant (DKT). Over the ensuing years, in comparison with dialysis expansion, the transplant rate has remained low with an average of 60 transplants annually.[2] In 2009, the incidence rate of local transplant was only 3 pmp, including both LKT (31%) and DKT (26%). The number of patients benefiting from the local kidney transplant program is therefore small, and an assessment of the cost-effectiveness (CE) of transplantation was important.

The CE of center hemodialysis and continuous ambulatory peritoneal dialysis in Ministry of Health (MOH) hospitals[4] had previously been evaluated in 2001 but no evaluation of kidney transplantation had been performed. Although studies have established the CE of kidney transplantation in

Received 18 August 2015. Revision received 9 October 2015.

Accepted 15 October 2015.

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Funding: The study was made possible by research grants from the National Institutes of Health, Post Graduate Renal Society of Malaysia and Malaysian Society of Nephrology.

The authors declare no conflicts of interest.

S.B. participated in the research design, performance of research, data analysis, and writing of the article. Y.-C.Y. participated in the research design, performance of research, data analysis, and writing of the article. G.A. participated in the research design, performance of research, data analysis, and writing of the article. H.-S.W. participated in the performance of research and writing of the article. S.A. participated in the research design, performance of research, data analysis, and writing of the article. A.G. participated in the research design, performance of research, data analysis, and writing of the article.

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ISSN: 2373-8731

DOI: 10.1097/TXD.0000000000000553

developed countries, such as the United States,[5,6] Canada,[7] United Kingdom,[8] and Netherlands,[9] there are limited published economic evaluations from low- and middle-income countries. To our knowledge, fewer than 10 studies on this topic exist outside of high-income countries, and to date, no studies have examined quality of life (QOL) pretransplantation and posttransplantation in a middle-income country. Therefore, we embarked on this study with the aim to evaluate the costs and outcomes of DKT and LKT in adult and pediatric ESRD patients in Malaysia.

MATERIALS AND METHODS

Study Design and Population

The study used both prospective and retrospective data collection for 4 groups of transplant recipients: adult LKT, adult DKT, pediatric LKT, and pediatric DKT. The primary outcomes of interest were costs and utility of transplantation, derived from the results of survival and QOL analysis. Analysis was conducted based on intention-to-treat. The time horizon of the study was the lifetime of the transplant recipient from transplant to death. The perspective of the study was that of the MOH because it is the main provider and fully funds all transplants performed in MOH hospitals. Hence, only health consequences and costs incurred by MOH were included. Transplants performed overseas were not included due to absence of accurate primary data on costing. In addition, since the Declaration of Istanbul, the number of transplants from overseas have declined dramatically from 47.5% in 2009[2] to 13.8% in 2013.[10] Sources of data used in the study are as shown in Table 1.

Inclusion criteria were patients with medical records (≥80% data availability) who received a kidney transplant in Malaysia between 1991 and 2009. All patients transplanted between 2008 and 2009 were included. For patients transplanted in 2009, there was 1-year prospective data collection, and for those transplanted in 2008, there was prospective data for the costs in the second year of transplant

TABLE 1.

Data Sources

Data	Data Type	Sources
(1) Medical resource use data		
(a) Recipients direct medical resource use (first year)	Primary	Data from all patients transplanted in 2009 using chart review method
(b) Recipients direct medical resource use (second year)	Primary	Data from all patients transplanted in 2008 using chart review method
(c) Recipients direct medical resource use (third year until death)	Primary	Data were collected via chart review method for resource use of a sample of 110 patients transplanted before 2008. Random sampling was conducted using the Malaysian Dialysis and Transplant Registry, [11] using a stratified cohort at 2-5, 5-10, and 10 y posttransplant.
(d) Living donor direct medical resource use	Primary	Data from all donors in 2008 and 2009 using chart review method.
(e) Deceased donor direct medical resource use	Primary	Medical records collected using chart review method
(2) Survival data		
(a) Survival	Secondary	Malaysian Dialysis and Transplant Registry [11]
(3) Quality of life data		
(a) QOL pretransplant	Primary	Survey of patients on the transplant waiting list in 2009
(b) QOL posttransplant	Primary	Survey of transplant recipients who were transplanted in 2008-2009
(c) Utility value set	Secondary	Published Malaysian data by Faridah et al[12]
(4) Overhead cost data		
(a) Hospital overheads cost	Primary	Survey of 6 MOH hospitals involved in the study.
(b) Land and building area	Primary and Secondary	Survey of 6 MOH hospitals involved in the study. Secondary data were used for Hospital Kuala Lumpur from Hooi et al,[4] inflation factors from Department of Statistics, 2009[13] and property price statistics from Valuation and Property Services Department, 2012[14]
(c) NTRC cost and resource use	Primary	Survey of NTRC operational costs and resource use
(d) eMOSS cost	Primary	Survey of Malaysian Dialysis and Transplant Registry operational costs including office rental, utilities, telephone, human resource, equipment, and database maintenance
(5) Cost and price data		
(a) Medicine prices	Secondary	Hospital pharmacy survey and MIMS Malaysia[15]
(b) Laboratory investigation prices	Secondary	Available published rates from laboratories (Pathlab, Pantai Premier), Hospital Universiti Kebangsaan Malaysia
(c) Procedures and surgery prices	Secondary	Malaysian Medical Association (MMA) schedule of fees 2008[16]
(d) Blood product prices	Secondary	National Blood Bank
(e) Transport prices	Secondary	For air transport, Malaysia Airlines airfares; for land transportation, Government mileage claim rates and St. John's Ambulance charges
(f) Clinic visits, referrals, general ward, and ICU stay prices	Secondary	MMA schedule of fees 2008[16] and published hospital rates by Tung Shin Hospital and Putrajaya Hospital private wing
(g) Costs of dialysis	Secondary	Hooi et al[4]

ICU, intensive care unit.

and retrospective data for first year costs. To obtain long-term transplant cost data, stratified sampling was performed for those transplanted before 2008. A master list of all local transplant recipients was generated from the Malaysian Dialysis and Transplant Registry (MDTR) database, and patients were stratified by the duration posttransplant, that is, 2 to 5, 5 to 10, and over 10 years posttransplant. Sample size obtained was 30 patients per stratum.

The study was registered and approved by the Medical Research and Ethics Committee under the National Institutes of Health (project ID: NMRR-08-1301-2669).

Survival Analysis

Graft and patient survival analyses were conducted using data from the MDTR that included all transplant recipients who received grafts from 1991 to 2009. The Kaplan-Meier product-limit survivor function approach was used to estimate mean survival time for the analysis because it best fits the available data and was consistent with previously reported survival estimates.[11]

Separate graft and survival analyses were performed for adult LKT, adult DKT, pediatric LKT and pediatric DKT. From the mean graft and life survival duration for each type of patient, we derived a mean duration of graft survival, followed by graft failure and survival time on dialysis thereafter until death. Although recipients could possibly receive another organ subsequent to graft failure, this is very rare in Malaysia and was not considered in the study.

QOL and Utility Analysis

The QOL was measured prospectively among adult subjects using the EQ-5D-3L instrument.[17] The Malay, Chinese, and English language EQ-5D-3L instruments have been validated for use in a Malaysian population.[12] Pretransplant QOL was obtained through a survey of dialysis patients on waiting list for DKT within the electronic Malaysian Organ Sharing System (eMOSS) in 2009. Posttransplant QOL was obtained through surveys of patients transplanted in 2008 and 2009 who completed 4 QOL questionnaires at 1, 3, 6, and 12 months posttransplant.

The utility score with a stable, functioning graft was assumed to be equal to that at 12 months posttransplant. Utility levels after graft failure were assumed to be the same as pretransplant utility while on dialysis. The QOL assessment was not performed for pediatric patients due to lack of an appropriate, validated questionnaire that could be readily converted to QALYs in a Malaysian pediatric population.

Costs

Costs considered in this study are direct medical costs incurred by the MOH over the lifetime of transplant patients, as well donors' costs and overhead costs of the transplant program. Patient level costs incurred by transplant recipients and organ donors were estimated by microcosting of resource utilization data extracted via reviews of medical records. Resources estimated through microcosting included hospitalization, medications, laboratory and radiological investigations, procedures, referrals, surgery, transportation and outpatient clinic visits incurred pretransplant, during the transplant admission, posttransplant care and the cost of dialysis from graft failure to death. For donors, the direct medical costs estimated through microcosting included work-up costs, nephrectomy operation and postoperative care.

Overhead costs of the transplant program consisting of hospitals overheads, and program costs of the National Transplant Resource Centre (NTRC) and the eMOSS were apportioned to transplant patients through top-down costing. Because the NTRC and eMOSS cover transplants for all organs, their costs were allocated to kidney transplantation according to the allocation factors (proportion of organs transplanted), and further apportioned to each transplant recipient. The eMOSS costs were allocated equally to all transplant recipients (DKT and LKT) because all patients, irrespective of organ source, are registered into the MOSS system. Conversely, NTRC costs were allocated to DKT recipients only as the NTRC manages the infrastructure for organ procurement from deceased donors (DDs).

Hospital overhead costs included the costs of land and building amortized over 30 years, as well as utilities, maintenance, departmental human resource, and program costs. These costs were then allocated to each patient by top-down costing using allocation factors, based on location of transplant center and home treatment center. Costs upon returning to dialysis until death used previously published data.[4] More details on the cost data and data sources are shown in Table 1.

Prices of resources were obtained from both public and private sector sources (see Table 1). Where MOH resource costs were not available, shadow pricing from the private sector was used. All costs were standardized to year 2009 Malaysian Ringgit (RM) and the equivalent costs in 2009 US dollars were obtained using a conversion rate of US $1 = RM3.4245.[1]

Cost Analysis

Cost-effectiveness of kidney transplantation was analyzed separately for all 4 groups of recipients and reported as cost per life year (LY). In addition, cost per quality-adjusted LY (QALY) for adult DKT and adult LKT was also calculated.

TABLE 2.

Kidney Transplant Recipient Characteristics

	Adult		Pediatric	
Characteristics	**LKT**	**DKT**	**LKT**	**DKT**
N	63	55	39	49
Mean age at transplant, years (SD)	33.4 (10.3)	41.8 (8.9)	12.3 (3.4)	14.0 (2.4)
Sex, n (%)				
Male	37 (58.7)	29 (52.7)	25 (64.1)	24 (49.0)
Female	26 (41.3)	26 (47.3)	14 (35.9)	25 (51.0)
Mean time on dialysis, years (SD)	2.5 (2.4)	12.5 (4.8)	2.0 (1.4)	5.5 (2.0)
Primary renal disease, n (%)	62	47	37	51
Glomerulonephritis	24 (38.7)	15 (31.9)	15 (40.5)	26 (51.0)
Hypertension	3 (4.8)	6 (12.8)	0	0
Diabetes mellitus	5 (8.1)	1 (2.1)	0	0
Obstructive nephropathy	0	0	3 (8.1)	4 (7.8)
Renal Hypoplasia	0	0	9 (24.3)	2 (3.9)
Other	4 (6.4)	3 (6.4)	2 (5.4)	5 (9.8)
Unknown	26 (41.9)	22 (46.8)	8 (21.6)	14 (27.4)
Pretransplant dialysis modality, n (%)	62	47	33	49
Hemodialysis	56 (90.3)	40 (85.1)	12 (26.4)	24 (49.0)
Peritoneal dialysis	6 (9.7)	7 (14.9)	21 (63.6)	25 (51.0)
Preemptive transplant, n (%)	1 (0.8)		4 (4.5)	

TABLE 3.

Quality of Life of Pretransplant Dialysis and Posttransplant Patients

Adult LKT	Pretransplant[a]	1 mo[b]	P[c]	3 mo[b]	P[c]	6 mo[b]	P[c]	1 y[b]	P[c]
N	207	15		18		19		15	
EQ-5D (% problems)									
• Mobility	21.74	40.00		16.67		10.53		6.67	
• Self-care	5.80	13.33		0.00		0.00		0.00	
• Usual activity	15.46	13.33		5.56		0.00		0.00	
• Pain	18.36	33.33		16.67		5.26		6.67	
• Anxiety/depression	15.46	20.00		11.11		0.00		0.00	
Utility index	0.91	0.87	0.297	0.95	0.218	0.98	0.031	0.99	0.031
Adult DKT	**Pretransplant[a]**	**1 mo[b]**	**P[c]**	**3 mo[b]**	**P[c]**	**6 mo[b]**	**P[c]**	**1 y[b]**	**P[c]**
N	207	14		15		15		12	
EQ-5D (% problems)									
• Mobility	21.74	14.29		13.33		13.33		0.00	
• Self-care	5.80	0.00		0.00		0.00		0.00	
• Usual activity	15.46	7.14		13.33		0.00		0.00	
• Pain	18.36	35.71		33.33		0.00		0.00	
• Anxiety/depression	15.46	14.29		6.67		0.00		0.00	
Utility index	0.91	0.92	0.688	0.93	0.628	0.95	0.266	1.00	0.022

[a] Survey of unrelated dialysis patients on the eMOSS waiting list.

[b] 2009 transplant cohort.

[c] Difference in means compared with the pretransplant utility index.

As recommended by Malaysian and international guidelines, costs and outcomes were adjusted to 2009 values at a discount rate of 3% per annum in base case analysis.[18,19]

Univariate sensitivity analysis was performed to determine the impact of cost variations on the CE of each patient and transplant type. Costs were varied by ±25% from their mean values in the analysis. Lastly, sensitivity analysis was conducted by calculating the CE using undiscounted costs and outcomes and for variables with uncertain values.[18-20] These included varying the measures of utility used in the calculation of QALYs, costs of NTRC on the DD kidney transplant program, and hospital overhead costs. Statistical analysis was performed using Stata 11.2 SE statistical software.[21]

RESULTS

A total of 206 patients were included—118 adults (55 DKT, 63 LKT) and 88 children (49 DKT, 39 LKT). The study sample included all 96 KT recipients who were transplanted in the years 2008 to 2009 and 110 subjects randomly selected from 1991 to 2007 using stratified sampling based on duration posttransplant. The mean age of adult recipients was 33.4 ± 10.3 years and 41.8 ± 8.9 years in LKT and DKT, respectively (Table 2). Among pediatric recipients, mean age was 12.3 ± 3.4 years and 14.0 ± 2.4 years for LKT and DKT, respectively. Fifty-six percent of all recipients were men. The cause of ESRD in 30% of adults and 50% of children was chronic glomerulonephritis. However, the cause of ESRD was unknown in a large percentage due to late presentation. Mean duration of dialysis pretransplant in adults was 2.5 years for LKT, 12.5 years for DKT, whereas it was 2.0 years for LKT, 5.5 years for DKT among pediatric recipients.

Survival and QOL Outcomes

The QOL measured by the EQ-5D-3L was significantly higher for all adult recipients at 1 year posttransplant compared with pretransplant (Table 3). Baseline pretransplant utility was 0.91. At 1 year posttransplant, utility was significantly higher at 0.99 ($P = 0.031$) for LKT and 1.0 ($P = 0.022$) for DKT.

Table 4 shows the number of LYs posttransplant. The average discounted LY for adult and pediatric LKT was 13.90 and 14.77, respectively (undiscounted LY, 18.26 and 19.80). In adult and pediatric DKT, the average discounted LY was 11.14 and 10.63, respectively (undiscounted, 13.76 and 12.99, respectively). Based on EQ-5D-3L index utility scores in adults, average discounted QALYs were 13.56 for LKT and 10.83 for DKT (undiscounted, 17.67 and 13.29, respectively).

Cost and Cost Utility

Average undiscounted costs for adult patients in the first year were US $24 452(RM83 735) for LKT and US $42 185 (RM144 475) for DKT including costs from pretransplant work-up, transplant operation, and costs to the end of the first year. Average annual costs declined to US $5247(RM17 970) and US $8427 (RM28 857), respectively, from second year onward (Table 5). In pediatric patients, average costs from first year were US $25 188 (RM86 258) and US $29 005 (RM99 328) for LKT and

TABLE 4.

Calculated QALYs and LY

	Adult LKT	Adult DKT	Pediatric LKT	Pediatric DKT
Undiscounted				
Life years	18.26	13.76	19.80	12.99
QALY (EQ-5D)	17.67	13.29	N/A	N/A
3% Discounted				
Life years	13.90	11.14	14.77	10.63
QALY (EQ-5D)	13.56	10.83	N/A	N/A

N/A, not applicable.

TABLE 5.

Estimated Average Annual Cost per Patient

Resource Category	Mean Annual Costs per Patient (% of Total)							
	Adult LKT First Year	Adult LKT Second Year Onward	Adult DKT First Year	Adult DKT Second Year Onward	Pediatric LKT First Year	Pediatric LKT Second Year Onward	Pediatric DKT First Year	Pediatric DKT Second Year Onward
Hospitalization								
US $ (%)	1208 (4.9)	70 (1.3)	2526 (6.0)	115 (1.4)	1280 (5.1)	139 (1.9)	1961 (6.8)	547 (4.5)
RM	4137	241	8652	393	4382	475	6715	1874
Outpatient								
US $ (%)	804 (3.3)	149 (2.8)	714 (1.7)	242 (2.9)	956 (3.8)	234 (3.2)	866 (3.0)	239 (1.9)
RM	2752	509	2446	829	3275	802	2966	818
Investigations and procedures								
US $ (%)	6155 (25.2)	724 (13.8)	9284 (22.0)	1195 (14.2)	7363 (29.2)	1379 (18.9)	9616 (33.2)	3357 (27.3)
RM	21 078	2480	31 793	4094	25 213	4721	32 931	11 496
Drugs[a]								
US $ (%)	10 319 (42.2)	3188 (60.9)	21 040 (49.9)	5863 (69.6)	9158 (36.4)	4429 (60.9)	9754 (33.6)	7291 (59.4)
RM	35 336	10 918	72 050	20 079	31 363	15 166	33 403	24 965
Others[b]								
US $ (%)	912 (1.1)	12 (0.2)	298 (0.7)	25 (0.3)	180 (0.7)	13 (0.2)	209 (0.7)	17 (0.1)
RM	912	42	1021	84	615	44	714	57
Overhead[c]								
US $ (%)	2578 (10.5)	1044 (21.0)	2208 (5.2)	986 (11.7)	2230 (8.8)	1085 (14.9)	1606 (5.5)	841 (6.8)
RM	8828	3780	7561	3378	7637	3717	5501	2882
Donor cost								
US $ (%)	3122 (12.8)		6119 (14.5)		4022 (16.0)		4993 (17.2)	
RM	10 692	N/A	20 953	N/A	13 772	N/A	17 099	N/A
Total cost								
US $	24 452	5247	42 189	8427	25 188	7278	29 005	12 291
RM	83 735	17 970	144 475	28 857	86 258	24 925	99 328	42 092

[a] Includes immunosuppressive agents, antiviral and antifungal prophylaxis, antihypertensive agents, and antibiotics.

[b] includes referral, transportation.

[c] includes land, buildings, utilities, maintenance, emoluments, eMOSS, and NTRC.

N/A, not appplicable.

DKT, respectively. Average annual costs declined in the second year onward to US $7278 (RM24 925) and US $12 291 (RM42 092), respectively. In both adult and pediatric patients, drugs accounted for the major component of costs. Average lifetime discounted costs from pretransplant workup to death were US $119 702(RM409 921) for adult LKT, US $147 152(RM503 922) for adult DKT, US $154 181 (RM530 252) for pediatric LKT and US $159 313(RM545 566) for pediatric DKT (Table 6).

As shown in Table 6, the cost per LY for adult LKT was US $8609(RM29 482) and US $13 209(RM45 234) for adult DKT. For pediatric recipients, the cost per LY was US $10 485(RM35 905) for LKT and US $14 985(RM51 317) for DKT. Cost-utility analysis in adult transplants using the EQ-5D-3L showed the cost per QALY for LKT was US $8826(RM30 224) compared with US $13 592(RM46 547) for DKT.

At zero discount rates, the cost per LY of adult LKT and DKT was US $8287 (RM28 380) and US $12 463 (RM42 680), respectively, as shown in Table 7. For pediatric recipients, the cost per LY of LKT and DKT was US $9955 (RM34 092) and US $13 706 (RM46 956), respectively, as seen in Table 8.

Univariate sensitivity analyses showed that cost per LY was most sensitive to variations in the annual follow-up costs

TABLE 6.

Costs, Outcomes, and Cost-Effectiveness

	Adult LKT	Adult DKT	Pediatric LKT	Pediatric DKT
Undiscounted costs and outcomes				
Total lifetime cost				
US $	151 336.88	171 517.83	197 119.03	178 102.17
RM	518 253.13	587 362.81	675 034.13	609 910.88
LYs	18.26	13.76	19.80	12.99
QALYs	17.67	13.29	N/A	N/A
Discounted costs and outcomes (3%)				
Total lifetime cost				
US $	119 702.30	147 152.10	154 840.78	159 312.54
RM	409 920.53	503 922.38	530 252.25	545 565.81
LYs	13.90	11.14	14.77	10.63
QALY	13.56	10.83	N/A	N/A
Cost-effectiveness				
Cost per LY				
US $	8609.11	13 208.85	10 484.60	14 985.33
RM	29 481.90	45 233.71	35 904.50	51 317.27
Cost-utility				
Cost per QALY				
US $	8825.85	13 592.28	N/A	N/A
RM	30 224.13	46 546.75		

N/A, not applicable.

TABLE 7.

Scenario Sensitivity Analysis of Adult Transplantation

Variable	Base Case Value	Sensitivity Value	Cost per LY, Adult LKT	Cost per LY, Adult DKT	Cost per QALY, Adult LKT	Cost per QALY, Adult DKT
Undiscounted cost and outcomes	3%	0%	US $8287 RM28 380	US $12 463 RM42 680	US $8564 RM29 326	US $12 909 RM44 209
Utility measure	EQ-5D index patient level values	VAS score patient level values	N/A	N/A	US $9615 RM32 926	US $15 486 RM53 031
Applying the overhead costs of a new Information Technology-based specialty hospital	US $798-843 RM2731-2886	US $2393-2528 RM8194-8657	US $8469 RM29 002	US $13 064 RM44 739	US $8682 RM29 732	US $13 443 RM46 037
NTRC costs per DKT donor	US $5442 RM18 635	US $2721 RM9317.67	US $8609 RM29 482	US $12 957 RM44 372	US $8826 RM30 224	US $13 333 RM45 660

N/A, not applicable.

with a functioning graft as shown in Figures 2A to D. These variations were +/-25% of the costs shown in Table 9 Cost per LY ranged from US $7573 (RM25 933) to US $9646 (RM33 031) for adult LKT, US $11 837 (RM45 234) to US $14 580 (RM49 930) for adult DKT, US $9104 (RM31 178)) to US $11 865 (RM40 631) for pediatric LKT, and US $12 428 (RM42 559) to US $17 543 (RM60 075) for pediatric DKT. Detailed data inputs and cost per LY values from univariate sensitivity analysis can be viewed in Table 9. Scenario sensitivity analyses by varying overhead costs of hospitals and the NTRC did not substantially diverge from the cost per LY from base case analysis as seen in Tables 7 and 8.

DISCUSSION

A review on the global role of kidney transplantation has highlighted that less-developed countries face problems such as inadequate infrastructure, insufficient trained workforce, and lack of a legal framework governing brain death.[22] These limitations may be further compounded by patient anxieties regarding successful transplant outcomes, physician bias, incentives favoring dialysis, and geographical remoteness.

In Malaysia, numerous initiatives to support kidney transplantation have been introduced over the last 15 years. These include the establishment of NTRC, tissue and organ procurement teams in major MOH hospitals, MOSS, and a National Transplant Coordinating Committee to coordinate and improve transplant-related activities and requirements. In 2007, the National Organ, Tissue and Cell Transplantation Policy was introduced to provide guiding principles for organ, tissue, and cell transplantation in Malaysia. A specific budget for transplant-related needs has been set aside by the MOH. The MOH collaborates with professional societies and nongovernmental organizations to promote transplantation. Local religious leaders have supported deceased organ donation with a decree issued by the National Fatwa Council in 1970. Despite all the aforementioned initiatives, there has been no evaluation of the transplant program to date.

This study was the first in Malaysia and Southeast Asia to explore the costs and outcomes of kidney transplantation. Our study has found that the average costs ranged from US $8609 (RM29 482) per LY for adult LKT to US $14 985 (RM51 317) per LY for pediatric DKT. Average cost per QALY was US $8825(RM30 224) for adult LKT and US $13 509 (RM46 546) for adult DKT. The cost per year of transplantation compares favorably with the annual cost of chronic hemodialysis of US $11 843(RM40 557) and US $11 137(RM38 138) as reported by Hooi et al[4] adjusted to 2009.[13] However, this is only a preliminary comparison as the study did not set out specifically to do a CE analysis of transplantation compared to dialysis. This study is planned for a later date.

The major component of cost was related to medications. There was a variation in treatment-related costs over different periods. Between 1991 and 1999, the majority of patients were prescribed cyclosporine, prednisolone and azathioprine. After the introduction of tacrolimus and mycophenolate mofetil in Malaysia in 2000, most new patients were on a combination of these two agents with prednisolone. However, the impact of the changing patterns in immunosuppressive regimens on costs and clinical outcomes was not studied separately. The second largest component of costs

TABLE 8.

Scenario Sensitivity Analysis of Pediatric Transplantation

Variable	Base Case Value	Sensitivity Value	Cost per LY, Pediatric LKT	Cost per LY, Pediatric DKT
Undiscounted cost and outcomes	3%	0%	US $9955 RM34 092	US $13 706 RM46 936
Applying the overhead costs of a new Information Technology-based specialty hospital	US $798-843 RM2731-2886	US $2393-2528 RM8194-8657	US $10 427 RM35 708	US $14 984 RM51 313
NTRC costs per DKT donor	US $4425 RM15 154	US $2213 RM7577	US $10 485 RM35 905	US $14 771 RM50 583

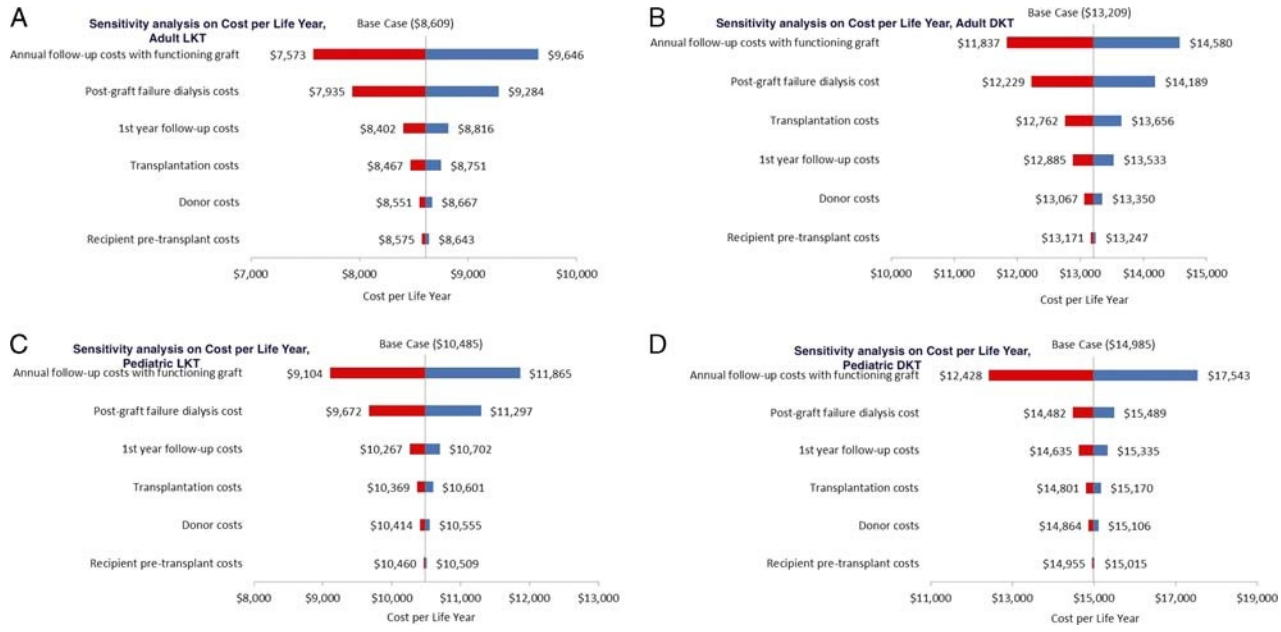

FIGURE 1.

was for investigations and procedures. These costs were greater for the pediatric group due to the need of general anesthesia for most procedures.

The third most important cost component is total overhead costs which includes costs of land, buildings, utilities, emolument, eMOSS, and NTRC. Because this cost is fixed irrespective of volume of transplant, CE can be improved by increasing the number of transplants.

In this study, the increased QOL of patients posttransplant was notable. There was a relatively high baseline utility value of 0.91 in the pretransplantation cohort which was partly explained by the exclusion of patients aged more than 60 years and those with major comorbidities from the DD transplant waiting list. Furthermore, it has been shown in other studies that Malaysian patients tend to report higher utility values than subjects from other countries.[2,12,23] This may be due to our Asian background where acceptance of life events is unusually high, there are cultural taboos in certain ethnic groups about reporting illness and hence, there is a tendency to overrate QOL despite having significant morbidity and complaints. Therefore, QOL assessment is difficult, and the impact of transplant in the Asian patient may appear attenuated. Nonetheless, despite the high baseline utility value in this study, utility values increased significantly to 0.99 and 1.00 at 1 year among adult LKT and DKT patients, respectively. This finding was similar to the data on QOL reported in MDTR 2012 where 90% of transplant patients recorded the maximum QOL score of 10 on the Spitzer's QOL index.[2] From our own unpublished data, patients report marked improvement in their QOL posttransplant despite only a 0.08 to 0.09 improvement in utility values.

Currently in Malaysia, cost data are not available from administrative databases. Hence, a major strength of this study was the microcosting approach relying on significant data collection through manual patient chart review and liaison with various administrative bodies for detailed case report form entry to determine resource use (Table 1). Economic valuation of resource use was based on market prices with adjustments for inflation and time preference. The study relied on the MDTR database, a long-term registry which formed the primary source for survival outcome. Our study was comprehensive by including broader program costs such as the national DD organ procurement and allocation systems, that is, NTRC and eMOSS. We also included lifetime costs from time of transplant to death.

Primary limitations of this study are those common to health economic analyses which include extrapolation over patients' lifetimes and necessity to combine various data sources.[24] We set out to conduct stratified random sampling to assess resource use of patients transplanted earlier than 2008 but disqualified 31% of the original sample because of incomplete data, leading to resampling. Hence, sampling bias may exist. Second, due to logistics for QOL evaluation in DKT, the pretransplant cohort (patients from DD transplant waiting list) was not the same as the posttransplant cohort.

Costs used were another limitation. Where public sector costing information was not available, shadow pricing from private centers was used. For calculation of costs over lifetime, dialysis costs were adjusted for inflation[13] from the previous economic evaluation of dialysis in Malaysia.[4] Although it would have been the ideal comparison, the lack of readily available and current dialysis cost data did not permit CE analysis of transplant versus dialysis within the same study. Furthermore cost per QALY cannot be compared because this was not measured in the previous economic evaluation of dialysis.

Another obvious limitation is lack of generalizability to other countries due to differences in study methodology, patient populations, clinical practices and economic settings. However, it is still useful to examine trends for costs between countries. Our study results were similar to other studies showing highest costs of transplant in the first year with a steep decline from second year onward (Table 10). In our study, cost reductions in the second year ranged from 58% to 80%.

TABLE 9.

Cost inputs, Lifetime Costs and Cost per LY, 3% Discount Rate

	Input Value			Total Lifetime Cost			Cost per LY		
Cost Category	Base Case	Low Sensitivity	High Sensitivity	Base Case	High Estimate	Low Estimate	Base Case	High Estimate	Low Estimate
Adult DKT									
Donor costs	21 582	16 186	26 977	503 922	498 527	509 318	45 234	44 749	45 718
Recipient pretransplant costs	5816	4362	7270	503 922	502 468	505 376	45 234	45 103	45 364
Transplantation costs	68 244	51 183	85 305	503 922	486 861	520 983	45 234	43 702	46 765
First year follow-up costs	49 462	37 096	61 827	503 922	491 557	516 288	45 234	44 124	46 344
Annual follow-up costs with functioning graft	26 186	19 639	32 732	503 922	451 599	556 246	45 234	40 537	49 930
Postgraft failure dialysis cost	149 526	112 144	186 907	503 922	466 541	541 304	45 234	41 878	48 589
Adult LKT									
Donor costs	11 013	8260	13 766	409 921	407 167	412 674	29 482	29 284	29 680
Recipient pretransplant costs	6506	4879	8132	409 921	408 294	411 547	29 482	29 365	29 599
Transplantation costs	27 049	20 287	33 812	409 921	403 158	416 683	29 482	28 996	29 968
First year follow-up costs	39 488	29 616	49 360	409 921	400 049	419 792	29 482	28 772	30 192
Annual follow-up costs with functioning graft	15 698	11 773	19 622	409 921	360 570	459 271	29 482	25 933	33 031
Postgraft failure dialysis cost	128 462	96 346	160 577	409 921	377 805	442 036	29 482	27 172	31 792
Pediatric DKT									
Donor costs	17 612	13 209	22 015	545 566	541 163	549 969	51 317	50 903	51 731
Recipient pretransplant costs	4376	3282	5470	545 566	544 472	546 660	51 317	51 214	51 420
Transplantation costs	26 897	20 173	33 622	545 566	538 841	552 290	51 317	50 685	51 950
First year follow-up costs	50 956	38 217	63 695	545 566	532 827	558 305	51 317	50 119	52 516
Annual follow-up costs with functioning graft	38 694	29 020	48 367	545 566	452 457	638 675	51 317	42 559	60 075
Postgraft failure dialysis cost	73 288	54 966	91 610	545 566	527 244	563 888	51 317	49 594	53 041
Pediatric LKT									
Donor costs	14 185	10 639	17 732	530 252	526 706	533 799	35 905	35 664	36 145
Recipient pretransplant costs	4993	3745	6241	530 252	529 004	531 501	35 905	35 820	35 989
Transplantation costs	23 468	17 601	29 335	530 252	524 385	536 119	35 905	35 507	36 302
First year follow-up costs	44 025	33 019	55 031	530 252	519 246	541 259	35 905	35 159	36 650
Annual follow-up costs with functioning graft	22 051	16 538	27 564	530 252	460 447	600 058	35 905	31 178	40 631
Postgraft failure dialysis cost	164 360	123 270	205 450	530 252	489 162	571 342	35 905	33 122	38 687

This study has demonstrated favorable costs and improved QOL with kidney transplantation and hence justifies all the initiatives to promote transplantation. However, cultural and religious barriers still remain. In addition, health care professionals themselves may represent another significant barrier to organ donation. A recent local study conducted in 2 tertiary hospitals has identified several shortcomings including misunderstanding of the concept of brain stem death, general passivity, and lack of knowledge to initiate the process of organ donation among health care professionals.[29]

Slow growth in LKT may be due to increased availability of dialysis treatment options in Malaysia. This has reduced the perceived need for relatives to donate kidneys. As opposed to dialysis which is now provided mainly by the private sector[2], there are no financial incentives for health care professionals to promote kidney transplantation. To increase the living donor pool, Malaysia embarked on ABO-incompatible kidney transplantation in 2011. Increasing preemptive transplants would also improve CE of living donor transplantation because of improved transplant outcomes.[30] However, this is often not feasible due to delayed referral of patients to nephrologists. Therefore, it is clear that much more effort is required to educate both the public as well as health care professionals regarding chronic kidney disease and transplant options.

Finally, this study will provide an information base for further research into the health economics of RRT in Malaysia.

CONCLUSIONS

Kidney transplantation in Malaysia is cost-favorable and results in better QOL for ESRD patients. This study has provided evidence for local health authorities to continue to support the existing national kidney transplant program. Our study also forms the basis for further research to establish the CE of kidney transplantation against alternative forms of RRT.

ACKNOWLEDGMENTS

This study would not have been possible without the support and collaboration of many individuals and professional bodies. The authors would in particular like to

TABLE 10.

Interstudy Comparison of Costs in Adult Kidney Transplantation

Country, Author, Year of Publication	Perspective and Discount Rate	First Year Cost, US $	Second year cost, US $	Cost/LY, US $	Cost/QALY, US $
Malaysia	Health care provider; 3% on costs and outcomes	LKT: RM83 735[a] (US $24 452)	LKT: RM17 970[a] (US $5427)	LKT: RM29 482 (US $8609)	LKT: RM30 224 (US $8826)
Bavanandan et al (current study)		DKT: RM144 475[a] (US $42 189)	DKT: RM28 857[a] (US $8427)	DKT: RM45 234 (US $13 209)	DKT: RM46 547 (US $13 592)
Greece	Health care provider; 5% on costs and outcomes	LKT and DKT: €31 714 (US $44 143)	N/A	N/A	First year transplant: €45 523 (US $63 363)
Kontodimopoulos and Niakas, 2008[25]					
Australia	Health care provider; 5% on costs and outcomes	LKT: AU $70 553 (US $55 624)	LKT: AU $10 749 (US $8475)		
Howard et al, 2009[26]		DKT: AU $65 375 (US $52 542)	DKT: AU $10 749 (US $8475)		
USA	Insurance, Medicare and patient; 5% on costs	US $87 400	US $13 749		
Yen et al, 2005[27]					
Japan		LKT and DKT: ~US $50 000	LKT and DKT: ~US $19 000		
Nakajima et al, 2001[28]					
Canada	Societal; Undiscounted	LKT and DKT: CAN $66 290[a] (US $48 397)	LKT and DKT: CAN $27 875[a] (US $20 351)		First year transplant: CAN $102 000[a] (US $74 469)
Laupacis, 1996[7]					Second year transplant: CAN $44 000[a] (US $32 133)

[a] Undiscounted costs.

N/A, not applicable.

thank: all nephrologists and allied healthcare professionals who helped in data collection, especially members of the Collaborative Kidney Transplant Economic Study Group: Hooi LS, Liu WJ (Hospital Sultanah Aminah Johor Bahru), Susan Pee (Hospital Sultan Ismail, Johor Baru), Ong LM, Rozina Ghazalli, Lynster Liaw, Liew YF (Hospital Pulau Pinang), Zawawi Nordin (Hospital Kuala Terengganu), Clare Tan, Laura Ngu (General Hospital Kuching), Sukeri Mohamad, Zuad Firdaus Rapiah (Hospital Raja Perempuan Zainab II), Ching CH (Hospital Sultanah Bahiyah Alor Setar), Thong KM, Lim YN, Masaamah Masood (Hospital Kuala Lumpur), Lee ML (Hospital Tuanku Jaafar), Chitra Ramasamy (Hospital Selayang), The National Transplant Resource Centre, Malaysia, The Malaysian Dialysis and Transplant Registry, S. Manjulaa Devi and Nurul Hizwani Azahar, MOH renal pharmacists, Yee Siau Lin of Azmi Burhani Consulting for assistance with statistical analysis, The National Clinical Research Centre, Malaysia, The Malaysian Society of Nephrology, Post Graduate Renal Society Malaysia and National Institutes of Health for financial support, The EuroQol Group for permission to use the EQ-5D-3L instrument, Sarah White and Steve Chadban, University of Sydney, Australia for reviewing the manuscript and valuable comments. Finally, the authors thank the Director-General of Health in Malaysia for permission to publish this paper.

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