Correlation Of Vascular Stenosis With Hemodialysis Parameters In Native Arterio-Venous Fistula (AVF), Pre- And Post Percutaneous Transluminal Angioplasty (PTA)

By

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LIST OF ABBREVIATIONS

AVF : Arteriovenous Fistula

AVG: Arteriovenous Graft

Vp : Venous dialysis pressure

VpA : Venous dialysis pressure pre-PTA

VpB : Venous dialysis pressure post-PTA

Vp0 : Venous static pressure

Qb : Blood pump flow rate

QbA : Blood pump flow rate pre-PTA

QbB : Blood pump flow rate post-PTA

Qa: Access flow

VesD : Vessel diameter

VesDA: Vessel diameter pre-PTA

VesDB: Vessel diameter post-PTA

NV: normal vessel,

SVa: stenosis vessel pre PTA,

SVb: stenosis vessel post PTA

%S: percentage stenosis

ESRD: End stage renal disease

RRT: Renal replacement therapy

GFR: Glomerular filtration rate

AMIEN: Advanced Minimally Invasive Endovascular and Neurointervention

VIARAD: Visual Interaction Assistant for Radiology system

DSA: Digital Substraction Angiography

PACS: Picture Archiving Communication System

HPT: Hypertension

DM: Diabetes mellitus

HCL: Hypercholesterolemia

HD: Heart disease

ABSTRAK

Pengenalan masalah : Permasalahan salur darah sempit dan beku sering berlaku pada saluran darah fistula para pesakit hemodialisis. Rawatan awal melalui prosedur bukaan salur darah sempit (PTA) dapat membantu, tetapi timbul persoalan sejauh mana prosedur ini dapat meningkatkan fungsi hemodialisis. Setakat ini belum banyak kajian yang merungkaikan persoalan ini dan dengan itu kami menjalankan kajian yang bertajuk "Korelasi diantara salur darah sempit fistula dan parameter hemodialisis, sebelum dan selepas prosedur bukaan salur darah".

Objektif: Menentukan kaitan antara peratusan salur darah sempit fistula dengan fungsi hemodialisis.

Metodologi: Seramai 47 pesakit menjalani prosedur bukaan salur darah sempit fistula (PTA) di unit AMIEN HUSM dari bulan Jun 2014 sehingga Oktober 2015; 14 subjek ditolak kerana tidak memenuhi kriteria kajian, dan 19 hilang data menjadikan jumlah sampel sebanyak 14 sahaja. Diameter salur darah sempit fistula sebelum dan selepas prosedur bukaan salur darah sempit (PTA) diukur melalui sistem PACS, manakala informasi berkenaan parameter hemodialisis dikumpul dengan membuat panggilan telefon ke pusat hemodialisis subjek.

Keputusan: Kajian ini menunjukkan korelasi yang lemah diantara peratusan salur darah sempit dengan kadar pam darah (Qb). Tiada korelasi diantara peratusan salur darah sempit dengan tekanan vena hemodialisis (Vp). Teknikal sukses sebanyak 57.1% (P=0.001).

Kesimpulan: Kajian ini mendapati korelasi yang lemah diantara peratusan bukaan salur darah sempit dengan kadar pam darah dialisis (Qb) tetapi tidak pada tekanan vena hemodialisis (Vp).

ABSTRACT

Introduction: Stenosis and thrombosis of Arterio-Venous Fistula (AVF) has been an ongoing problem in hemodialysis patients. Early treatment by Percutaneous Transluminal Angioplasty (PTA) helps in maintaining AVF patency. However, how much PTA would improve the hemodialysis function was still questionable and only few literatures discussed on this matter. Hence, we performed a study on “Correlation of Vascular Stenosis with Hemodialysis Parameters in Native Arteriovenous Fistula (AVF), Pre and Post Percutaneous Transluminal Angioplasty”.

Objective: To determine association between percentage of residual stenosis with hemodialysis success.

Methodology: A total of 47 patients underwent Percutaneous Transluminal Angioplasty (PTA) in AMIEN Unit HUSM from June 2014 till October 2015; 14 were excluded and 19 lost to follow up leaving 14 subjects to study. All measurements of stenosis diameter were made from the PACS system whereas hemodialysis parameters were gathered through phone call to the subjects’ regular hemodialysis centre.

Results: This study has revealed a weak correlation between percentage of stenosis with blood pump flow rate (Qb) in pre and post PTA. No correlation between percentage of stenosis with venous dialysis pressure (Vp) in pre and post PTA. The achieved technical success was 57.1% (P = 0.001).

Conclusion: There is weak correlation between degree of stenosis with blood pump flow rate (Qb) but not observed in venous dialysis pressure (Vp).

Chapter 1

Introduction

Chapter 1

Introduction

End stage renal failure is a debilitating and life long illness. There are multifactorial factors which lead to this illness and the most commonly found reason is diabetes. The affected population is primarily older people but there is a prevailing trend involving patients of younger age. In Malaysia, the number of population diagnosed with ESRF has increased. In 2008, data from the National Renal Registry Malaysia reported an increase of dialysis acceptance rate to 116 per million population compared to 3 per million population recorded in 1980 (Lim *et al*., 2008).

The treatment for ESRD is a renal replacement therapy (RRT) which includes haemodialysis, peritoneal dialysis (CAPD) and renal transplant. Haemodialysis is most commonly practiced among large population due to its availability and accessibility. Haemodialysis requires vascular access. The most favourable vascular access is surgically created arteriovenous fistula (AVF) as it provides good patency with low complication rate (Tordoir *et al*., 2007) (NKF, 2006). Despite that, AVF still pose risks of developing stenosis and thrombosis; if undetected and untreated may cause AVF dysfunction. Hence, the importance of monitoring and detecting earlier signs of AVF stenosis.

There are two methods of detecting AVF dysfunction which include monitoring and surveillance. It is found that monitoring by means of physical examination is less advantageous compared to surveillance method as the former detects stenosis or thrombosis later.

Percutaneous transluminal angioplasty (PTA) is a minimally invasive procedure in which it restores the stenosed or thrombosed AVF. So far, this has become the most suggested first line procedure prior to resort to surgical revision. Beathard (1992) argues for PTA as a first line treatment for AVF dysfunction in view of shorter procedure, minimal stress to the patient, no requirement for hospitalization and this procedure enables immediate dialysis without the need for a central venous catheter. This procedure also reduces the chances of infection and preserves the rest of upper extremity veins

Reviewed literatures on post PTA successfulness primarily provides accounts on technical and hemodynamic success. Nevertheless, the term technical success was interchangeably used with anatomical success, whereas hemodynamic success was interchangeably used with clinical success. To avoid confusion, our study uses the term technical and hemodynamic success.

Numerous work in the past have reported significant successful rate of PTA in terms of technical success (Long *et al*., 2011; Tang *et al*. (1998); Tessitore *et al*., 2003) and hemodynamic success (Ahya *et al*., 2001; Long *et al*., 2011; Tang *et al*., 1998). A prospective study with 62 subjects by Tessitore *et al*. (2003) showed a technical success rate of 93.3%. Similar results were also observed in few retrospective studies with a technical success of more than 90% (Aktas *et al*., 2015; Long *et al*., 2011) , clinical success of 97.2% (Aktas *et al*., 2015), 75% (Long *et al*., 2011) and both technical and clinical success of 73% (Tang *et al*., 1998).

Nonetheless, not much studies have been done to observe in particular the correlation between percentage of stenosis and the hemodynamic improvement it caused in pre and post PTA of the intervened dysfunctional AVF. Ahya *et al*. (2001) found no correlation between changes in percentage stenosis and the improvement of blood flow post PTA, however it showed a significant correlation (p value 0.001) between pre and post PTA blood access flow regardless of the percentage of stenosis changes. In contrary to a study by Beathard (1992) there was a significant correlation between changes in percentage stenosis with venous dialysis pressure (p value <0.001).

In this study, we are looking at both venous pressure (Vp) and blood pump flow rate (Qb) as the parameters for hemodynamic success. Thus, the objective of this study is to determine association between percentages of stenosis with hemodialysis success in pre and post PTA.

The rationale of this study is to provide an overview on the importance of Vp and Qb parameters for hemodynamic success post PTA and surveillance for early detection of AVF dysfunction. In line with that, should there be any suspicion of stenosis, an early referral for fistulogram and further PTA might reduce the chances of failed or unsalvageable AVF. Moreover, dedicated surveillance will detect the early stage of stenosis, provides early intervention, higher PTA success and eventually increases the AVF longevity.

Chapter 2

Literature Review

Chapter 2

Literature Review

2.1 Introduction to End Stage Renal Failure (ESRD)

End Stage Renal Disease is the manifestation of chronic kidney disease.

2.1.1 Chronic Kidney Disease

Chronic Kidney Disease refers to kidney damaged with the presence of albuminuria or a reduction in kidney function with glomerular filtration rate (GFR) of less than 60 mL/min per 1.73m2 for 3 months duration or more. There are multistages of chronic kidney disease; stage1; GFR more than 90 mL/min per 1.73 m , stage 2; GFR 60–89 mL/min per 1.73 m , stage 3; GFR 30–59 mL/min per 1.73 m , stage 4; GFR 15–29 mL/min per 1.73 m and stage 5 (renal failure) is GFR of less than 15mL/min per 1.73 m (Levey and Coresh, 2012).

2.1.2 ESRD

Progression of chronic kidney disease to stage 5 known as ESRD with GFR less than 15mL/min per 1.73m left the renal function incompatible with life and requires treatment to replace renal function (Haynes and Winearls, 2010) either by means of dialysis, or transplantation (Levey and Coresh, 2012).

There are multifactorial causes which lead to the development of ESRD such as diabetes mellitus, hypertension, lupus nephritis, glomerulonephritis and renal stone. Hypertension and diabetes mellitus in chronic kidney disease predispose to faster progression to ESRD ("Association of Level of GFR with Complications in Adults Part 6.," 2002). It is found that diabetes accounts for higher prevalence of ESRD with 46.7% compared to hypertension which is reported at 28.4% (Wright *et al*., 2010).

In Malaysia, the number of population diagnosed with ESRD has increased. The data reported by the National Renal Registry Malaysia in 2008 points to the escalating number of dialysis acceptance rates from 3 per million population in 1980 to 116 per million population in 2008 (Lim *et al*., 2008).

2.2 Dialysis

Dialysis is one form of renal replacement therapy which is widely available as compared to renal transplant. Dialysis removes uremic toxins, excess extracellular fluid and electrolytes (sodium and potassium) by equilibrating the patient's blood to dialysate fluid with a semi-permeable membrane in between (Haynes and Winearls, 2010).There are two types of dialysis namely haemodialysis and peritoneal dialysis; the former is preferable due to its easy access and less risk of infection.

2.2.1 Haemodialysis

Haemodialysis involves an extracorporeal blood circuit and an artificial membrane to allow most small uremic toxin molecules across but small enough to ensure essential proteins are not removed. Dialysate fluid is passed in the opposite direction on the other side of the membrane so a diffusive gradient is maintained leading to toxin removal into the dialysate. The trans-membrane pressure can be increased to force extra fluid across the membrane allowing the extracellular volume to be controlled and toxins to be removed by filtration.

There have been debates concerning suitable timing of starting haemodialysis treatment. Most patients (66.4%) commenced haemodialysis with an estimated GFR between 5.0 and 10 mL/min/1.73 m2 (Wilson *et al*., 2007). It is found that patients who started dialysis at an eGFR of ≤5 ml/min per 1.73 m2 have reduced risk of mortality. An incremental increase in mortality risk however is observed in patients whose dialysis started at an eGFR >10 to 15 ml/min per 1.73 m^2 (Wilson *et al*., 2007). Patients' prognosis is to be better with lower initial GFR (Yamagata *et al*., 2012). In contrast to a study conducted by Korevaar *et al*. (2001), there is no significant differences in survival rate between late starters and timely starters.

2.3 Vascular Access

The availability of vascular access in haemodialysis patient is very important as it ensures patient received adequate treatment as per scheduled (commonly three times a week). There are two types of vascular access for haemodialysis patient. These types of access include temporary vascular access (central venous catheterization of the internal jugular, subclavian or femoral veins) and permanent vascular access (arteriovenous fistula, arteriovenous graft). Among all, arteriovenous fistula (AVF) is the best form of haemodialysis access (Zaleski, 2004). The NKF (1997) DOQI guidelines recommend that AV fistulae should be the first option in view of early patency was found in 94.0% of the AVF created (Iyem, 2011).

2.3.1 Arteriovenous Fistula (AVF)

AVF creation was first introduced by Brescia and Cimino in 1966. It is created surgically as a vascular access for hemodialysis treatment. Despite the introduction of AV grafts (PTFE graft), native AVF is still preferable due to its higher patency, low incidence of stenosis, thrombosis and infection.

There are three types of anastomosis techniques in AVF creation; namely (i) side to side anastomosis, (Sprouse Ii *et al.*) end to end anastomosis and (Sprouse Ii *et al.*) side to end anastomosis. The third technique is most commonly adopted as it avoids creation of acute angle and should thrombosis occurs, it only affects the venous limb (Konner *et al.*, 2003)

Location of fistula are grouped into: (i) distal fistula, comprises of distal radiocephalic fistula (DRCF) and radiocephalic Fistula (RCF), (Sprouse Ii *et al.*) middle radio-cephalic fistula (MRCF) and (Sprouse Ii *et al.*) proximal fistula, includes Brachiocephalic Fistula (BCF) and Brachiobasilic Fistula (BBF)(Wan Najmi, 2012)

A minimum of 28 days after creation need to be allowed for AVF to mature before it is used for hemodialysis (Rajabi-Jaghargh and Banerjee, 2015).

2.3.2 AVF Dysfunction

A dysfunctional AVF is defined as an access that is unable to provide the minimum flow (350-450 mL/min) during the 3 to 5 hour dialysis and it is clinically evident by changes in thrills pattern, difficult cannulation, recirculation, excessive bleeding from the venepuncture sites and thrombosis formation (Rajabi-Jaghargh and Banerjee, 2015).

2.3.3 AVF stenosis and thrombosis

Over time, AVF patency will be reduced due to stenosis and thrombosis formation. The pathophysiology behind this is the turbulence flow of blood created by the AVF itself which activates platelets and endothelial cells (Konner *et al*., 2003). In addition, multiple punctures over the AVF has resulted in iatrogenic remodelling of the vessel (Krönung, 1984) and formed a defect which later on replaced by thrombus (Konner *et al*., 2003). AVF thrombosis is also triggered by a critical reduction of fistula blood flow (Konner *et al*., 2003).

Basically, AVF stenosis can occur anywhere along the fistula; venous limb, ostium and arterial limb (Figure 4.3) and can be divided into inflow or outflow stenosis. An inflow stenosis is where the thrombosis formed around the anastomosis and proximal to the venous needle. An outflow stenosis is located further away from the anastomosis site and distal to the venous needle (Rajabi-Jaghargh and Banerjee, 2015). Inflow stenosis is prone to occur at the Radio-cephalic AVF, whereas the outflow stenosis is more likely to occur at the Brachiocephalic AVF (Rajabi-Jaghargh and Banerjee, 2015). The creation of the upper arm fistulae shows greater tendency to develop thrombosis (Turmel-Rodrigues *et al*., 2000) compared to forearm fistula (Zaleski, 2004).

2.4 Detection of AVF dysfunction

Early recognition of AVF dysfunction is crucial by means of continuous *monitoring* and *surveillance*. This is to preserve the AVF from functional loss or unsalvageable.

2.4.1 Monitoring

Regular physical examination of the AVF can easily be performed by the patient or by the attending staff of hemodialysis unit. It could be observed that a well-functioning fistula will have a soft continuous thrill along its outflow segment, compressible, empties on arm elevation and low pitched continuous bruit on auscultation.

Absence of thrills, a strong water hammer pulse and failure to collapse on arm elevation are more suggestive of outflow stenosis. Meanwhile a weak pulse, loss of augmentation and high pitched bruit are more suggestive of inflow stenosis. Other signs of AVF dysfunction include persistent cannulation difficulties (Tessitore *et al*., 2014) and prolonged bleeding post cannulation (Sigala *et al*., 2014; Tessitore *et al*., 2014).

AVF dysfunction has a strong association with central vein stenosis. This can be suspected in the event of unilateral arm swelling and multiple collaterals over the chest.

2.4.2 Surveillance

Fistula surveillance is divided into two; flow surveillance and pressure surveillance.

2.4.2.1 Flow surveillance

Flow surveillance include two parameters; blood pump flow rate (Qb) and access blood flow (Qa).

a) Blood pump flow rate (Qb)

Blood pump flow rate (Qb) is under documented as a surveillance parameter to detect dysfunctional fistula, whereas more research is found dedicated to access blood flow rate (Qa).

However a prospective study by Tessitore *et al*. (2003) have adopted the changes in Qb as part of their surveillance programme. In their study, subjects with decreased Qb for two consecutive hemodialysis sessions were included as candidates for PTA.

b) Access blood flow rate (Qa)

There were much literature with positive reviews on the usefulness of Qa in detecting dysfunctional fistula at early stage. The Qa is measured using ultrasound where direct and indirect measurements were performed. Direct measurement used Doppler ultrasound, whereas indirect measurement used ultrasound dilution, transcutaneous flow rate, glucose infusion, differential conductivity and ionic dialysance.

A Qa < 500 ml/min by Tonelli 2001 shows 81% positive stenosis on angiogram (Tonelli *et al*., 2001). Polkinghorne, 2006 also gave similar result where seven patients with baseline of Qa <500 ml/min showed significant stenosis at angiogram. Meanwhile, a higher strength of Qa < 900 mL/min were found positive for stenosis in a study by Tessitore *et al*. (2014).

Qa measurement showed accuracy of 73% to 80% for inflow stenosis especially when combined with physical examination (Tessitore *et al*., 2011). Blood access flow less than 1000 mL/min or 20% reduction, leads to prediction of a hemodynamically significant AVF stenosis (Schwab *et al*., 2001). Furthermore, there was a high positive predictive value of Qa to detect significant stenosis at 87% (Moist *et al*., 2003).

2.4.2.2 Pressure surveillance

Pressure Surveillance is the measurement of inherent pressure gradient between the artery and the vein across the arterial anastomosis. The change in intraaccess pressures (IAP) in an AVF depends on the site of stenosis and the presence or absence of collateral veins (Vachharajani, 2012). Direct pressure gradient measurement within the fistula provided more information regarding stenosis than ultrasound (Zaleski, 2004). According to Beathard, 1992 the normal mean Vp was 77.4+-27.4mmHg using a 16 Gauge needle, and abnormal Vp was more than 100 mmHg for three consecutive treatment (Beathard, 1992). Previous study with 112 subjects showed a high positive predictive value of Vp in detecting AVF stenosis (Moist *et al*., 2003). Similarly, a progressive increased in venous dialysis pressure (Vp) on consecutive dialysis session was associated with AVF stenosis (Konner *et al*., 2003).

On the other hand, Polkinghorne, 2006 found that Vp was a poor screening test for AVF dysfunction in which only 3 of 15 patients with high Vp were positive on angiogram (Polkinghorne *et al*., 2006). Instead, an increased derived static pressure (Vp0) of more than 0.5 with no drop in Qa level were associated with access loss or thrombosis (Tessitore *et al*., 2014).

Combination of physical examination and static venous pressure (Vp0) > 0.5 showed an excellent diagnostic performance for outflow stenosis with an accuracy >85% (Tessitore *et al*., 2011). An increased in static venous pressure (Vp0) was associated with significant stenosis at venous limb and anastomotic site as compared to dynamic venous dialysis pressure (Vp)(Smits *et al*., 2001).

2.5 Fistulogram

Suspicion of AVF dysfunction from monitoring and surveillance means will be confirmed by fistulogram. It is an imaging of the entire vascular access of AVF by injecting contrast preferably from the venous limb. From this study, the site and degree of stenosis can be evaluated.

A significant degree of stenosis has been widely defined in the literatures as a local reduction of luminal diameter of more than 50% as compared to the adjacent normal vessel

(Beathard, 1992; Long *et al*., 2011; Polkinghorne *et al*., 2006; Richard J. Gray, Amended 2014 ; Tessitore *et al*., 2003).

2.6 Percutaneous Transluminal Angioplasty (PTA)

Once AVF stenosis or thrombosis developed, choices of treatment include percutaneous transluminal angioplasty (PTA) or surgical revision. PTA is preferable method to restore blood flow for thrombosed or malfunctioning native fistula (Zaleski, 2004) because it is less invasive, highly repeatable and more access length sparing. Moreover, with PTA there will be no surgical wound, able to resume hemodialysis immediately through the intervened AVF, avoid the need for central catheter placement and reduced hospitalization (Bountouris *et al*., 2014). Napoli et al, .2010, suggested that PTA should be is the first to be done as assisted primary patency, whereas surgical revision is preserved if PTA failed (Napoli *et al*., 2010).

Definition of successful PTA is varied among different published literatures with interchangeable use of terms between technical and anatomical success, and hemodynamic and clinical success. Gary, 2003 has divided post treatment evaluation into three; anatomical success, hemodynamic success and clinical success (Gray *et al*., 2003). For the purpose of this study and to avoid confusion, we use the term of technical success and hemodynamic success.

2.6.1 Technical (anatomical) success

Technical success post PTA treatment is defined as the achievement of residual diameter stenosis of 30% (Liang *et al*., 2014) (Aktas *et al*., 2015) or less (Tessitore *et al*., 2003) (Moist *et al*., 2003) (Tessitore *et al*., 2004). On the other hand, Valji, 1995 has defined technical success of PTA as a complete opening of the stenotic AVF with evidence of palpable thrills (Valji *et al*., 1995).

2.6.2 Hemodynamic success

Hemodynamic success is the restoration of hemodynamic parameters from its predefined values (Richard J. Gray, Amended 2014). Following PTA, there will be reduction of venous dialysis or static pressures (Richard J. Gray, Amended 2014), reduced arterial inflow pressure and maintained dialysis blood flow rate (Tang *et al*., 1998). On the other hand, Gary, 2003 recommended the use of three parameters to determine PTA success which includes venous dynamic pressure, venous static pressure and access volume flows (Gray *et al*., 2003). In our setting, venous dialysis pressure (Vp) and blood pump flow rate (Qb) are two readings that readily available on hemodialysis machine during ongoing hemodialysis. They were routinely documented on patients' record book. Neither static venous pressure (Vp0) nor blood flow access (Qa) was routinely recorded. Hence further explanation is more on Vp and Qb.

a) Venous dialysis pressure (Vp)

Post- PTA showed a drop in venous dialysis pressure significantly (Richard J. Gray, Amended 2014) (Schwab *et al*., 1989).A study by Beathard,1992, post PTA showed subsequent reduction of venous pressure on follow up; 36.5% at 1 week, 32.3% at 1 month and 22% at 3month (Beathard, 1992).

b) ***Blood pump flow rate (Qb)***

To my best knowledge, not much study focused on the Qb changes in pre and post PTA study. A pilot study by Tessitore *et al*. (2003) all 32 patients who had PTA treatment showed a returned of Qb to the prescribed level with an increased by 29.0 +- 35.2 ml/min within a week post PTA.

2.6.3 *Clinical success*

Clinical success definition was taken into different perspective manner. Gary, 2003 defined clinical success of PTA as the presence of uniform thrills and the resolution of pre-PTA clinical signs such as pain, extremity edema, prolonged post dialysis bleeding and difficult access cannulation (Gray *et al*., 2003; Sprouse Ii *et al*., 2004). Whereas Valji et al., defined clinical success as the ability to resume successful dialysis within 24 hours of post treatment (Valji *et al*., 1995). Another different definition is the ability to provide adequate dialysis (Aktas *et al*., 2015) or the ability to perform at least one full dialysis treatment at 300 mL/min without recirculation (Liang *et al*., 2014) after PTA.

Chapter 3

Objectives, Hypothesis

Chapter 3

Objectives, Hypothesis

3.1 General objective

To determine the association between percentages of stenosis with haemodialysis success in patients underwent PTA.

3.2 Specific objectives

1. To correlate percentage of stenosis with venous pressure (Vp) in pre and post- PTA.
2. To correlate percentage of stenosis with blood pump flow rate (Qb) in pre and post- PTA.
3. To compare mean percentage of stenosis in pre and post PTA.
4. To compare mean of venous pressure (Vp) in pre and post PTA.
5. To compare mean of blood pump flow rate (Qb) in pre and post PTA.

3.3 Research hypothesis

There is high correlation between degree of stenosis and changes in haemodialysis parameters in pre- and post- Percutaneous Transluminal Angioplasty (PTA) of native Arterio-Venous Fistula (AVF).

Chapter 4

Methodology

Chapter 4

Methodology

4.1 Study design

This cross sectional study was conducted in Advanced Minimally Invasive Endovascular and Neurointervention (AMIEN) unit in Hospital Universiti Sains Malaysia (HUSM) from June 2014 till October 2015. This study received ethical approval from Human Research Ethics Committee of HUSM. Subjects obtained from cases referred to AMIEN unit.

4.2 Population and Sample

4.2.1 Reference population

All End Stage Renal Disease (ESRD) patients on regular hemodialysis.

4.2.2 Source population

All ESRD patients who referred to AMIEN unit HUSM for dysfunctional AVF and underwent PTA.

4.2.3 Inclusion criteria

1. All patients 18 years old and above.
2. All ESRD patients with dysfunctional upper limb AVF underwent PTA.
3. The venous pressure (Vp) and blood pump flow rate (Qb) can be traced from hemodialysis centre.

4.2.4 Exclusion criteria

1. ESRD patient on Arterio-Venous Graft (AVG).

2. ESRD patient with central vein stenosis.

3. Technical and clinical failure post PTA.

4.2.5 Sampling method

Sampling method was by purposive method.

4.2.6 Sample size calculation

For objective 1 and 2:

Sample size calculation was made based on reference from website: www.cct.cuhk.edu.hk with power of study (1-β) of 80%, significance level(α) of 0.05 and expected correlation (r) ≈ 0.5. Sample size was calculated with reference based on Lachin (1981) Controlled Clinical Trials 2: 93-113. The corrected sample size was 35 subjects.

For objective 3, 4 and 5:

Sample Size Calculator version 1.7 from website: www.medic.usm.my/biostat was used to calculate the sample size using two means comparison with power of study (1-β) of 80%, significance level (α) of 0.05, standard deviation of difference (σ) of 6.6 (Ahya *et al*., 2001), expected difference / effect size(Δ) of 3.9 and added drop out 20%. The corrected sample size was 57 subjects.

4.3 Research tools

4.3.1 Ultrasound

Preliminary ultrasound was usually performed before proceeded with fistulogram and PTA. This is done to locate the stenosis area and as a guidance for venous limb cannulation. We use the Ultrasound Colour and Power Doppler model ACUSON X300-SIEMENS, serial number 340358 from German.

To perform this examination, patient is put on supine position with the upper limb of interest is in abducted position. Gel is then applied at the area of concerned. Linear probe of 75MHz is used and the scanning performed to assess the patency of venous limb, anastomotic site (ostium) and arterial limb. Once area of puncture determined (Figure 4.1), the upper limb is cleaned and draped to make sure the sterility is maintained throughout procedure. Ultrasound probe is then cleaned and covered with sterile probe cover. Using 18G branula, venous limb cannulated under ultrasound guidance (Figure 4.2), either in longitudinal or axial plane in preference of the operator. The point of puncture is made towards the ostium, so that both ostium and venous limb can be assessed during fistulogram. Stopper is applied and branula secured with tagaderm plaster.

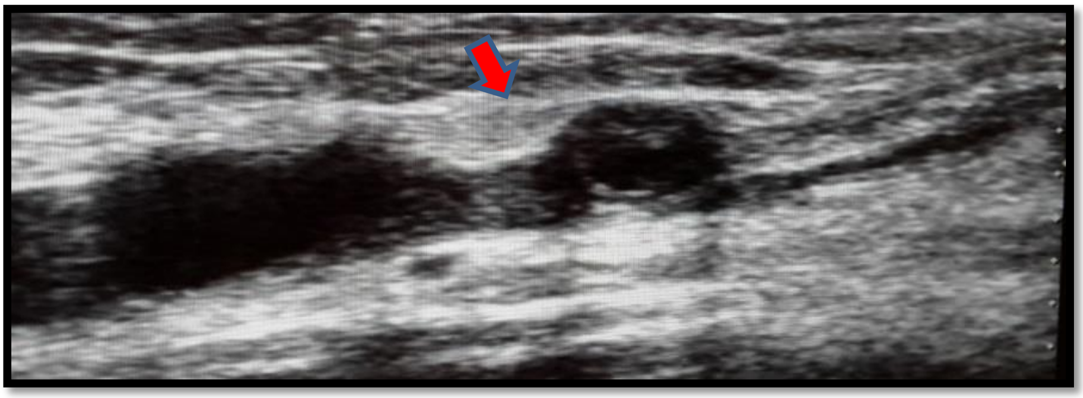

Figure 4.1: Preliminary ultrasound shows juxta-anastomosis site of stenosis (red arrow).

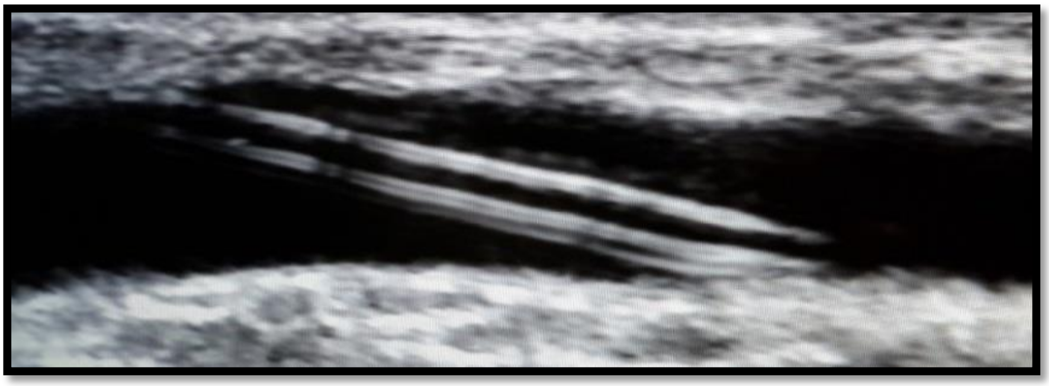

Figure 4.2: Venous limb cannulation with branula within the vessel lumen.

4.3.2 Fistulogram

Fistulogram is performed under Digital Subtraction Angiography (Moist *et al.*) guidance. We use Angiography Intraoperative Biplane AXIOM Artist Zee-SIEMENS, serial number 154004 from German. The purpose is to locate the site of stenosis (Figure 4.3) and to measure diameter of the affected vessel so that the appropriate selection of catheter and balloon can be made.

A 10 mls syringe filled with iodinated contrast (Visipaque 320mg/I) is connected to the branula through butterfly needle. Contrast was injected under fluoroscopy guidance and images were taken.

After fistulogram, central venogram of the ipsilateral site is proceeded. Sample with central venous stenosis is excluded. Assessment of central vein patency is important as it is closely related to AVF patency. Central vein represent the final common pathway for blood flow from the peripheral vessels to the heart. As the central vein stenosis progresses, back flow of blood to the AVF triggers further thrombosis formation and frequently end up with AVF dysfunction.

Once fistulogram done, the images were evaluated to locate the site of stenosis; ostium, venous limb or arterial limb (Figure 4.6). Measurement for diameter of stenosis and diameter of adjacent normal venous limb were then documented. If fistulogram finding is permissible, PTA will be proceeded. If the findings showed that it was not amenable for PTA in which there was a total occlusion, surgical revision were advised.