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Inferiority of arteriovenous grafts, in comparison to autogenous fistulas, is underestimated by standard survival measures alone

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Title

The inferiority of arteriovenous grafts, in comparison to autogenous fistulas, is underestimated by standard survival measures alone

Running Head

The superiority of autologous AVF

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Author Contribution

Stephen Thwaites: Conceptualization, data curation, formal analysis, methodology, project administration, writing – original draft, writing – review and editing

Stephen Holt: Writing – review and editing

Ming K Yui: Writing – review and editing

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ABSTRACT

Background

It has been argued that a prosthetic arteriovenous graft (AVG) is a reasonable alternative to an arteriovenous fistula (AVF) for dialysis. We aimed to compare the patency rates and requirements for intervention of newly formed AVF and AVG.

Methods

A retrospective analysis was undertaken of AVF and AVG formed between January 1, 2013 and December 31, 2015 at two tertiary referral centres and followed up until December 31, 2017.

Outcome measures included successful use for dialysis, patency rates and the number of interventions required to maintain dialysis access per patient year.

Results

Four hundred and seventy AVF and 92 AVG were constructed. Of 470 AVF, 324 (68.9%) were used compared to 80/92 (87%) AVG were used. One year assisted primary patency of AVF was 75% (CI 71%-79%) compared to 47% (CI 36%-57%) for AVG. Secondary patency rates for AVF at one, two and three years were 77% 71% and 69%, respectively. At the same time points, secondary patency rates for AVG were 77%, 60% and 46%, respectively (log rank $P = 0.034$). AVG required 2.4 times the number of interventions per patient-year (PPY) than AVF. Surgical thrombectomy of AVG was at a rate of 0.49 PPY compared with 0.042 PPY for AVF.

Conclusion

AVG have a substantially higher rate of thrombosis than AVF, evident from early in the life of the graft.

AVF demonstrate superior patency rates to AVG throughout the life of the access, with far fewer interventions per patient year than grafts.

KEYWORDS

Arteriovenous fistula, arteriovenous graft, patency, intervention rates

INTRODUCTION

The National Kidney Foundation Kidney Disease Outcomes Quality Initiative (KDOQI), the United States' National Vascular Improvement initiative, Fistula First, and the KHA-CARI Guidelines in Australia recommend dialysis by autogenous arteriovenous fistula (AVF) ¹⁻³. These guidelines have been promulgated in order to reduce the use of prosthetic arteriovenous grafts (AVG) and tunnelled central venous catheters, both of which are associated with increased risks of infection, hospitalisation, death and other complications ⁴⁻⁶.

Despite this, more than one in six prevalent haemodialysis patients in the United States use an AVG ⁷. While the prevalence of dialysis by AVG in Australia is less than 10% ⁸ there are marked variations in practice between institutions, with some exhibiting a significantly higher proportion of graft use than the national average.

The aim of this study was to evaluate differences in outcomes and rates of intervention between AVF and AVG in two large tertiary metropolitan hospitals.

METHODS

All patients undergoing surgery to form a new permanent haemodialysis access between January 1, 2013 and December 31, 2015 were retrospectively identified from the records of two teaching hospitals in a major Australian city. Approval was obtained from the respective institutional ethics committees; patient consent was not required.

A new access was defined as one where a new usable segment was formed, either with an autogenous vein (AVF) or a prosthetic graft (AVG). As such, operations to revise an anastomosis of an existing access were excluded from the study.

Accesses were preferentially placed in the most distal position possible, as assessed by a specialist surgeon. AVF formation was performed in the presence of a palpable pulse and an outflow vein >2.5 mm in diameter, as measured by pre-operative B-mode ultrasound, with a tourniquet. The vein was anastomosed to the artery in an end-to-side manner, using 6-0 or 7-0 polypropylene suture. Central vein imaging was not routinely performed prior to surgery. AVG were mostly early cannulation polyurethane grafts (Thoratec, Pleasanton, United States) and placed in the upper arm, with inflow via the brachial artery. The decision to form a fistula or insert a graft was at the discretion of the surgeon.

Primary patency was defined as the length of time from access formation to access failure or intervention to maintain patency. Rates of assisted primary patency (thrombosis-free access survival) and secondary patency (permanent access failure) were also measured. All patients were followed up for at least two years or until a censoring event. An access was censored if a patient died, underwent renal transplantation, was lost to follow up or reached the end of the study (December 31, 2017) with a patent access.

Patients had in-centre haemodialysis and home haemodialysis. Accesses were monitored clinically; intervention was performed on accesses at the discretion of the clinician for AVF that failed to mature or were identified as dysfunctional. Serial surveillance ultrasonography was not routinely performed on accesses in pre-dialysis patients or on functioning accesses that were being used for dialysis. The second stage of a brachiobasilic transposition was not included as an additional operation. Endovascular techniques included angioplasty and stenting. Thrombosed accesses underwent surgical thrombectomy.

Measured values are reported as percentages for categorical data and medians with interquartile range (IQR; 25th to 75th quartile) for continuous data. Intergroup differences were compared by the Chi-squared or Fisher's exact tests for categorical variables and the Wilcoxon test for continuous variables.

Primary, assisted primary and secondary patency rates were analysed by the Kaplan-Meier method with log-rank testing to compare patency between groups.

Statistical analysis was performed using Stata 14 (Stata Corp, Texas, USA). A value of $P < 0.05$ was considered statistically significant.

RESULTS

Four hundred and fifty-nine patients underwent a total of 562 operations at two institutions to form an AVF or AVG (Table 1). At the time of surgery, the prevalence of diabetes was approximately 48.8%; the difference between groups was not statistically significant ($P = 0.174$, Table 2).

Patients receiving prosthetic grafts were more likely to have required renal replacement therapy – in particular via permanent haemodialysis access (an AVF or AVG) - immediately prior to their new access than those in the AVF group. In contrast, those who had an AVF formed were more likely to have a tunnelled cuffed haemodialysis catheter immediately prior (43.8% vs 27.2%, Table 2).

Of 470 autogenous fistulas, 184 were radiocephalic, one was radiobasilic, 187 were brachiocephalic and 97 were brachiobasilic. Arteriovenous grafts were predominantly placed in the upper arm; seven were loop grafts in the forearm and six were thigh loop grafts.

There were institutional differences in access placement. Eighty-five of 92 AVG were inserted in one hospital and seven at the other. In those institutions, the two-year secondary patency of autogenous AVF was 64.9% (57.3%-71.5%) and 75.4% (CI 69.5%-80.4%), respectively, (log rank $P = 0.032$, data not shown). The increased use of AVG at one hospital was based on a local preference to avoid central venous catheter insertion, especially after an unsalvageable thrombosis of an existing fistula or graft.

Within the recruitment period (Jan 1, 2013 - Dec 31, 2015) 104 patients had a second access; 34 of these were grafts. The number of operations to form a new access in each patient during the recruitment period ranged from 1 to 5.

At the time of access formation, a greater proportion of patients who received AVG than AVF lived more than 100km from their parent hospital (35.9% vs 19%, $P < 0.001$, Table 2). Categorised by access type however, distance from hospital did not affect AVF survival (log rank $P = 0.809$) or AVG survival (log rank $P = 0.731$, data not shown).

Median time of follow-up was 709.5 days (IQR 204.3-1157.8 days) for AVF and 455.5 days (IQR 159-892 days) for AVG ($p = .01$). During the period of observation (January 1, 2013 to December 31, 2017), 107/400 patients (26.8%) who had an AVF and 27/59 (45.8%) of patients who had an AVG died (Table 1). Twenty patients had not commenced, or returned to, dialysis after their access surgery. Twenty-two patients were lost to follow up.

Of 470 AVF created, 324 (68.9%) were used; primary failure occurred in 88 (18.7%). Fifty-six AVF (11.9%) were functional at the time of censoring of data, but had not been used. Reasons included death before commencement of dialysis via the AVF ($n=19$), transplantation ($n=12$), loss to follow-up ($n=7$), reaching the end of the observation period without commencing haemodialysis ($n=17$) and, in one patient, refusal to use the access created.

Eighty of 92 (87%) AVG were used; primary failure occurred in nine (11%). One patient died with a patent AVG that had not been used, one patient received a transplant before the AVG was used and one patient elected to continue on haemodialysis via central line until the AVG thrombosed permanently. Median time from formation to use was 111 days for AVF (IQR 64.5-228 days), and 1 day for AVG (IQR 1-2 days, $P < .001$).

Primary patency rates of AVF and AVG diverged early (Fig. 1). One year assisted primary patency of AVG was 47% (CI 36%-57%) compared to 75% (CI 71%-79%) for AVF. Due to salvage thrombectomy, secondary patency for AVG and AVF was similar for the first 18 months; thereafter permanent AVG failure rates accelerated and the survival curves diverged (Fig. 2). Secondary patency rates for AVF at one, two and three years were 77% 71% and 69%, respectively. At the same time points, secondary patency rates for AVG were 77%, 60% and 46%, respectively (log rank $P = 0.034$, Fig. 3).

When seven lower limb accesses were excluded from analysis, the primary patency rates of 185 forearm AVF and 284 upper arm AVF were found to be similar (log rank $P = 0.087$); both were superior to that of 86 upper limb AVG. Freedom from thrombosis was again significantly worse in upper limb AVG, while the secondary patency rate of upper limb AVG was inferior to that of forearm AVF but not statistically different to that of upper arm AVF (Fig. S1-S3 and Tables S1-S3).

To determine if permanent haemodialysis access immediately prior to AVG insertion affected patency, the AVG cohort was analysed separately. For those who had an AVF or AVG immediately prior ($n=49$) compared to those who didn't ($n=43$), primary patency of AVG at six months (49.4% and 43.2%, respectively) and twelve months (34.7% vs 31.2%, respectively) was not statistically different (log rank $P = 0.363$, data not shown).

In all, 470 AVF were followed for a total of 330821 days until loss of secondary patency or the censoring of data (including the end of the follow-up period). Ninety-two AVG were followed for a total of 50053 days.

Of the 92 AVG that were inserted, 55 (59.8%) received surgical and/or endovascular intervention, while 177/470 AVF (37.7%) required intervention (Table 3). The number of interventions per access ranged from 1-7 for AVG and 1-10 for AVF (data not shown).

For dysfunctional accesses, AVG required 2.4 times the number of interventions per patient per year than AVF (Table 3). This was largely due to the frequency of operations to maintain or re-establish patency, to preserve limb function or to preserve life (0.686 per patient-year (PPY) versus 0.147 per patient-year). In patients with AVG, these operations were most typically performed for access thrombosis (67 thrombectomies were performed in 40 patients) and infection (n=9). In contrast, 38 thrombectomies were performed on 470 AVF, a rate of 0.042 PPY compared to 0.49 PPY for AVG. Other indications for surgery on AVF included stenosis (n=77), hand ischaemia (n=7) and ligation for irremediable central vein stenosis (n=2, Table S4).

DISCUSSION

This study examined the outcomes of 459 patients having permanent haemodialysis access formed over a three year period, then followed for up to five years.

Autogenous AVF had a primary failure rate of 18.6%, and a secondary patency rate of 71% at two years. These compare favourably to results in a meta-analysis of AVF by Al-Jaishi et al. in which a 23% primary failure rate and a 2-year secondary patency rate of 64% was reported ⁹.

In our cohort, AVG had a 13% primary failure rate, which is similar to the reported literature ¹⁰, but a secondary patency rate similar to AVF at 18 months. The divergence in secondary patency rates between AVF and AVG witnessed between 12 and 24 months is reflected in others' experiences ^{11,12}.

Arteriovenous grafts have long been discussed as a reasonable alternative to an autogenous fistula. In certain circumstances, it has been argued that an AVG is at least equivalent, if not preferable, to an autogenous AVF ^{13,14}. While prosthetic grafts allow earlier cannulation than AVF, reduce the duration of CVC use ^{2,15} and have a lower primary failure rate than AVF, they are associated with a higher incidence of bacteraemia, access thrombosis and poorer survival compared to AVF ¹⁶⁻¹⁸.

The disparity in thrombosis-free survival between AVF and AVG is evident within the first few months of placement, and becomes more pronounced with time. In addition, the number of interventions per patient-year is consistently, and substantially, higher for AVG than autogenous AVF ^{12,15,19,20}, notwithstanding the inclusion of immature AVF requiring intervention, as this study has done.

In 2001, Oliver et al compared the outcomes of 82 patients with upper arm AVG and 145 patients with upper arm AVF, with a median follow-up of 505-705 days, depending on the access type ¹⁵. Including primary failure, AVG had a higher rate of thrombosis than brachio basilic AVF (relative risk of 1.6) and

required 1.7 procedures per access year to remediate thrombosis compared to 0.3 per year for brachiobasilic AVF and 0.03 per year for brachiocephalic AVF.

Despite refinements in functional access surveillance and ultrasound reporting of AVF, has much changed? Eighteen years after Olivier's paper, Drouven et al performed a retrospective analysis of the outcomes of 55 forearm loop PTFE grafts and 75 brachiobasilic fistulas ¹⁹. Compared to autogenous AVF, AVG were associated with an overall higher rate of percutaneous angioplasty (1.77 vs 1.05 per patient year (ppy), $p = .022$), access thrombosis (0.54 vs 0.11 ppy, $p < .001$) and endovascular salvage of thrombosed accesses (0.25 vs 0.03 ppy, $p < .001$).

Both of these studies reflect the results of a randomised controlled trial of brachiobasilic AVF versus forearm loop grafts, reported by Keuter in 2008 ²⁰. The incident rate of surgical thrombectomy within 12 months of access formation was 0.59 per patient year for AVG and 0.073 per patient year for AVF ($p < .001$).

On Kaplan-Meier analysis, secondary patency of AVG may parallel AVF for the first 12-18 months but this headline rate belies the substantially greater susceptibility of AVG to thrombosis and conspicuously higher resource use to resuscitate occluded grafts. Not only does such thrombosis and its correction inconveniences the patient, but it burdens the healthcare system with unplanned consumption of interventional and financial resources ²¹.

The main limitation of this study is that it is retrospective in nature, with variations in baseline patient characteristics, and differences in practices between institutions. In particular, the requirement for, and duration of, renal replacement therapy preceding access formation were dissimilar (the rates of permanent haemodialysis access immediately prior to new access formation are a case in point). The absolute number of operations preceding entry into the study for each subject was unable to be obtained consistently and was not reported.

CONCLUSION

In this retrospective study with a relatively large cohort, followed for up to 5 years, we have shown that AVG have a substantially higher rate of thrombosis than AVF, evident from early in the life of the graft. This and other studies demonstrate the superiority of AVF with respect to access patency, especially beyond 18 months, and rates of re-intervention. In our opinion, AVG should only be considered when all other upper limb autogenous access options have been exhausted.

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None.

Disclosure Statement

Declaration of Interest: None

Conflict of Interest: None

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Legends for Figures

Fig 1. Primary patency rates of arteriovenous fistulas (AVF) and prosthetic arteriovenous grafts (AVG). Log rank, $P < 0.001$

Fig 2. Assisted primary patency rates of arteriovenous fistulas (AVF) and prosthetic arteriovenous grafts (AVG). Log rank, $P < 0.001$

Fig 3. Secondary patency rates of arteriovenous fistulas (AVF) and prosthetic arteriovenous grafts (AVG). Log rank, $P = 0.034$

Table 1. AVF Operations to Establish New Permanent Haemodialysis Jan 1, 2013- Dec 31, 2015

	AVF		AVG		p-value
	Number	%	Number	%	
Total patients	400		59		
Male	248	62	29	49.2	0.065
Outcomes at the end of follow-up					
Dead	107	26.8	27	45.8	0.024
Dialysis	170	42.5	22	37.3	
Transplant	83	20.8	8	13.6	
Not yet on HDx	20	5	0	0	
Lost to follow-up	20	5	2	3.4	

Table 2. Accesses

	AVF		AVG		p-value
	Number	%	Number	%	
Total Accesses	470		92		
Male	293	62.3	46	50	0.027
Age at time of procedure, years (Median, IQR)	60.7 (49.6-70.4)		64.7 (54.8-72.2)		0.106
Age range (years)	19-87.2		19-85.7		
Diabetic	236	50.2	39	42.4	0.174
Never smoked	272	57.9	57	61.9	0.724
Former smokers	153	32.6	26	28.3	
Current smokers	45	9.6	9	9.8	
Residential distance of patient from parent hospital					
< 50 km from parent hospital	360	76.6	55	59.8	0.001
50-100km from parent hospital	21	4.5	4	4.3	
> 100 km from parent hospital	89	19	33	35.9	
Renal replacement therapy immediately prior to new access formation:					
Central venous catheter	206	43.8	25	27.2	<.001
AVF/AVG	17	3.6	49	53.3	
Peritoneal dialysis or transplant	55	11.7	11	12	
None	192	40.9	7	7.6	
Median duration (IQR) of prior renal replacement therapy (days) [no. patients for whom data is available]	584 (155-2503) [n = 239]		2241 (649-4060) [n = 83]		<.001
Access used	324	68.9	80	87	<.001
Median time (IQR) from AVF formation to use (days)	111 (64.5-228)		1 (1-2)		<.001
Median time (IQR) of follow up (days)	709.5 (204.3-1157.8)		455.5 (159-892)		0.011

Table 3. Intervention Requirements for AVF

	AVF	AVG
Number	470	92
Total days* of follow-up	330821	50053
Number of accesses requiring intervention during follow-up	177 (37.7%)	55 (59.8%)
Operations	133	94
Angioplasties	227	37
Operations PPY [#]	0.147	0.686
Surgical thrombectomies PPY	0.042	0.49
Operations for other reasons PPY	0.105	0.196
Angioplasties PPY	0.251	0.27
Total Interventions PPY	0.397	0.956

* Σ Days until loss of secondary patency, censoring of data (transplant, death, lost) or end of follow-up

[#] Per Patient Year

List of Supporting Information

Figure S1. Primary patency of forearm AVF, upper arm AVF and upper limb AVG

Figure S2. Assisted primary patency of forearm AVF, upper arm AVF and upper limb AVG

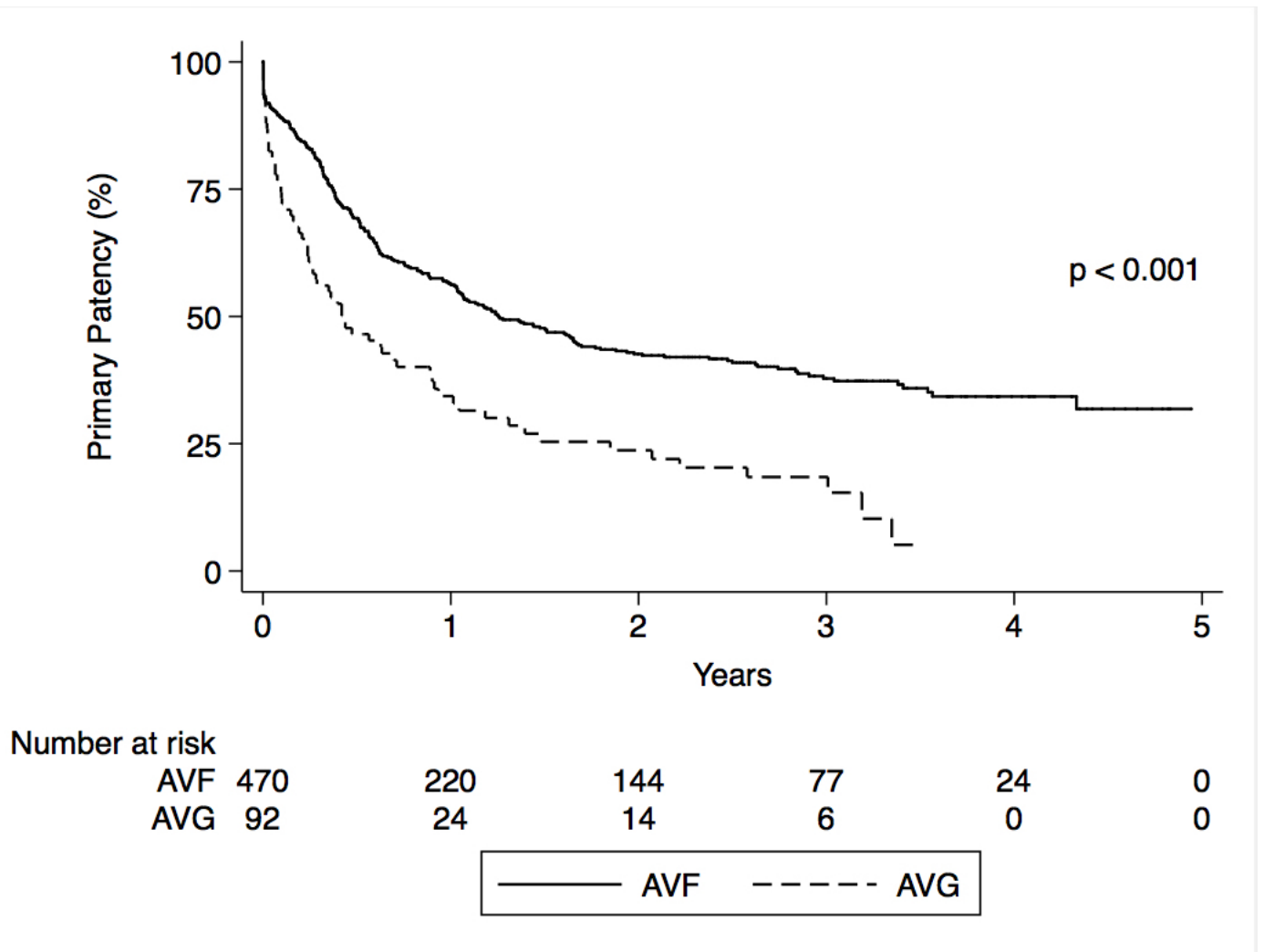
Figure S3. Secondary patency of forearm AVF, upper arm AVF and upper limb AVG

Table S1. Comparison of primary patency between upper limb AVG, upper limb AVF and forearm AVF, as shown in Fig S1.

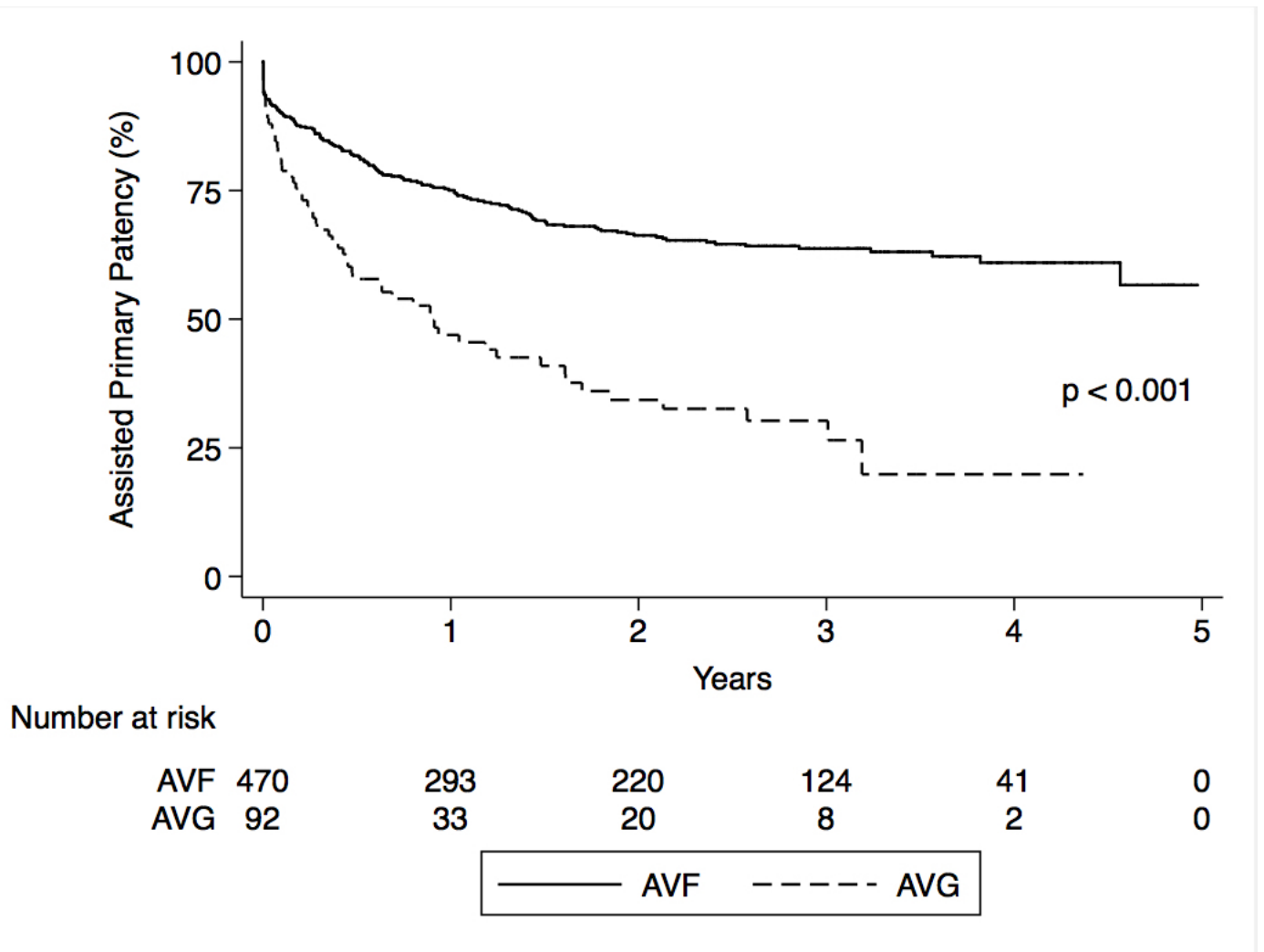
Table S2. Comparison of assisted primary patency between upper limb AVG, upper limb AVF and forearm AVF, as shown in Fig S2.

Table S3. Comparison of secondary patency between upper limb AVG, upper limb AVF and forearm AVF, as shown in Fig S3.

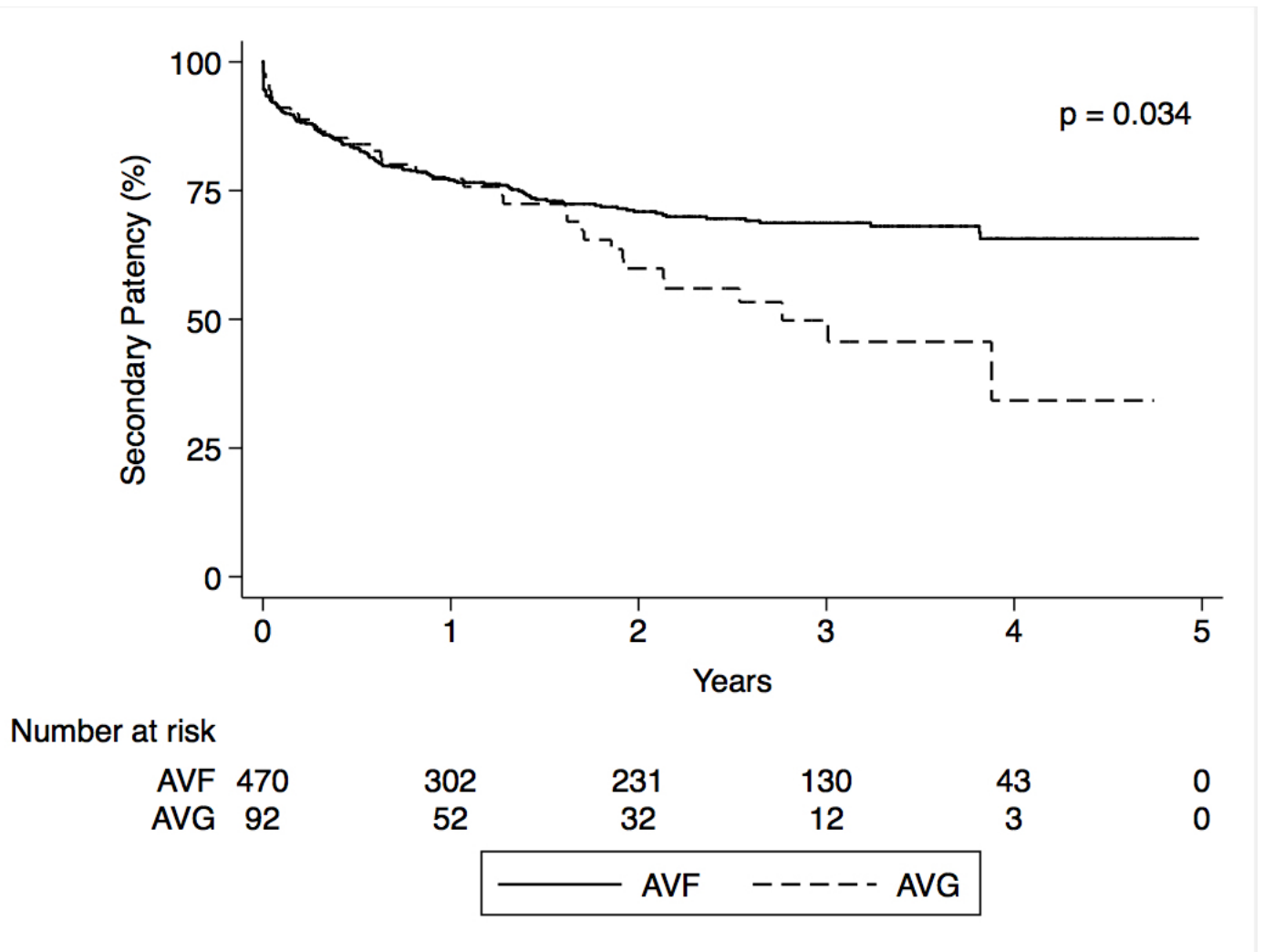
Table S4. Indications for operations on AVF and AVG.



ANS_16472_Fig 1 Primary Patency jpeg.jpg



ANS_16472_Fig 2 Assisted Primary Patency jpeg.jpg



ANS_16472_Fig 3 Secondary Patency Jpeg.jpg