

## Retrospective Study on Role of Atorvastatin in Arterio-Venous (Brachiocephalic) Fistula Maturation

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### Abstract

### Original Research Article

**Introduction:** Patients on haemodialysis require either an intravenous cannula or an arterio-venous (AV) fistula for haemodialysis. Multiple factors are involved in the maturation of an AV fistula and this retrospective study was designed to look into the relationship of atorvastatin usage affecting AV fistula maturation. **Methods:** A retrospective cohort of 89 patients who underwent arterio-venous fistula creation from the year 2023 - 2024 in Hospital Sultan Haji Ahmad Shah (HoSHAS), Temerloh were analysed in this study. Patients were divided into 2 groups: (1) patients that were on regular atorvastatin, (2) patients not on atorvastatin. **Results:** A total of 89 patients underwent AV fistula creation. Patients in group 1 had an overall success rate of 53% with 3 failures. Meanwhile, the patients in group 2 had a success rate of 46% with 7 failures. **Discussion:** Significant statistical difference observed in outcome of AV fistula maturation in the group of patients that received atorvastatin. (p value 0.011). However, a number of confounding factors such as the dose of atorvastatin, surgeon factor, ages of the patients, dose of atorvastatin and patients with chronic kidney disease (CKD) or End Stage Renal Failure (ESRF) could affect the outcome of this study. **Conclusion:** Results of this study showing positive relationship of atorvastatin usage with Brachiocephalic fistula (BCF) maturation.

**Keywords:** Arteriovenous Fistula (AV Fistula), Atorvastatin, Hemodialysis, Maturation, Chronic Kidney Disease (CKD), End Stage Renal Failure (ESRF).

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## INTRODUCTION

Kidney disease is a rising and notable problem worldwide. In Malaysia, 9.07% of the population suffer from chronic kidney disease (CKD) and 0.36% are Stage V CKD or ESRF [1]. The incidence of ESRF is growing rapidly from 18 per million in 1993 to 231 per million in 2013. It is estimated that the incidence of ESRF is expected to increase exponentially in years to come [2]. As renal transplants in Malaysia are a distant dream for most of these patients, with a waiting period of 13-15 years, these patients require an alternate form of renal replacement therapy (haemodialysis or peritoneal dialysis).

An arterio-venous (AV) fistula is a connection that is created surgically between an artery and a vein. These AV fistulas mature via a process called venous arterialisatation which allows the anastomosed venous limb to be enlarged and able to withstand the high flow rates necessary to sustain haemodialysis. Multiple factors play an important role in the maturation of an AV

fistula. There are a few options for sites of fistula creations: brachiocephalic, brachio basilic and radiocephalic fistulas. In our district centre (non-vascular centre), the majority of our patients undergo brachiocephalic fistula (BCF) creations. BCF creations are opted in our centre as it requires fewer interventions [5] to maintain long term patency. Hence, due to our patient demographics, who are from a district and rural backgrounds with logistic drawbacks, BCF creations are the standard and selected choice for fistula creations for our patients.

With AV Fistula creations, primary failure is a concerning sequelae as it has an economic impact and results in higher healthcare costs [6]. Primary failure is defined as thrombosis or the inability to cannulate the AV fistula within 3 months of creation. Primary failure is assessed post-surgery. Post AV fistula creations, patients are reviewed after 6 weeks to assess fistula maturity and patency.

Multiple factors are involved in the maturation of an AV fistula. These can be divided into patient factors and surgical factors. Patient factors include; age, gender, comorbidities (diabetes, hypertension, peripheral vascular disease, obesity, smoking). Surgical factors include; surgeon experience, intraoperative vein diameter, size and degree of atherosclerosis of the feeding artery.

Statins have a beneficial pleiotropic effect for vascular remodelling. The vasculoprotective and anti-inflammatory effects of statin therapy are attributed to both lipid-reducing and non-lipid-related mechanisms. Statins decrease smooth muscle cell proliferation and migration and chemotaxis of immune cells, which are all important players in vascular remodelling. The use of these drugs is also associated with improved endothelial cell function, by lower circulating levels of oxidized LDL, upregulation of endothelial nitric oxide synthase, inhibition of endothelin-1, and reduced adhesion of leukocytes to the endothelium [3].

## METHODS

### Study Participants

This retrospective study included patients who underwent brachiocephalic fistula (BCF) creations (one – stage) in Hospital Sultan Haji Ahmad Shah, Temerloh from the year 2023 to 2024. Patients were divided into 2 groups: (1) patients that were on regular atorvastatin, (2) patients not on atorvastatin.

Patients were referred by renal physicians to our AVF clinic in HoSHAS for AV fistula assessment. Screening of potential patients was done by the surgeon using an ultrasound. Criteria accepted for brachiocephalic fistula creations included: cephalic vein diameters of 2mm and more, absence of brachial artery calcifications, good radial artery pulse (2+), surgery done on the hand without an ipsilateral internal jugular dialysis catheter and patients without clinical heart failure. Selected patients had no recent procedures or blood taking done on the side of the BCF creation side and were all educated regarding renal replacement therapy options and they have opted and agreed for haemodialysis.

Surgeries were performed by 3 credentialed general surgeons with less than 5 years of experience in fistula creations. Surgeries were performed under local anaesthesia with 2% lignocaine. Surgical site was prepped with povidone iodine and chlorhexidine. Vascular anastomoses were done using standardized techniques of cephalic vein and brachial artery isolation using sharp dissections. Arteriotomy size on the brachial artery were as of the cephalic vein size. Tension free end to side anastomosis were done using prolene 7-0 sutures. Their anastomoses were done using a standardized parachute technique. This technique involves the preparation of the brachial artery and the cephalic vein, followed by an array of “parachute” sutures along the anastomotic line while ensuring no suture entanglement

and maintaining visualisation of the lumen. Heparinized saline was used to wet the sutures to ensure that the vessel could be parachuted down smoothly with no resistance.

Post operatively, patients were educated by the medical officer in charge regarding post operative care. Patients were advised with a standardized template that included, avoiding compressive or restrictive dressing over the fistula site, arm is to be kept extended and to allow only up to at 30° elbow flexion, arm is rested for the duration of six weeks till the post operative ultrasound assessment and to avoid lifting weights more than 5 kgs on the side of the surgery. Wound inspections were done on day 3 at the nearest clinic and as sutures were placed subcuticular, removal of sutures was not required.

All patients were reviewed six weeks after surgery to assess fistula patency and maturity. Post operative assessment included clinical assessment and a sonographic assessment of the fistula by a surgeon. Ultrasound assessment was done with a linear ultrasound probe using a Finus 70 model by Focus and Fusion. Patients with an immature fistula during the initial assessment were reviewed again 6 weeks later. During assessment by the surgeon, fistula maturity was assessed according to The Kidney Disease Outcomes Qualitative Initiative (KDOQI) by the National Kidney Foundation. Parameters assessed included:

- Clinical
  - Fistula thrills intensity
- Sonography
  - Vessel diameter (>6mm)
  - Fistula blood flow (>600mls/min)
  - Fistula depth from skin surface (<6mm from skin)
  - Functional fistula length (>6cm)

Total of 151 patients underwent arterio-venous fistula creation from the year 2023 – 2024 in our facility. However, after exclusion only 89 patients were selected in this study. Patients who were excluded from this study included:

- Patients who underwent radiocephalic or brachiocephalic fistula creations (20 patients)
- Patients on other types of lipid lowering drugs - simvastatin (28 patients)
- Immature fistulas at 3 months of creation that required further radiological or surgical intervention (4 patients needed superficialization or fistuloplasty)
- Patients defaulted follow up (8 defaulted follow up)
- Deceased patients (2)

### Definitions

Primary failure was defined as an AV fistula that had failed to mature; fistula diameter <6mm or blood flow less than 600mls/min within 3 months of creation [4].

### Statistical Analyses

Statistical analyses were performed using Microsoft excel, and results were considered significant when p-value is <0.05. Results were tabulated and interpreted using a paired t-test.

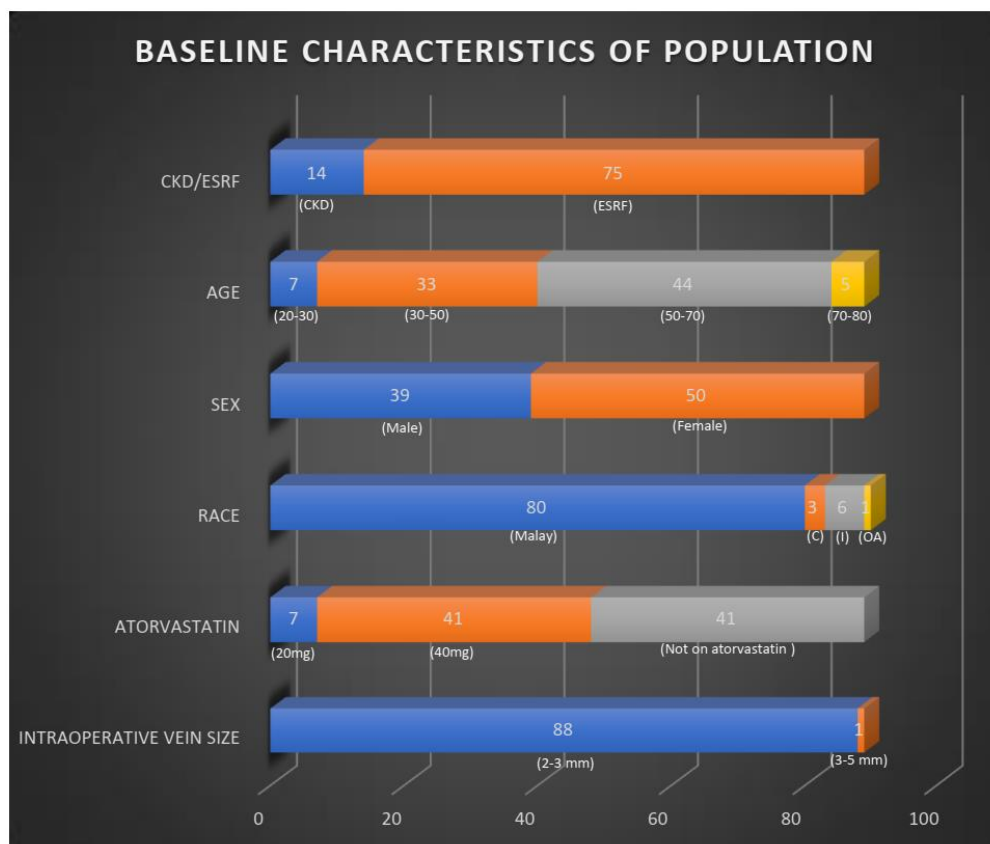
## RESULTS

A total of 89 patients were included in this retrospective study. Patients were divided into 2 groups: (1) patients that were on regular atorvastatin, (2) patients not on atorvastatin.

The final study population of these 89 patients were formed by patients of different races; Malay, Chinese, Indian and indigenous people (Orang Asli). Patients' ages varied from 22 to 78 years old and comprised both chronic kidney disease and end stage renal failure patients. Patients all had an intraoperative vein diameter of at least 2mm. Patients who were on regular atorvastatins were on either 20mg or 40mg on a regular nightly dose.

Baseline characteristics of study population

Sex	
- Male (%)	39 (43%)
- Female (%)	50 (56%)
Race	
- Malay (%)	80 (89%)
- Chinese (%)	3 (3.3%)
- Indian (%)	6 (6.6%)
- Indigenous people (Orang Asli) (%)	1 (1.1%)
Age	
- 20 – 30 years old	7 (7.8%)
- 30 – 50 years old	33 (49.4%)
- 50 – 70 years old	44 (37%)
- 70 – 80 years old	5 (5.6%)
Atorvastatin	
- 20mg ON (%)	7 (7.8%)
- 40mg ON (%)	41 (46%)
- Not on atorvastatin (%)	41 (46%)
Intraoperative vein diameter	
- 2-3mm (%)	88 (98.8%)
- 3-5mm (%)	1 (1.12%)
Issue	
- Chronic kidney disease (CKD)	14 (15.7%)
- End stage renal failure (ESRF)	75 (85.2%)

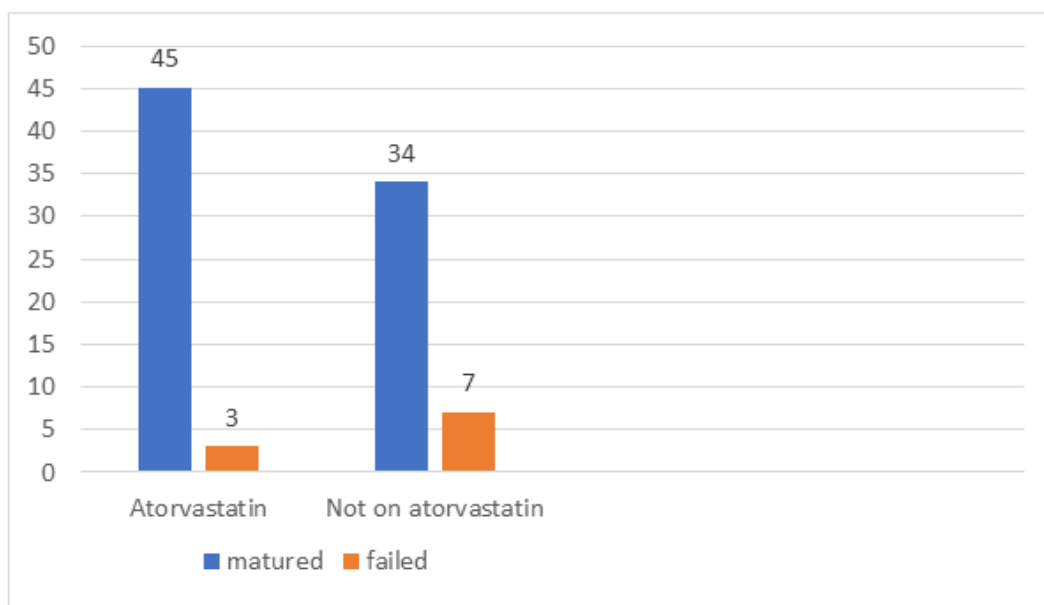


### Effect of atorvastatin on fistula maturation

In our study, primary failure occurred in 10 out of 89 patients. Out of these 10 patients with primary failure, 7 were not on atorvastatin, whereas the group

treated with atorvastatin only had 3 primary failures. Significant reduction of primary failure can be seen in the group on atorvastatin ( $p = 0.011$ ).

	Maturation by 6 weeks	Failure
- On atorvastatin	45	3
- Not on atorvastatin	34	7



Type of statins used	Maturation by 6 weeks		Primary Failure	
	2023	2024	2023	2024
Atorvastatin				
- 20mg	2	4	1	-
- 40mg	16	23	2	-

## DISCUSSION

Our study only focuses on the role of atorvastatin in promoting maturation and reducing rates of primary failure. The reason atorvastatin was chosen as a drug to study is due to its regular use for patients with dyslipidemia, as per the local guidelines. Our work demonstrated that atorvastatin plays an important role in reducing primary failure. In general, all fistula creations come with a risk of primary failure of up to 28 – 53% [7]. Brachiocephalic fistulas have a relatively higher primary failure rate up to 38% [5]. Multiple factors contribute to its maturation and failure. In our facility, we have managed to achieve an overall primary failure of only 11%.

Although atorvastatin was the only drug being studied, other studies have shown the superiority of atorvastatin as compared to its counterparts. HMG-CoA reductase is an enzyme that converts HMG-CoA into mevalonic acid that produces cholesterol. Elevated levels of LDL are related to the failure of AV fistulas. Hence, HMG-CoA reductase inhibitors play an important and crucial role in reducing serum lipid levels. Atorvastatin

inhibits HMG-CoA reductase enzyme and reduces overall LDL levels. As compared to other groups of statins, atorvastatin is more effective at reducing LDL cholesterol levels. Atorvastatin also has an extended half-life (15-30 hours) as compared to other statins and has more enhanced affinity for HMG-CoA reductase [3].

Additionally, atorvastatin has an added benefit of improving endothelial function and increases brachial artery vasodilation. This role that statins play is due to the improvement in the endothelial function that results in vasodilation and improvement in blood flow. Studies have shown the effect that atorvastatin plays in improving endothelial function and providing an anti-stenotic effect on the brachial artery [8].

Atorvastatin is generally a safe drug with minimal side effects with notable efficacy for the treatment of dyslipidemia [17]. As most of our patients were on regular use of atorvastatin pre operatively, they tolerated the medication with no significant complaints during follow up assessments. As these patients were primarily on atorvastatin for dyslipidemia and primary

prevention of cardiovascular disease, significant side effects associated with this medication were highlighted to the primary physician of the patient in the primary health care centre for further evaluation and change in medication if needed. Some of these side effects included; myalgia and gastrointestinal discomfort. Additionally, atorvastatin and other groups of statins are known to have a negative effect on the derangement of liver enzymes and may require dose reduction and liver function monitoring. Postoperative liver function tests were not monitored in this study at our facility as patients were subsequently discharged to the primary health care or renal physician for regular follow up and monitoring. Despite these adverse effects, studies have shown that generally statins, including atorvastatin had low risk of adverse effects and the benefit-to-harm balance of statins is generally favourable [18]. Incidence of adverse effects is associated with increase in the dose of atorvastatin, however doses up to 40mg have shown to be as effective as higher doses in lipid level reduction as well as decreased adverse effects [19].

The role of atorvastatin as an adjunct should be considered for patients undergoing AV fistula creations to promote maturation in order to reduce the cost of further interventions and surgeries required for fistula salvage procedures. In our population of patients, the nearest tertiary centre for fistuloplasties and salvage procedures is located 130 km (80 miles) away. Given the demographic of our patients that comprise a majority of poor income groups [14] these added interventions result in additional travel and treatment expenses. As repeated interventions of a failing AVF reduces the success rate of the following intervention, some patients may ultimately require a new AV fistula creation as it is more cost effective than recurrent salvage procedures [15]. The costs of an AV fistula creation in a government hospital in Malaysia for a Malaysian citizen is around RM 1300 and further angioplasties and surgeries range between RM 1300 – 4700 [16]. Despite subsidisation by the government to reduce the burden of healthcare cost on the patient, it is evident that there is still a significant economic impact that follows the complications of a failing AV fistula.

The limitations of this study are that there are a number confounding variables that could have affected the outcomes. The first drawback is the (1) low number of cases in this study. As our hospital is not a vascular centre, the allocation for AV fistula creations is limited to only one operating slot in a week. Additionally, the low number of cases in our centre is also due to a relatively low density population of 46 people/km<sup>2</sup> in the state of Pahang [9] (1.66 million in the year 2024) with poor socioeconomic backgrounds and logistic vulnerabilities [10]. The second variable in our study were the (2) different doses of atorvastatin (20mg / 40mg) the patients were on, as they were initiated by renal physicians or primary healthcare physicians for treatment of dyslipidemia and for primary prevention of

cardiovascular diseases before the time of fistula creation. Another significant variable in this study is the (3) operating surgeons. Surgery was carried out by 3 different credentialed general surgeons with an experience of performing at least 10 successful brachiocephalic fistula surgeries before being credentialed. Despite the difference in the surgeons' experience, the standardization of the technique of BCF creations helped to reduce bias in the outcome of this study. (4) A wide range of age groups of patients ranging from 22 to 78 years of age were recruited in our study. Lastly, our patients also comprised both (5) chronic kidney disease and a majority of End Stage Renal Failure patients. Patients with ESRF have shown to have better maturation outcomes than those with CKD [11].

## CONCLUSION

Atorvastatin is shown to have beneficial effects on AV fistula maturation and prevention of primary failure. Failure or delayed maturation of the AV fistula results in further treatment and procedures to salvage the fistula, with a resultant increase in healthcare costs and potential delay in haemodialysis.

AV fistula failures have a significant economic burden [12] (follow up interventions) and greatly affect the quality of life of the patient [13]. The consequent interventions definitely come across as a burden to patients, especially for the population in our setting with logistic challenges to seek further treatment in a distant tertiary centre. Hence, additional measures should be considered in order to ensure early fistula maturation. As atorvastatin has relatively minimal side effects, it should be considered as an adjunct to be routinely prescribed in patients undergoing AV fistula creations. Not to mention the effect of repeated interventions has a significant emotional toll on the patient [20].

The data from our study provides a basis for future randomized control studies to be carried out with a larger sample size to further study the role of atorvastatin in helping the maturation of Brachiocephalic Fistulas and other AV Fistulas.

## REFERENCES

1. Ismail, H., Manaf, M. R. A., Gafor, A. H. A., Zaher, Z. M. M., & Ibrahim, A. I. N. (2019). Economic burden of ESRD to the Malaysian health care system. *Kidney International Reports*, 4(9), 1261-1270. <https://pmc.ncbi.nlm.nih.gov/articles/PMC6732754/>
2. Bujang, M. A., Adnan, T. H., Hashim, N. H., Mohan, K., Kim Liong, A., Ahmad, G., ... & Haniff, J. (2017). Forecasting the incidence and prevalence of patients with end-stage renal disease in Malaysia up to the year 2040. *International journal of nephrology*, 2017(1), 2735296. <https://pmc.ncbi.nlm.nih.gov/articles/PMC5350290>





- dyslipidemia. *Indian Heart Journal*, 70, S8-S12.  
<https://pmc.ncbi.nlm.nih.gov/articles/PMC6310693/>
20. Patel, S. T., Hughes, J., & Mills Sr, J. L. (2003). Failure of arteriovenous fistula maturation: an unintended consequence of exceeding dialysis outcome quality Initiative guidelines for hemodialysis access. *Journal of vascular surgery*, 38(3), 439-445.  
<https://www.sciencedirect.com/science/article/pii/S0741521403007328>