CHAPTER 17

CENTRE EFFECT IN RENAL TRANSPLANTATION IN AUSTRALIA 1993 - 1998

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Background

Centre-specific outcomes are reported regularly by ANZDATA to enable individual renal transplant centres to compare their own outcome with those of other centres and with the Australian average. Since its inception, this mode of reporting has identified discrepancies in outcome amongst the various centres. It is unclear however, whether these discrepancies represent differences in patient characteristics between centres or reflect differences in quality of care.

Twenty-one Australian transplant centres performed a total of 2,304 primary renal transplants between January 1st, 1993 and September 30th, 1998. Sixteen of these centres are primarily adult renal transplant centres, and five primarily paediatric renal transplant centres. The five paediatric transplant centres were excluded from the analysis.

Recipients under 18 years of age and transplanted in a primarily adult renal transplant centre were also excluded. Of the remaining 2,187 patients, 201 (9%) were subsequently excluded from the analysis because of missing data relating to recipient or donor characteristics. The number of transplants performed by each centre during this period ranged from 24 to 403.

The primary outcome examined was 12-month graft survival, defined as time elapsing between transplantation and patient death with a functioning graft, or graft failure. Graft failure was defined as the need for permanent dialysis or re-transplantation. Patients who were alive with a functioning graft were censored at the date of last follow-up or at twelve months if their follow-up was greater than twelve months.

Figure 17.1

12-Month Graft Survival by Recipient Factors

		Number	Survival [95% Confidence Interval]		Log Rank Test
Age	18.0 to 59.9 years	1,627	91.7%	[90.3%, 93.0%]	p=0.0116
	≥ 60.0 years	359	87.5%	[83.6%, 90.5%]	
Gender	Male	1,177	91.7%	[90.0%, 93.2%]	p=0.1366
	Female	809	89.8%	[87.5%, 91.7%]	
Race	Aboriginal/Torres Strait Isl.	73	88.4%	[78.1%, 94.0%]	p=0.3901
	Other	1,913	91.0%	[90.0%, 92.2%]	
Primary Renal Disease	Glomerulonephritis	977	92.5%	[90.6%, 94.0%]	p=0.1263
	Reflux Nephropathy	234	91.1%	[86.9%, 94.1%]	
	Polycystic Kidney Disease	249	90.0%	[85.4%, 93.3%]	
	Diabetic Nephropathy	191	87.7%	[82.1%, 91.7%]	
	Other	335	88.8%	[84.9%, 91.8%]	
Time on Dialysis	< 1.0 years	692	93.3%	[91.2%, 95.0%]	p=0.0004
	1.0 to 2.9 years	845	91.2%	[89.1%, 93.0%]	
	≥ 3 years	449	86.6%	[83.1%, 89.5%]	
Peak Panel Reactive Antibodies	0%	630	93.8%	[91.6%, 95.5%]	p=0.0072
	1 - 10%	623	90.2%	[87.6%, 92.3%]	
	> 10%	733	89.1%	[86.5%, 91.1%]	
Diabetes Mellitus *	Yes	243	91.3%	[89.8%, 92.5%]	p=0.1908
	No	1,743	88.7%	[83.9%, 92.1%]	
Vascular Disease #	Yes	194	83.8%	[77.8%, 88.3%)	p=0.0002
	No	1,792	91.7%	[90.3%, 92.9%]	

* Type 1 or Type 2, at the time of commencement of renal replacement therapy.

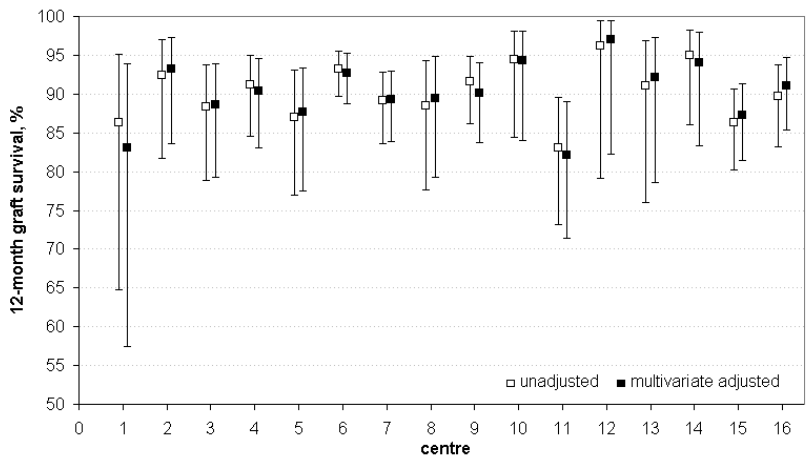
Ischaemic Heart Disease, Cerebrovascular Disease or Peripheral Vascular Disease at the time of commencement of renal replacement therapy.

Figure 17.2

12-Month Graft Survival by Donor and Other Factors

		Number	Survival [95% Confidence Interval]		Log Rank Test
Age	< 18.0 years	193	90.1%	[84.9%, 93.6%]	p=0.0010
	18.0 to 49.9 years	1,220	92.8%	[91.2%, 94.1%]	
	≥ 50 years	573	87.3%	[84.2%, 89.8%]	
Gender	Male	1,089	91.4%	[89.6%, 93.0%]	p=0.4105
	Female	897	94.8%	[92.5%, 96.5%]	
Organ Source	Cadaveric	1,493	89.7%	[88.0%, 91.1%]	p=0.0009
	Living Donor	493	94.8%	[92.5%, 96.5%]	
Cause of Donor Death	Living Donor (no death)	493	94.8%	[92.5%, 96.5%]	p=0.0002
	Brain Damage	869	87.7%	[85.0%, 89.9%]	
	Accident	563	92.4%	[89.9%, 94.4%]	
	Other	65	89.0%	[84.2%, 92.5%]	
Cold Ischaemia Time	≤ 10 hours	693	93.3%	[91.1%, 94.9%]	p=0.0266
	11 - 20 hours	844	90.0%	[88.0%, 91.7%]	
	> 20 hours	449	88.5%	[83.8%, 91.9%]	
HLA Mismatches	0	105	95.2%	[88.9%, 98.0%]	p=0.0007
	1	213	94.8%	[90.8%, 97.1%]	
	2	484	93.4%	[90.8%, 95.3%]	
	3	572	90.9%	[88.2%, 93.0%]	
	4	342	87.9%	[83.9%, 90.9%]	
	5	192	86.3%	[80.6%, 90.5%]	
	6	77	84.2%	[73.8%, 90.7%]	
Year of Transplant	1993	280	87.1%	[82.6%, 90.6%]	p=0.0401
	1994	310	92.9%	[89.4%, 95.3%]	
	1995	325	89.2%	[85.3%, 92.1%]	
	1996	369	90.8%	[87.3%, 93.3%]	
	1997	413	91.3%	[88.1%, 93.6%]	
	1998	289	95.1%	[91.8%, 97.1%]	

Figure 17.3 Centre-specific 12-month Graft Survival



Recipient and Donor Factors Influencing Outcome

Factors found to be predictive of reduced 12-month graft survival on univariable analysis were older recipient age, presence of vascular disease in the recipient at the time of commencement of renal replacement therapy, higher peak panel reactive antibody levels, longer time on dialysis prior to transplantation, older donor age, cadaveric donor source, brain damage as the cause of donor death, greater number of HLA mismatch, longer cold ischaemia time and earlier year of transplantation (fig 17.1 and 17.2). On multivariable analysis, longer time on dialysis prior to transplantation (HR: 1.77 (95% CI: 1.18, 2.65) for ≥3 years compared to <1 year), presence of vascular disease in the recipient at the time of commencement of renal replacement therapy (HR = 1.71 (95% CI: 1.21, 2.43) compared to no vascular disease), older donor age category (HR = 1.93 (95% CI: 1.40, 2.64) for ≥50.0 years compared to <18 years), cadaveric organ source (HR = 1.58 (95% CI: 1.01, 2.48) compared to living donor), greater number of HLA mismatches (HR = 1.24 (95% CI: 1.11, 1.38) for every HLA mismatch) and earlier year of transplantation (HR = 1.14 (95% CI: 1.04, 1.25) for every year) were independent predictors of 12-month graft survival.

Of the factors that were predictive of reduced 12-month graft survival on multivariable analysis, time on dialysis prior to transplantation, donor age, organ source and number of HLA mismatches were significantly different between centres. For time on dialysis prior to transplantation, the percentage of patients on dialysis ≥3 years overall was 22.6% and ranged from 11.8% to 56.7% between centres (p=0.000 for difference). The percentage of donors ≥50 years overall was 28.9% and ranged from 20.1% to 42.1% between centres (p=0.001 for difference). The percentage of

cadaveric donors transplanted overall was 75.2% and between centres ranged from 50.0% to 96.7% (p=0.000 for difference). For number of HLA mismatches the percentage of patients with four to six mismatches overall was 30.8% and ranged from 12.5% to 42.8% between centres (p=0.000 for difference). No significant difference was seen for presence of vascular disease in the recipient at the time of commencement of renal replacement therapy (p=0.196) or year of transplantation (p=0.427) between centres.

Centre Comparisons

The average 12-month graft survival for all centres was 91.7% (95% CI: 89.8%, 93.3%). Observed 12-month graft survival amongst individual transplant centres ranged from 83.1% to 96.4%. Outcomes in two centres were significantly worse than that of the average for all centres. In these centres, the 12-month graft survival was 83.1% [95% CI: 73.1%, 89.6%, p=0.013] and 86.3% [95% CI: 80.3%, 90.6%, p=0.036]. The estimated 12-month graft survival from the multivariable Cox regression model ranged from 82.1% [95% CI: 71.4%, 89.0%] to 97.0% [95% CI: 82.2%, 99.5%]. One centre was significantly worse than that of the average for all centres with a 12-month graft survival of 82.1% [95% CI: 71.4%, 89.0%, p=0.007]. A comparison of the unadjusted and multivariable adjusted 12-month graft survival is given in Figure 17.3.

When sampling variability between centres is accounted for using the hierarchical multivariable Cox regression model, estimated 12-month graft survival ranged from 89.2% [95% CI: 83.0%, 91.8%] to 92.2% [95% CI: 90.3%, 94.5%]. No centre was significantly worse or better than the average for all centres. A comparison of the multivariable adjusted 12-month graft survival which does not (fixed effects model) and does (random effects model) take into account sampling variability that can occur due to the small number of transplants that are performed by some centres is given in Figure 17.4.

Figure 17.4 Effect of Sampling Variability

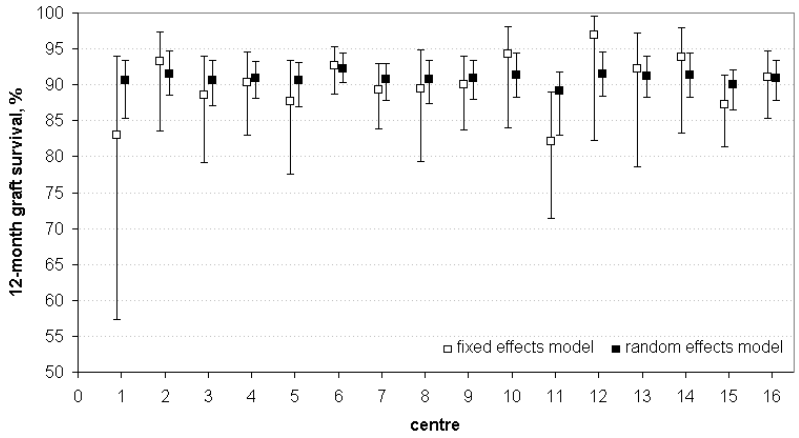


Figure 17.5 Effect of Transplantation Volume

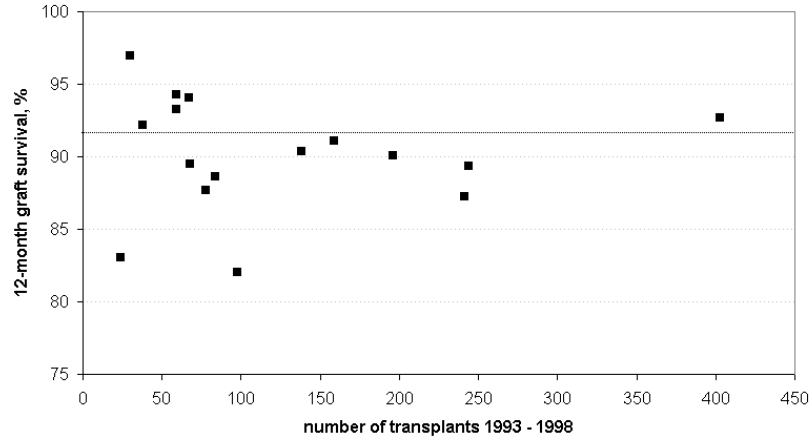


Figure 17.6 Date Ascertainment by Centre Volume

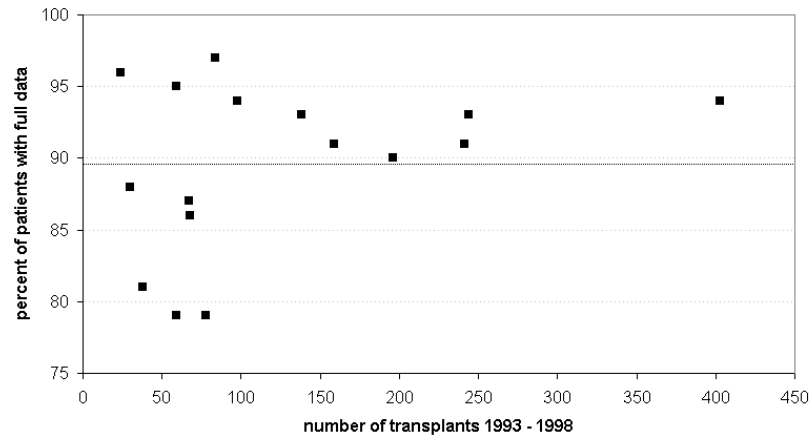
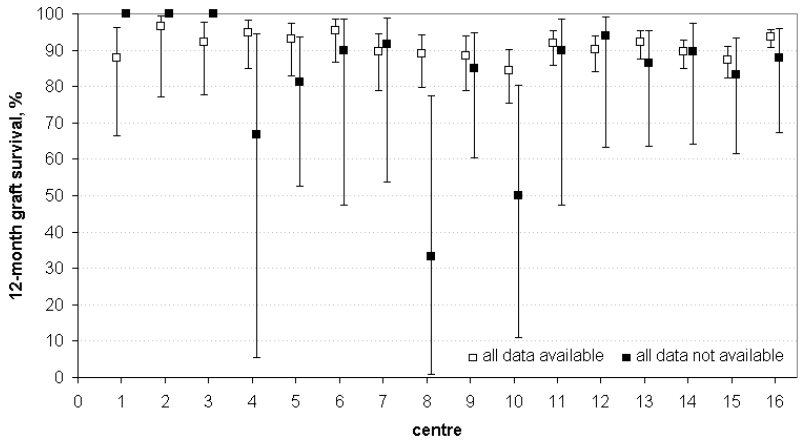


Figure 17.7 Effect of Patient Exclusion Due to Inad equate Data Ascertainment



Drawing conclusions about smaller centres can be problematic due to the imprecise estimates of their performance. Large differences may be seen between observed and expected outcomes in smaller centres as a result of sampling variability rather than any true difference in performance between centres. The hierarchical model employed in this analysis accounts for such variation between centres. This methodology tends to draw the relatively imprecise estimates of smaller volume centres towards the average outcome while exerting less effect on the relatively more precise estimates from larger centres.

Number of transplants performed by a centre was not found to be predictive of 12-month graft survival either before or after adjusting for relevant confounders (unadjusted - HR = 0.99 (95% CI: 0.84, 1.15), p=0.86; multivariate adjusted - HR = 0.98 (95% CI: 0.84, 1.14), p=0.80) (fig 17.5).

Ascertainment Bias

On average 9% of patients had missing data on relevant risk factors required for the multivariable analysis, but this ranged from 4% to 21% for individual centres. There was a tendency for small centres (<100 transplants) to have more patients with missing data compared to medium size centres (100-200 transplants) and large centres (>200 transplants). Small centres had on average 13% of patients with missing data, while medium centres had 7% and large centres 8%. The difference however was not statistically significant (fig 17.6).

For the 201 patients who were excluded from the analysis due to incomplete information for the multivariable analysis, the average unadjusted 12-month graft survival was 86.0% (95%CI: 80.3%, 90.1%), and ranged from 33.3% to 100% amongst individual transplant centres. This was significantly less than the unadjusted average 12-month graft survival for all patients included in the analysis, which was 90.9% (95% CI: 89.6%, 92.1%; p value =0.02 for log rank test). For the effect of missing data on estimates of 12-month survival within each centre (fig 17.7).

The presence of missing data, and therefore the exclusion of these patients from the analysis, is potentially an important source of bias, particularly for the interpretation of outcome for the smaller centres. Although only 9% of patients were excluded from the analysis, the unadjusted 12-month graft survival for this group was significantly less than for those with complete information relating to recipient and donor factors. Such a bias would result in a more favourable outcome than was truly the case in centres with greater numbers of patients with missing data.

Conclusion

This study has shown that for patients transplanted between 1993 and 1998, 12-month graft survival amongst Australian renal transplant centres were not different from the average outcome for all centres, after accounting for key outcome predictors known prior to transplantation and random variability between centres. In addition the number of transplants performed by a centre was not predictive of 12-month graft survival. An important limitation of this conclusion is that the impact of missing data can result in significant bias and limit the validity of a multivariable analysis.