Incidence, Risk Factors and Outcomes of Stroke in Scotland's Renal Transplant Recipients

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Background

- Chronic kidney disease is an established risk factor for cerebrovascular disease
- Stroke rate rises as GFR falls - peaking at end-stage renal disease (ESRD) and case fatality rates reported following stroke in dialysis patients are dismal
- The risk of stroke is reduced following renal transplantation , however the effect on survival is poorly studied
- Using national datasets, we merged data from the Scottish Renal Registry (SRR) and the Scottish Stroke Care Audit (SSCA) to determine incidence, risk factors and outcomes following stroke in renal transplant recipients.

Aims

- Describe the stroke incidence rate of renal transplant recipients (RTR)
- Determine risk factors associated with stroke
- Compare stroke care pathways of RTR against the general population (GP)

Method

- Permission was sought via the NHS National Services Scotland Privacy Advisory Committee to allow access to national datasets
- The SRR was interrogated between 01 January 2005 to 31 Dec 2013 to identify all records of RTRs and merged with data held in the SSCA. To ensure complete capture of stroke diagnoses the Scottish discharge (SMR01) and death records (NRS) were included (figure 1).
- RTRs were defined as those with a renal transplant at study inception, or undergoing transplantation during follow-up. Stroke was defined as first stroke during follow-up or where stroke was listed as the primary cause of death.
- Incidence rate was calculated as number of stroke events divided by the summed person-years of observation.
- Demographics were compared and Cox proportional hazard analyses performed to assess factors influencing time to stroke.
- Finally, we employed propensity score matching (PSM) to compare the circumstances and outcome following stroke in RTR to the GP at a ratio of 5:1
- Analyses were performed using SAS 9.4 and the R package 'MatchIt' for PSM

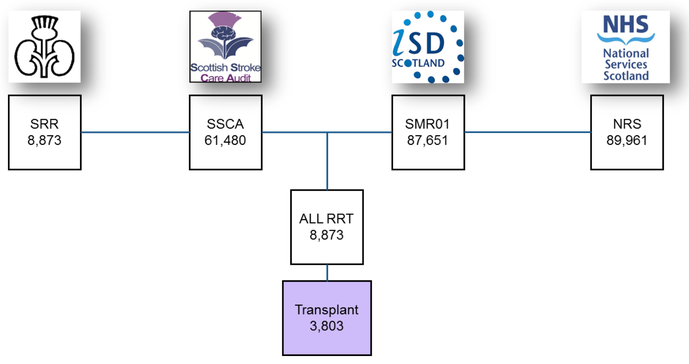

Figure 1 *Data sources accessed to identify all transplant recipients, stroke cases and death following stroke (not identified prior to death) in Scotland 2005-2013*

Results

- 3,803 RTR were identified, mean age 39 (IQR 23.4)years, 40.6% were female.
- Cumulative follow-up was 19,234 years.

Variable	No Stroke	Stroke	p-value
	3719	*84*	
Median age, years [IQR]	39.4 [23.4]	47.6 [18.1]	*<0.0001*
Female – n [%]	1509 [40.6]	33 [39.3]	*0.911*
Primary Renal Diagnosis – n [%]			
Glomerulonephritis	970 [26.1]	20 [23.8]	*0.707*
Interstitial	1450 [39.0]	32 [38.1]	*0.910*
Multisystem	441 [11.9]	10 [11.9]	*1.000*
Diabetes	389 [10.5]	12 [14.3]	*0.278*
Years of RRT prior to Transplant, median [IQR]	5.2 [9.3]	11.5 [9.1]	*<0.0001*
Past Medical History – n [%]			
Atrial Fibrillation	109 [2.9]	6 [7.1]	0.042
Ischaemic Heart Disease	677 [18.2]	26 [31.0]	0.007
Stroke	64 [1.7]	10 [11.9]	<0.0001
Diabetes	757 [20.4]	26 [31.0]	0.029
Hypercholesterolemia	367 [9.9]	7 [8.3]	0.853
Hypertension	2628 [70.7]	62 [73.8]	0.715
Lab Values – median [IQR]			
Haemoglobin, g/dL	12.37 [1.5]	12.4 [1.6]	0.842
Serum Albumin, g/L	39.4 [4.5]	38.8 [3.7]	0.251
Serum Phosphate, mmol/L	1.21 [0.4]	1.06 [0.3]	0.002

Table 1 *Demographics of transplant recipients, stroke v no stoke*

- Stroke episode were identified in 84 patients (2.2%) and incidence rate was 4.37 events/1000 patient-years (background Scottish population rate for same time period 2.4/1000 patient years)
- Demographics between those with and without stroke are compared in table 1
- Older age, longer RRT exposure, atrial fibrillation, ischaemic heart disease, prior stroke, diabetes and lower serum phosphate are more common in those with stroke, p<0.05
- Multivariable regression analyses adjusting for conventional stroke risk factors demonstrated significance for advancing age, prior stroke and low haemoglobin, table 2

Variable	HR	95% CI	p-value
Age – per year	1.04	1.02-1.06	<0.0001
Female Sex	1.07	0.66-1.75	0.7773
Past Medical History			
Atrial Fibrillation	1.32	0.52-3.37	0.5575
Stroke	4.84	2.27-10.29	<0.0001
Diabetes	1.06	0.63-1.80	0.8205
Ischaemic Heart Disease	1.45	0.87-2.44	0.1555
Lab Values			
Haemoglobin, g/dL	0.80	0.66-0.95	0.0134
Serum Phosphate, mmol/L	0.62	0.23-1.63	0.3286

Table 2 *Multivariable regression of stroke predictors in RTR*

- There were significant difference between RTR who suffered stroke and the general population. Propensity score matching removed this variability, allowing examination of outcomes following stroke, table 3

Variable	General Population	Transplant Population	p-value	General Population	p-value
n	*61087*	*56*		*280*	
Median Age, years [IQR]	71 [18.0]	63 [16.0]	<0.0001	63 [16.0]	0.6677
Female Gender [%]	31365 [51.4]	21 [37.5]	0.044	98 [35.0]	0.7603
Rural Residence [%]	10015 [16.4]	6 [10.7]	0.3642	26 [9.3]	0.8026
Socio-economical Deprivation [%]	29709 [48.6]	30 [53.6]	0.5048	162 [57.9]	0.558
Past Medical History [%]					
Atrial Fibrillation	5019 [8.2]	4 [7.1]	1.000	22 [7.9]	1.000
Stroke	3555 [5.8]	5 [8.9]	0.3877	27 [9.6]	1.000
Cardiovascular Disease	10225 [19.7]	15 [26.8]	0.2438	79 [28.2]	0.8721
Hypertension	25818 [42.3]	41 [73.2]	<0.0001	205 [73.2]	1.000
Diabetes	8536 [14.0]	20 [35.7]	<0.0001	109 [38.9]	0.7637

Table 3 *Comparison of GP to RTR before and after propensity score matching*

- There were no significant differences in admission length, case mix, stroke subtype and management between groups.
- Mortality is higher in RTR compared to matched non-ESRD patients; both at discharge (19.6 v 9.3%, p=0.03, figure 2) and at follow-up (66.1 vs 36.1%, p<0.0001)
- Stroke in RTR is independently associated with a higher risk of death on multivariable regression analysis (HR 4.8, 95% CI 3.4-6.9) adjusting for age, sex, duration of RRT, prior AF, stroke, ischaemic heart disease and diabetes

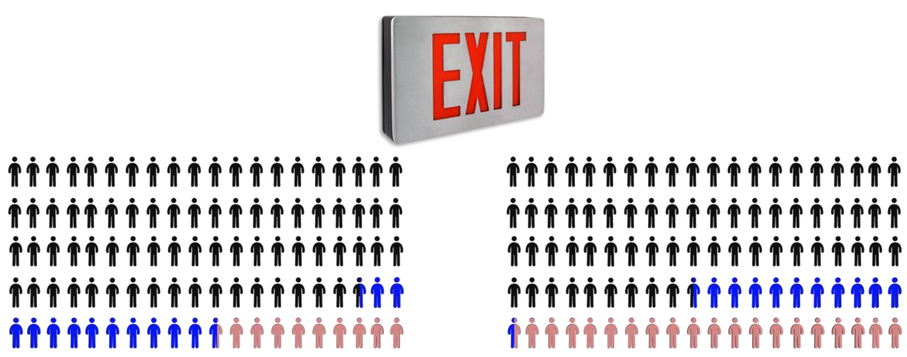

Figure 2 *Discharge destination following stroke in general population (left) and RTR (right). Black = usual residence, Blue= ongoing NHS care, Red = Death*

Discussion

- Stroke incidence in RTR is almost double the background rate in Scotland
- In RTR the rate of short and long term death following stroke is higher than their matched non-ESRD cohort
- Stroke in RTR associated with classical cardiovascular risk factors and a longer duration of renal replacement therapy

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