

# Predictors of radio-cephalic arteriovenous fistulae patency in an Asian population

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## ABSTRACT

**Purpose:** To identify predictors of arteriovenous fistula (AVF) patency in Asian patients with autogenous radio-cephalic arteriovenous fistula (RCAVF).

**Methods:** Retrospective review of 436 RCAVFs created between 2009 and 2013. Predictors of patency were identified with univariate and multivariate analysis. Kaplan-Meier survival analysis and log-rank test were used to calculate patency rates.

**Results:** Overall secondary patency rate was 72% at 12 months, 69% at 24 months, 58% at 36 months, 57% at 48 months, 56% at 60 months and 54% at 72 months. Univariate analysis showed that factors which predict for patency include male gender ( $p = 0.003$ ), good diabetic control ( $p = 0.025$ ), aspirin use ( $p = 0.031$ ), pre-dialysis status ( $p = 0.037$ ), radial artery diameter ( $p = 0.029$ ) and non-calcified radial arteries ( $p = 0.002$ ). Age ( $p = 0.866$ ), cephalic vein diameter ( $p = 0.630$ ) and surgeon grade ( $p = 0.472$ ) did not predict for primary AVF failure. Multivariate analysis revealed the male gender to be an independent predictor for patency (odds ratio 1.99,  $p = 0.01$ ). Subset analysis showed a significantly larger average radial artery diameter of 2.3 mm amongst males, as compared to 1.9 mm amongst females ( $p = 0.001$ ) and no statistical difference in the average cephalic vein diameter.

**Conclusions:** Within our Asian study population, 12-month patency rate of RCAVF is 72%, 69% at 24 months, 58% at 36 months, 57% at 48 months, 56% at 60 months and 54% at 72 months. Male gender is an independent predictor for RCAVF patency. In females or patients with calcified radial arteries, a more proximal AVF should be considered.

**Keywords:** Arteriovenous fistula, Haemodialysis, Patency, Radio-cephalic, Vascular access

## Introduction

Arteriovenous fistulae (AVFs) are the preferred access for haemodialysis in patients with end-stage renal failure (ESRF) but have a considerable failure rate. Current Society of Vascular Surgery guidelines on AVF recommend that whenever possible, autogenous AVF be placed as far distally in the upper extremity as possible to preserve proximal sites for future accesses (1).

In a large meta-analysis comprising of 62 unique cohorts and 12,383 patients, the rate of primary fistula failure is 23% (2) whilst reported failure rates of radio-cephalic AVFs (RCAVF) is 15% (3). Although various local factors such as surgical technique, arterial flow, venous compliance and systemic factors

such as patient demographics and co-morbidities are known to influence AVF maturation (4, 5), accurately predicting whether an AVF will mature and be useable for haemodialysis vascular access is still a challenge. In this study, we aim to identify predictors of AVF patency in Asian patients with RCAVFs.

## Methodology

We performed a retrospective review of all patients who underwent creation of RCAVF between 2009 to 2013 at Tan Tock Seng Hospital (Singapore), a 1600-bed tertiary referral university hospital. All procedures were performed under local anaesthesia, with vascular anastomosis being Cimino-Brescia side-to-end radial-cephalic anastomosis. Factors investigated include patient demographics, co-morbidities, previous central venous interventions, ESRF status, current medication regime, pre-operative ultrasound vein map, surgeon grade (sub-specialty vascular consultants and vascular registrars under training who were closely supervised) and requirement for any assisted patency interventions such as tributary ligation, fistuloplasty or AVF revision. Secondary patency interventions include surgical thrombectomy and endovascular thrombolysis. Pre-operative ultrasound vein mappings were performed at our local vascular diagnostic laboratory by trained vascular scientists according to Society of Vascular Ultrasound guide-

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lines, using Philips iU22 ultrasound machines (California, USA) with the patients lying supine and upper limb tourniquet close to the axilla.

In our study, definitions of patency, as defined within the literature (4), are as follows:

- Primary patency – the interval from the time of access creation to the time of measurement of patency without the need for any intervening manipulations.
- Assisted primary patency – the interval from time of access placement to the time of measurement of patency, including intervening manipulations (surgical or endovascular) to maintain functionality of a patent access.
- Secondary patency – the interval from time of access placement to the time of measurement of patency, including intervening manipulations (surgical or endovascular) to re-establish functionality in thrombosed access.
- Primary failure – this is an AVF for which, despite interventions, it was not possible to use the AVF successfully for haemodialysis.

### Statistical analysis

Factors investigated were evaluated using descriptive statistics. Percentages were used for categorical data and means with standard deviations (SDs) for continuous data. Comparisons between groups for categorical data were made using Chi-square tests while comparisons between groups for continuous data were made using Student's t-test. Univariate analysis was performed to identify factors associated with AVF maturation failure, with a further cut-off p value of 0.1 being used for multivariate logistic regression to identify independent risk factors associated with AVF maturation failure of therapy. Odds ratios (ORs) and their 95% confidence intervals (CIs) were calculated. All p values  $\leq 0.05$  were considered statistically significant and all p values were two-tailed. Kaplan-Meier survival analysis was used to calculate patency, and the log-rank test was used to compare patency rates between the male and female gender. SPSS 13.0 (Chicago, IL, USA) was used for statistical analysis.

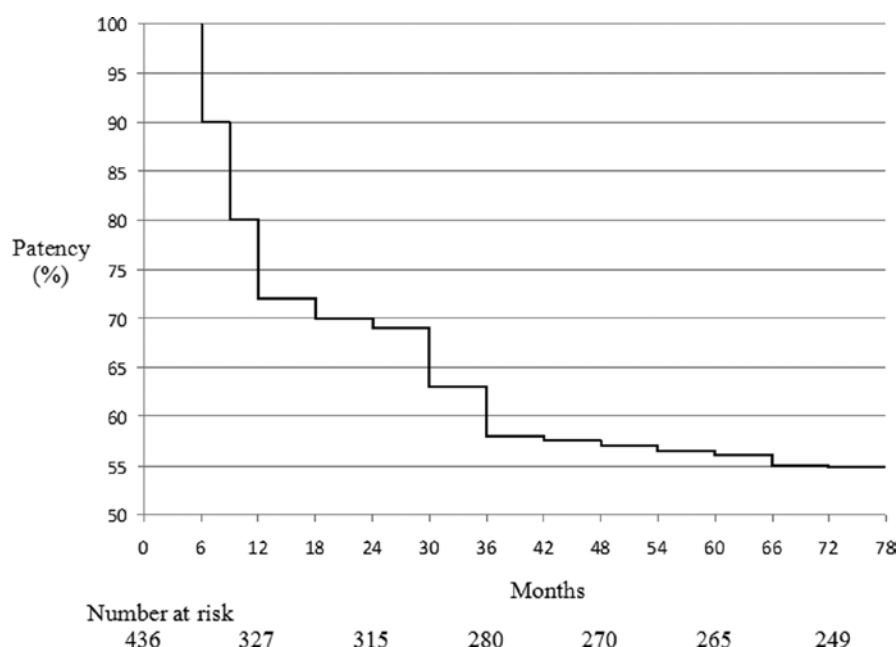
### Results

There were 1049 autogenous AVFs created between January 2009 to December 2013, of which there were 436 RCAVFs (42%). Within the study population of patients with RCAVFs created, 70% were male, average age was 58 years and 76% of patients had their AVFs created on the left arm (Tab. I). The ethnicity make-up of the study population, with 71% Chinese, 21% Malay and 8% Indian, was similar to that of the general Singapore population. In terms of co-morbidities, 27% of the patients were chronic smokers, with 72% having underlying type 2 diabetes mellitus (T2DM) and out of which, 88% had good T2DM control with HbA1c  $< 7\%$ . The majority of patients also had underlying hyperlipidaemia (93%) and hypertension (98%) whilst 15% of the study population had concurrent peripheral arterial disease. Almost half (45%) the patients had underlying ischaemic heart disease, with a similar percentage of patients (45%) on anti-platelet medication (either aspirin or clopidogrel). The follow-up period ranged from 12 to 72 months.

**TABLE I - Study population characteristics and outcome**

Demographics	
Study population	436
Study period	2009-2013
Male: Female	70%:30%
Chinese: Malay: Indian	71%:21%:8%
Average age (range)	58 (22-90) years
Right arm: Left arm	24%:76%
Smoker	99 (27%)
Co-morbidities	
Type 2 diabetes mellitus (T2DM)	315 (72%)
Good T2DM control (HbA1c $< 7\%$ )	276 (88%)
Hyperlipidaemia	405 (93%)
Hypertension	427 (98%)
Ischaemic heart disease	196 (45%)
Cerebrovascular disease	57 (13%)
Peripheral arterial disease	65 (15%)
Central venous interventions	
Permanent catheter (PC) in-situ	316 (72%)
PC ipsilateral to AVF	87 (20%)
Central vein stenosis	9 (2%)
ESRF status	
Average eGFR (range)	8.1 (2.3-38.6) mL/min
Haemodialysis commenced	316 (72%)
Medications	
Aspirin	148 (34%)
Clopidogrel	48 (11%)
Any other anti-coagulation	26 (6%)
Pre-operative vein map	
Average cephalic vein diameter (range)	2.4 (1.8-6.3) mm
Presence of tributaries within 10 cm of anastomosis	344 (79%)
Average radial artery diameter (range)	2.2 (1.9-3.8) mm
Circumferential radial calcification ( $> 50\%$ calcification)	78 (18%)
Surgeon grade	
Consultant:Registrar	72%:28%
Outcome at 12-months	
Primary patency	143 (33%)
Assisted primary patency	271 (62%)
Secondary patency	313 (72%)
Primary failure	116 (26%)
Death (non-AVF related)	7 (2%)

AVF = arteriovenous fistula; eGFR = estimated glomerular filtration rate; HbA1c = haemoglobin A1c; PC = permanent catheter; T2DM = type 2 diabetes mellitus.



**Fig. 1** - Combined patency rates of 436 radio-cephalic arteriovenous fistulae.

**TABLE II** - Analysis between secondary patency and primary failure

	Secondary patency (n = 313, 72%)	Primary failure (n = 116, 27%)	Univariate analysis p value <sup>a</sup>	Multivariate analysis OR (SD) p value
Demographics				
Male	231 (74%)	68 (59%)	0.003	1.99 (0.22); p = 0.01
Average age (years)	57.8	58.1	0.866 <sup>b</sup>	-
Co-morbidities				
Good T2DM control	228 (73%)	71 (61%)	0.025	-
Medication				
Aspirin	119 (38%)	31 (27%)	0.031	-
ESRF status				
HD commenced	166 (53%)	75 (65%)	0.037	-
Vein map				
Ave. cephalic diameter (mm)	2.5	2.3	0.630 <sup>b</sup>	-
Ave. radial diameter (mm)	2.3 (SD 0.50)	2.1 (SD 0.48)	0.029 <sup>b</sup>	-
Calcified radial artery	38 (12%)	29 (25%)	0.002	-
Surgeon grade				
Consultant	219 (70%)	86 (74%)	0.472	-

<sup>a</sup> Fisher's two-tailed.

<sup>b</sup> Student's t-test.

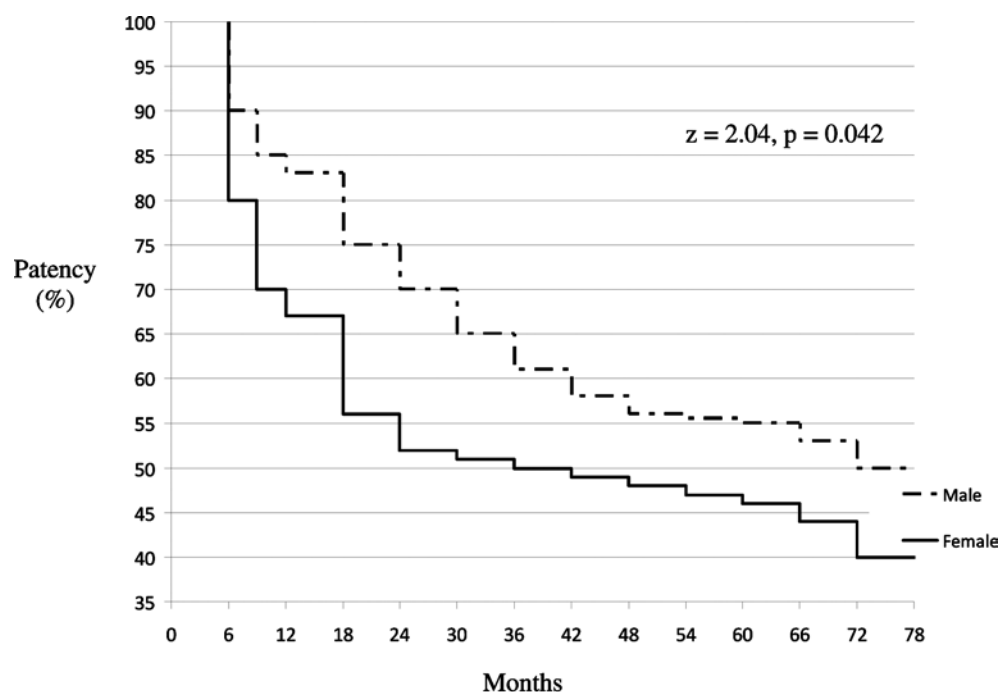
Ave. = average; ESRF = end-stage renal failure; HD = haemodialysis; OR = odds ratio; SD = standard deviation; T2DM = type 2 diabetes mellitus.

Almost three-quarters of the patients had haemodialysis commenced (72%), with 20% of patients having their permanent catheter (PC) ipsilateral to the AVF and only 2% having underlying central vein stenosis. The average estimated glomerular filtration rate (eGFR) at the time of AVF creation was 8.1 mL/min. Pre-operatively, the average cephalic vein diameter was 2.4 mm and 79% of patients had tributaries within 10 cm of anastomosis site. The average radial artery diameter was 2.2 mm, with 18% of patients having circumferential radial calcification (>50% calcification). Almost three-quarters of AVFs were created by consultants (72%)

whilst the remainder (28%) were created by registrars under supervision.

The 12-month primary patency rate within our study population was 33%, with assisted primary patency at 62% and secondary patency rate at 72%. Overall secondary patency rate was 69% at 24 months, 58% at 36 months, 57% at 48 months, 56% at 60 months and 54% at 72 months (Fig. 1). The primary failure rate was 26%. There were a total of eight non-AVF-related deaths (2%) within the study population.

Univariate analysis between patients with secondary patency and patients with primary failure (Tab. II) showed that factors



**Fig. 2** - Patency rates between male and female gender.

Number at risk							
Male	305	260	219	195	183	175	165
Female	131	92	77	69	65	60	56

**TABLE III** - Analysis between male and female vascular calibre

	Male (n = 305, 70%)	Female (n = 131, 30%)	p value (Student's t-test)
Vascular calibre			
Average radial diameter (mm)	2.3 (SD 0.49)	1.9 (SD 0.45)	0.001
Average cephalic diameter (mm)	2.5	2.3	0.219
Primary/assisted/secondary patent AVF			
Average radial diameter (mm)	2.3	2.1	0.139
Average cephalic diameter (mm)	2.5	2.4	0.511
Primary failure AVF			
Average radial diameter (mm)	2.3 (SD .45)	1.8 (SD 0.37)	0.001
Average cephalic diameter (mm)	2.4	2.2	0.398

AVF = arteriovenous fistula; SD = standard deviation.

which predict for patency include male gender ( $p = 0.003$ ), good T2DM control ( $p = 0.025$ ), aspirin use ( $p = 0.031$ ), pre-dialysis status ( $p = 0.037$ ), radial artery diameter ( $p = 0.029$ ) and non-calcified radial arteries ( $p = 0.002$ ). Age ( $p = 0.866$ ), cephalic vein diameter ( $p = 0.630$ ) and surgeon grade ( $p = 0.472$ ) did not predict for primary AVF failure. Multivariate analysis revealed the male gender to be an independent predictor for patency (odds ratio 1.99, standard deviation 0.22,  $p = 0.01$ ). Log-rank test to compare patency rates between the male and female gender showed a significant differing hazard rate from time of creation ( $z = 2.04$ ,  $p = 0.042$ ) (Fig. 2).

Subset analysis of vascular calibre difference between the male and female gender showed a significantly larger aver-

age radial artery diameter of 2.3 mm (standard deviation 0.49 mm) amongst males, as compared to the average radial artery diameter of 1.9 mm (standard deviation 0.45 mm) amongst females ( $p = 0.001$ ) (Tab. III). There was no statistical difference in the average cephalic vein diameter between the male and female gender within our study population.

## Discussion

This is the largest published series of radio-cephalic AVFs from an Asian centre (6). According to the US Renal Data System's annual report in 2014, the prevalence of ESRF has been continually rising (7). In 2012, incidence of ESRF

in Singapore is 285 per million, making it joint fourth in the world with Japan, whilst the prevalence of ESRF, at 1741/million population, is also fourth highest in the world. In 2013, 87% of ESRF patients in Singapore underwent haemodialysis as their primary renal replacement therapy (8). Undoubtedly, these statistics indicate the continuing worldwide need for additional resources and care on a broad, global level to meet the health needs of individuals with ESRF, with AVF patency being of utmost importance to the patient. Our 1-year patency rate of 72% is similar to that of rates within the literature (2, 3).

The most significant finding from our study is that the male gender is an independent predictor for RCAVF patency. Within the literature, female gender was identified as a significant predictor of graft patency, rather than AVF patency (9), with little specific evidence for AVF patency differences between genders (6, 10, 11). However, the gender difference within our study population may be attributed to the significant vascular calibre difference between the male and female gender. Although there is no statistical difference in the average cephalic vein diameter between the males and females within our study population, there is a significantly larger average radial artery diameter amongst males (2.3 mm), as compared to the females (1.9 mm). Smaller artery diameters have been associated with increased non-maturation rates and our findings are consistent with current guidelines, which suggest a minimum diameter of 2 mm for successful RCAVF creation (1, 12-16).

In terms of underlying co-morbidities, T2DM is known to have an effect on AVF patency (5, 17). Within our study population, a good T2DM control, as defined by HbA1c <7%, is shown to predict AVF patency on univariate analysis. Various reasons proposed within the literature include reduced arterial calcifications and increased vessel diameter and arterial peak systolic volume in non-diabetic patients, but most studies were comparisons between diabetic and non-diabetic patients instead of good T2DM control.

Although our study showed aspirin use to predict AVF patency on univariate analysis, a 2013 meta-analysis of 21 trials with 4826 patients showed that although antiplatelet treatment protects fistula against thrombosis or loss of patency, it has little or no effect on graft patency and uncertain effects on vascular access maturation for dialysis and major bleeding (18). Similarly, clopidogrel has been shown to reduce the frequency of early thrombosis of new AVFs but does not increase the proportion of fistulae that become suitable for dialysis (19). A 2015 Cochrane review on the use of medical adjuvant treatment to increase AVF patency showed current inadequate data within the literature to demonstrate beneficial effects of anti-platelet in AVF patency rates (20).

Society of Vascular Surgery's 2008 clinical practice guidelines recommend that patients with advanced chronic kidney disease (late stage 4, eGFR <20 to 25 mL/min) who have elected haemodialysis as their choice of renal replacement therapy be referred to an access surgeon in order to evaluate and plan construction of AV access (Grade 1 recommendation) (1). Within our local population, although the renal physicians refer to vascular surgeons early on in the ESRF disease process, most patients appear to have a strong cul-

tural inertia against creating a prophylactic vascular access when haemodialysis is not needed. In our study, non-commencement of haemodialysis prior to AVF creation predicts for patency on univariate analysis. This is likely to be secondary to the underlying pro-thrombotic state in patients undergoing dialysis (21-23). Thus, much patient education is needed to allow patients to understand the importance of AVF creation prior to the commencement of haemodialysis and early referral for vascular access will continue to be advocated.

Lastly, our study has shown surgeon grade to not affect RCAVF patency or failure rates. Within the literature, there have been conflicting studies with regards to the surgical experience in AVF creation. On one hand, it has been advocated that AVF creation should be performed by the most experienced member of a team dedicated to vascular access creation or at least under his/her supervision (24). On the other hand, newer studies suggest that the seniority of the operating surgeon does not appear to impact on the outcomes following AVF creation (25). At our institution, all AVFs are created by vascular consultant surgeons and all registrars perform the procedure under close supervision. Hence, perhaps the specialist care and close supervision accounted for surgeon grade not being a factor in predicting for AVF patency.

Limitations of our study include its retrospective design, with associated selection and information biases. We did not manage to review patient's body mass index, AVF size during trial of cannulation, time to patency or failure, length of patency, and surveillance duplex or dialysis flow rates. Currently, the Haemodialysis Fistula Maturation (HSM) Study, a large multi-centre study in the USA, aims to follow 600 patients over the course of 4 years, and will hope to identify factors affecting maturation of AVFs as well as the usefulness of early indicators in predicting fistula maturation (26).

## Conclusion

In this large Asian single-institutional review of 436 RCAVFs, overall secondary patency rate is 72% at 12 months, 69% at 24 months, 58% at 36 months, 57% at 48 months, 56% at 60 months and 54% at 72 months. Multivariate analysis revealed the male gender to be an independent predictor for patency, and subset analysis of vascular calibre difference between the male and female gender showed a significantly larger average radial artery diameter of 2.3 mm amongst males, as compared to the average radial artery diameter of 1.9 mm amongst females. There was no difference in the average cephalic vein diameter between the male and female gender within our study population. Age, cephalic vein diameter and surgeon grade did not predict for AVF failure. In females or patients with calcified radial arteries, instead of RCAVFs, a more proximal AVF should be considered.

## Disclosures

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Conflict of interest: None of the authors has financial interest related to this study to disclose.

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