ASSOCIATION OF CLINICAL AND RADIOLOGICAL FACTORS WITH THE OUTCOMES OF CENTRAL VENOPLASTY AMONG END-STAGE RENAL DISEASE PATIENTS IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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UNIVERSITI SAINS MALAYSIA

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by

DR OTHMAN BIN PUTEH

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DISCLAIMER

I declare that this dissertation records the results of the study performed by me and that it is of my composition.

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(OTHMAN BIN PUTEH)

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LIST OF SYMBOLS, ABBREVIATIONS, AND ACRONYMS

AMIEN	Advanced Minimally Invasive Endovascular and Neurointervention
AV	Arteriovenous
AVF	Arteriovenous Fistula
BCV	Brachiocephalic Vein
CVS	Central venous stenosis
DM	Diabetes Mellitus
HPT	Hypertension
HUSM	Hospital Universiti Sains Malaysia
IJV	Internal Jugular Vein
IVC	Inferior Vena Cava
KDOQI	Kidney Disease Outcomes Quality Initiative
NKF	National Kidney Foundation
PACS	Picture Archive Communication System
SCV	Subclavian Vein
SVC	Superior Vena Cava

ABSTRAK

Latar belakang: Stenosis vena pusat adalah komplikasi umum pada pesakit penyakit ginjal peringkat akhir yang menerima terapi hemodialisis dan venoplasty pusat kini merupakan rawatan utama. Namun, tidak semua pesakit yang menjalani venoplasty pusat mendapat hasil yang baik. Kajian ini bertujuan untuk menentukan hubungan antara faktor radiologi dan faktor klinikal yang menentukan kadar kejayaan venoplasty pusat.

Metodologi: Kajian keratan rentas retrospektif yang dilakukan di Advanced Minimally Invasive Endovascular and Neurointervention (AMIEN) Unit, Hospital Universiti Sains Malaysia (HUSM) pada 62 pesakit yang mengalami stenosis vena pusat atau oklusi dan dirawat dengan venoplasty pusat di Hospital HUSM 1 Januari 2016 hingga 31 Ogos 2020. Pemboleh ubah radiologi (lokasi, tahap dan jarak stenosis) dan pemboleh ubah klinikal (jantina, diabetes mellitus (DM) dan darah tinggi (HPT)) dinilai sebelum venoplasty pusat. Hubungan antara faktor radiologi dan klinikal dengan hasil venoplasty pusat dikira menggunakan Ujian Chi-Square.

Keputusan: Sebanyak 62 pesakit dimasukkan dalam kajian kami. Tidak ada hubungan yang signifikan antara lokasi urat, tahap jarak stenosis dengan hasil kejayaan. Walau bagaimanapun, penglibatan satu salur darah mempunyai kadar kejayaan yang jauh lebih tinggi (92.6%) berbanding dengan penglibatan beberapa salur darah (7.4%). Selain daripada faktor radiologi, faktor klinikal (jantina, DM, dan HPT) juga tidak menunjukkan perkaitan yang signifikan dalam menentukan hasil yang berjaya dengan nilai p masing-masing 0.159, 0.644 dan 0.283 (melebihi 0.05).

Kesimpulan: Tidak ada kaitan faktor demografi, klinikal dan radiologi dengan hasil venoplasty pusat di kalangan pesakit penyakit ginjal peringkat akhir. Kajian lebih lanjut perlu dilakukan dengan ukuran sampel yang lebih besar dan faktor penentu lain yang mungkin untuk membantu memudahkan prosedur di masa depan.

Kata kunci: Stenosis vena pusat, Venoplasti pusat, Panjang stenosis, Tahap stenosis, Lokasi stenosis.

ABSTRACT

Background: Central venous stenosis is a common complication in end-stage renal disease patients receiving hemodialysis therapy, and central venoplasty is currently the mainstay treatment. However, not all patients undergoing central venoplasty have a successful outcome. This study aims to determine the association between radiological factors and clinical factors determining the success rate of central venoplasty.

Methodology: A retrospective cross-sectional study was conducted in Advanced Minimally Invasive Endovascular and Neurointervention (AMIEN) Unit, Hospital Universiti Sains Malaysia (HUSM) on 62 patients with central venous stenosis or occlusion and were treated with central venoplasty in Hospital HUSM 1st January 2016 until 31st August 2020. Radiological variables (location, grade, and length of stenosis) and clinical variables (gender, diabetes mellitus (DM), and hypertension (HPT) were assessed before central venoplasty. The association between the radiological and clinical factors with the outcome of central venoplasty was calculated using Chi-Square Test.

Results: A total of 62 patients were included in our study. There was no significant association between the location of veins, degree, and length of stenosis with the successful outcome. However, a single vein had a significantly higher success rate (92.6%) than multiple veins (7.4%). Apart from the radiological factors, the clinical factors (gender, DM, and HPT) also show no significant association in determining successful outcomes with p values 0.159, 0.644 and 0.283 respectively (more than 0.05).

Conclusion: There is no association between clinical and radiological factors with the outcomes of central venoplasty among end-stage renal disease patients. A further study needs to be conducted with a larger sample size and other possible determining factors to help facilitate the procedure in the future.

Keywords: *Central venous stenosis (CVS); Central venoplasty, Length of stenosis, Degree of stenosis, Location of stenosis*

CHAPTER 1: BACKGROUND

1.1 Introduction

Central venous stenosis or obstruction(CVS) is defined as 50% or more narrowing of the superior vena cava (SVC), brachiocephalic vein (BCV), or subclavian veins (SV) (Cuthbert *et al.*, 2018). The pathophysiology of CVS is the development of venous intimal hyperplasia that can be due to multiple causes. The most common one is central venous catheterization. Other causes of CVS include central venous port catheters, pacemakers, and defibrillator wires (Modabber and Kundu, 2013). CVS will cause outflow obstruction of the arteriovenous fistula among hemodialysis patients, leading to venous hypertension. Untreated CVS will cause upper limb edema and compromise the function of the arteriovenous fistula. The incidence of CVS in hemodialysis patients is 29% (Lumsden *et al.*, 1997). According to Cuthbert et al., central venoplasty is a balloon angioplasty of the brachiocephalic, subclavian, or superior vena cava" (Cuthbert *et al.*, 2018). Nowadays, central venoplasty is the first-line management of CVS rather than surgical treatment because of less morbidity and mortality associated with venoplasty (Huang *et al.*, 2016). However, despite recognizing venoplasty as the mainstay of therapy, one-fifth of the total cases still needs to undergo re-plasty. Some are finally subjected to surgical repair (Medicine, no date; Kovalik *et al.*, 1994). Factors associated with successful venoplasty, such as location, length, and grade of stenosis, are still debatable. Some studies conclude that these factors influence the outcome, while some do not. Furthermore, most of these studies focus on fistuloplasty and not central venoplasty.

Problem statement and study rationale

Central venoplasty is the current mainstay treatment for CVS. However, not all CVS patients can be managed with this treatment successfully. Some of the patients will need surgical repair to solve their symptoms. This study aims to determine the association between radiological factors such as the location of the stenosis, the degree of stenosis, and the length of stenosis with the success rate of central venoplasty. Most of the previous studies on CVS are related to fistuloplasty and its' patency. We, however, assess all types of CVS.

Moreover, most previous studies assessed acute stenosis cases due to periodic assessment (prophylaxis, fistulogram, and ultrasound Doppler) and high awareness in European countries. This is not the same with our scenario in which most patients present with chronic obstruction. Some cases are total occlusion complicated with Arterioenous(AV) dysfunction. Other than that, we do not know the rate of central venoplasty success in our center, although an increasing number of cases of central venous occlusion undergoing central venoplasty lately. Thus, if the factors significantly affect the success rate of the procedure identified, we can propose a predictive model in the future for patient selection. Such a model will allow appropriate patient selection and maximize the outcome. We also measure the success rate of central venoplasty done in this center.

1.2 Objectives

1.2.1 General objective

To study the outcomes of central venoplasty among the end-stage renal disease patient in Hospital Universiti Sains Malaysia (HUSM), Kubang Kerian.

1.2.2 Specific objectives

1. To determine the association between the location of the stenosis, the degree of the stenosis, and the length of the stenosis with the outcome of central venoplasty.
2. To determine the association between clinical factors (gender, hypertension and diabetes mellitus, other causes) with the outcome of central venoplasty.

1.3 Research Questions

1. What is the success rate of central venoplasty in HUSM?
2. Is there any association between radiological factors such as the location of the stenosis, the degree of the stenosis, and the length of the stenosis with the outcome of central venoplasty in HUSM?
3. Is there any association between clinical factors such as gender, hypertension, and diabetes mellitus with the outcome of central venoplasty in HUSM?

CHAPTER 2: LITERATURE REVIEW

The National Kidney Foundation Kidney Disease Outcomes Quality Initiative(NKF KDOQI) guideline states that stenosis should be treated if there is a significant clinical, physiological, or anatomical abnormality ('Medium Term Strategic Plan to Reduce the Burden of Chronic Kidney Disease in Malaysia (2018-2025)). Clinical and physiologic abnormality is a decreased access blood flow (<600ml/min), elevated venous pressure, decreased dialysis dose, or abnormal physical examination, whereas anatomic abnormality is more than 50% stenosis. Patients who have central venous stenosis can either be symptomatic or asymptomatic. It can be detected using a diagnostic venogram or fistulogram before access placement for an immature fistula.

Signs and symptoms due to central venous stenosis depend on the anatomic location of the stenosis or obstruction. Narrowing or occlusion of the subclavian vein usually presents with edema or venous hypertension of the corresponding extremity or breast. Brachiocephalic vein stenosis affects blood flow from the ipsilateral side of the face and the upper limb and breast, leading to edema of the ipsilateral upper limb and facial edema. Approximately only 50% of patients with significant central venous stenosis will develop ipsilateral upper-extremity edema (Schwab *et al.*, 1988; Cuthbert *et al.*, 2018). When a functional ipsilateral upper extremity AV access has been created, edema tends to be more pronounced (Nakhoul *et al.*, 2005). Edema, with acute swelling, tenderness, pain, and erythema, which can mimic cellulitis, can occur when AV access is continuously used despite blockage. Breast enlargement associated with hemodialysis arteriovenous fistulae, especially with a history of subclavian catheterization, may indicate central vein stenosis (Techanithisawat, Boonjunwetvat, and Chatamra, 2020).

CVS can present with numerous dilated collaterals in the neck or chest with arm swelling or dilated tortuous draining veins of the fistula. SVC syndrome can also occur when a

bilateral innominate vein or SVC is stenosed or occluded (Mehta, 2017). It is a group of symptoms, most commonly shortness of breath followed by face or arm swelling. In an acute setting, early intervention by an interventional radiologist can relieve the symptom within 12 to 24 hours. Evidence of AV access dysfunction, decreased access flows, increased venous pressures during dialysis, and a history of excessive bleeding from the puncture site after removing the needle are the consequences of central venous stenosis.

Nowadays, central venoplasty is the first-line management of CVS rather than surgical treatment, given less morbidity and mortality associated with venoplasty (Huang *et al.*, 2016). However, despite recognizing venoplasty as the mainstay of therapy, one-fifth of the total cases still needs to undergo re-plasty. Some patients are finally subjected to surgical repair (Medicine, no date; Kovalik *et al.*, 1994). Several factors are associated with successful venoplasty, such as location, length, and grade of stenosis. Clinical factors such as patient gender and age, age of the Arteriovenous Fistula (AVF), AVF type (brachiocephalic, brachiobasilic, etc.), side of access (left or right arm), and diabetes mellitus also influence the success rate of plasty (Maeda *et al.*, 2005; Heye *et al.*, 2012). However, most of these studies focus on fistuloplasty rather than central venoplasty. In these studies, there is some mention of a strong association between the location of stenosis to the outcome of the angioplasty and patency (Medicine, no date; Heye *et al.*, 2012). Heye *et al.* (2012) also added that the initial grading of stenosis is linear to the success rate of fistuloplasty.

Location

Central and peripheral veins are the terms that are widely used in medicine. They are essential to the planning and management of dialysis vascular access. As can be seen from Figure 1 (Dolmatch *et al.*, 2018), the central thoracic veins include intrathoracic segments of the internal jugular veins (IJVs), subclavian veins (SCVs), BCVs, SVC, and the suprahepatic portion of the inferior vena cava (IVC). These veins are central to the superior thoracic aperture (C7–T1 intervertebral disc level), central to the lateral margin of the first rib margin, and superior to the diaphragmatic caval opening. Anomalies of the central thoracic veins have been described. The most common, found in 0.3% of people, is the persistence of the left SVC, typically seen along with a right-sided SVC. The left SVC is almost always an incidental finding and carries venous flow from the left BCV to the coronary sinus. Given its infrequent occurrence, the role of left-sided SVC in the thoracic central vein occlusion remains unknown. Other thoracic central vein anomalies are much less common and, therefore, not mentioned in these reporting standards (p.455).

Other than this, the axillary vein is sometimes included as part of the central vein (Mehta, 2017). The brachial and basilic veins join at the lower border of the teres major muscle to form the axillary vein, which passes anteriorly to the subscapularis muscle and posteriorly to the pectoralis minor muscle near its insertion at the coracoid process. The axillary vein continues to the lateral border of the first rib, where it becomes the subclavian vein (SV), which enters the thoracic inlet posteriorly to the clavicle and anteriorly to the first rib and scalenus anticus muscle (costoclavicular space) and joins the IJV after several centimeters to become the BCV. The right and left BCV to combine in the mediastinum to form the SVC. Mehta (2017), Glanz *et al.*, (1988), Trerotola *et al.*, (2004) mention the axillary vein as part of the central vein.

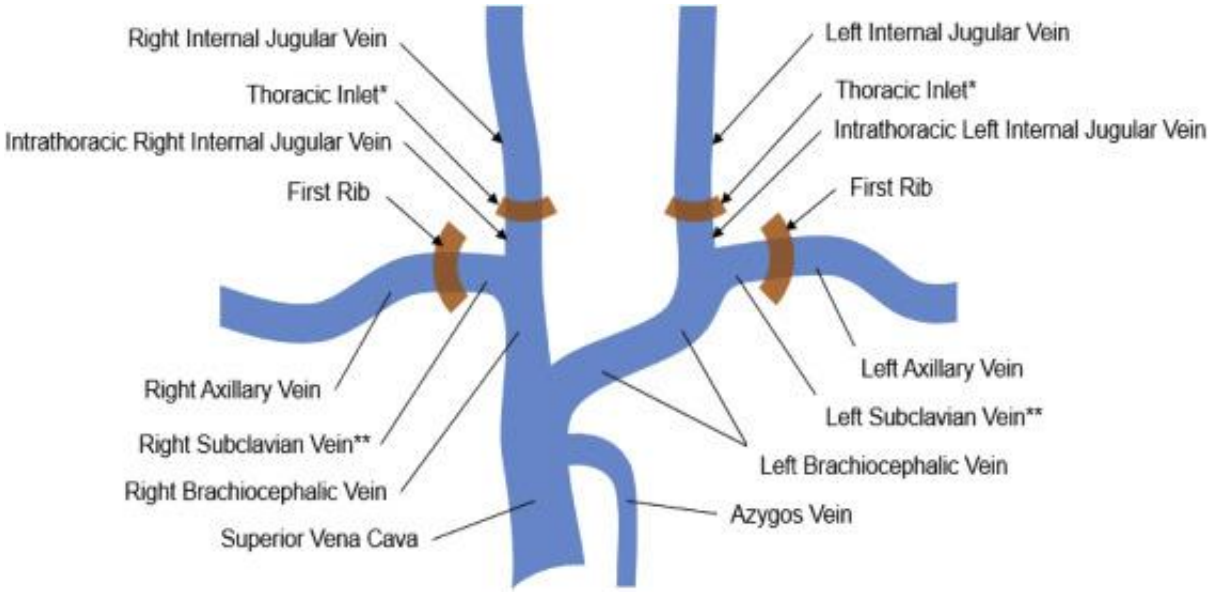

Figure 1: Thoracic central vein (Dolmatch *et al.*, 2018**)**

Based on the cavogram of the SVC, stenosis can be classified into four types (Neuen *et al.*, 2014). Type I, partial obstruction (up to 90% stenosis) of the SVC with patency of the azygos vein; type Il, near-complete to complete obstruction (90-1 00%) of the SVC with patency and blood flow through the azygos vein into the right atrium; type Ill, near-complete to complete obstruction (90-100%) of the SVC with reversal of azygos blood flow; type IV, complete obstruction of the SVC and one or more of the major caval tributaries, including the azygos system.

Grade of stenosis.

Ahn *et al.* (2014) advocate a venogram to determine the degree of stenosis of SV and IJV. It measures the diameter of a stenosed vessel compared to the patent vessel. In this study, duplex ultrasound is not used because of obstructing shadow from the clavicle. By these measurements, stenosis is divided into a high grade (Stenosis area >66%), medium grade (stenosis

33-66%), and low grade (stenosis <33%). However, several other studies use different classifications. Some states that venogram can be divided into normal, equivocal, and abnormal as the vein is more distensible(Barrett *et al.*, 1988). The absence of vessel narrowing is considered normal, while the vein is considered abnormal if there is a presence of irregularity or any narrowing. They classify equivocal changes as minor changes to the vessel other than stenosis. On the other hand, Maeda et al. (2005) only classify the stenosis grade into stenosis and occlusion. Despite multiple studies classifying the stenosed vein differently, central venoplasty is generally not performed on veins (central and peripheral) with less than 50% stenosis. Therefore, the most suitable classification is mild (stenosis less than 50%), moderate (stenosis between 50%-75%), as well as severe (more than 75% stenosis) (Romann *et al.*, 2016).

Length of stenosis

The length of the stenosis can be divided into short-segment and long-segment stenosis. Most institutions now define long-segment stenosis as a stenosed area longer than 5 cm long (Surgery and Washington, 1997; Cuthbert et al., 2018; Sidhu et al., 2016).

Successful treatment of venoplasty is defined as the presence of less than 30% residual stenosis after treatment with venoplasty (Sidhu *et al.*, 2016; Cuthbert *et al.*, 2018). This is classified as technical success. Clinical success is the reduction of limb swelling or edema (Modabber and Kundu, 2013). However, clinical success is challenging to measure because detailed clinical history is sometimes not well recorded.

2.1 Conceptual framework

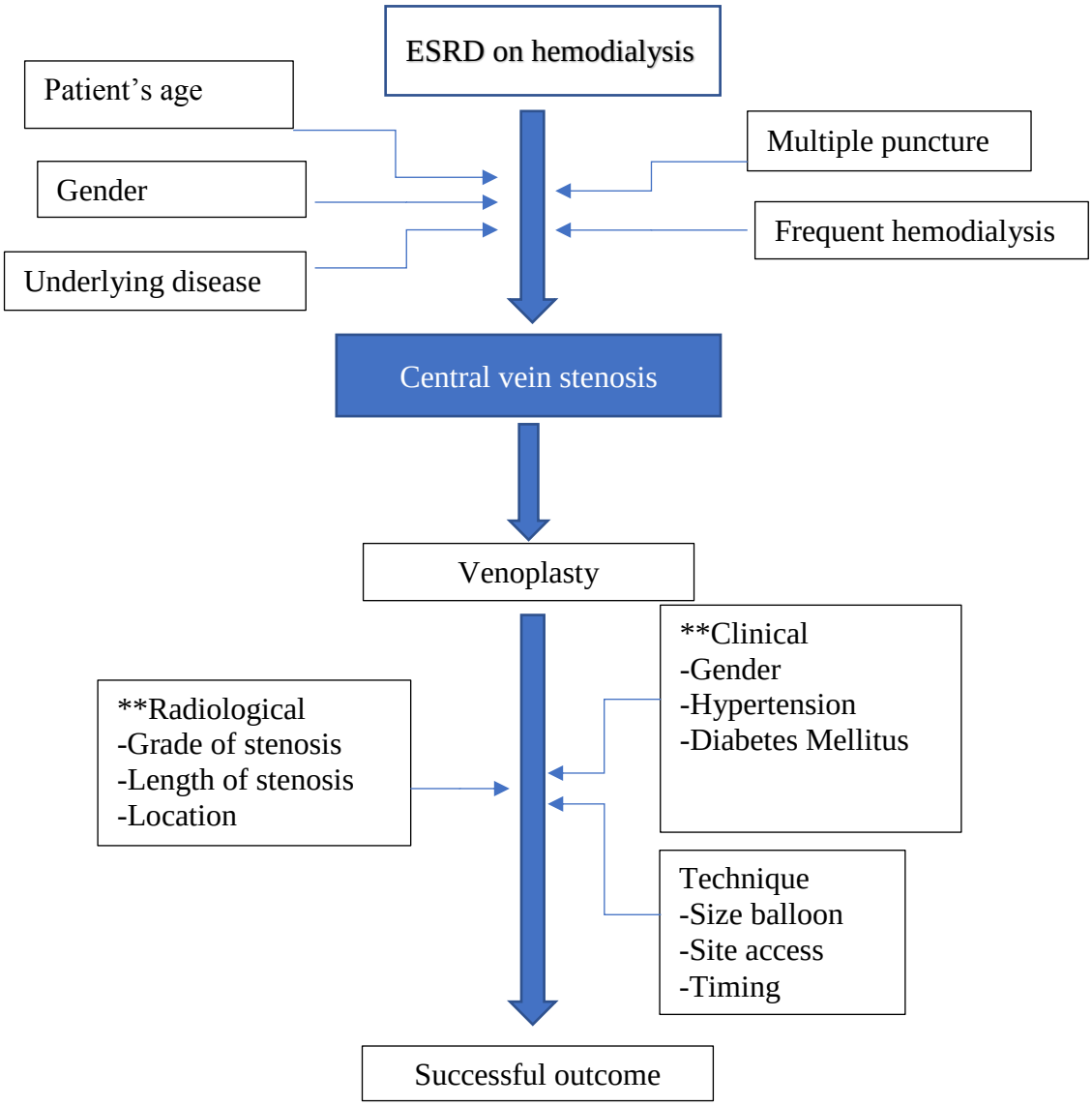

Figure 2: Conceptual framework

CHAPTER 3: METHODOLOGY

3.1 Study Design

Cross-sectional study using secondary data.

3.2 Study Location and Duration

This study was conducted in Advanced Minimally Invasive Endovascular and Neurointervention (AMIEN) Unit, Hospital HUSM. This study was conducted from 1st November 2020 to 30th October 2021. Data from 1st January 2016 until 31st August 2020 were reviewed.

3.3 Study Population and Sample

Reference population:

Patients who are having central venous stenosis or occlusion.

Source population:

Patients who have central venous stenosis or occlusion and were treated with central venoplasty in Hospital HUSM

Target population:

Patients who have central venous stenosis or occlusion and were treated with central venoplasty in Hospital HUSM from 1st January 2016 until 31st August 2020

Sampling frame:

Patients who underwent central venoplasty, according to the PACS list, from 1st January 2016 until 31st August 2020 and fulfilled the inclusion and exclusion criteria.

3.4 Inclusion Criteria

1. All patients underwent central venoplasty.
2. Age 18 years and above.
3. End-stage renal disease patient.

3.5 Exclusion Criteria

1. Inadequate/incomplete pre-plasty imaging or patient record.
2. Other causes of central venous occlusion such as:
    a) Complications of central venous port - Patients with central venous port devices subjected to prolonged chemotherapy drugs and parenteral nutrition may develop venous thrombosis rather than stenosis (Machat *et al.*, 2019).
    b) Mechanical trauma due to clavicle fracture.
    c) Effort-induced thrombosis (Paget von Schroetter syndrome) which affects healthy young individuals.
    d) Pancoast tumor and lung malignancy(Marulli *et al.*, 2016).
    e) Clotting factor deficiency such as Antithrombin III deficiency.
    f) Idiopathic due to thrombosis caused by occult malignancy or coagulation abnormality.
3. Mild central vein stenosis (less than 50% occlusion).

3.6 Sample Size Calculation

The sample size was calculated using the two-proportion formula.

$$n = (Z_{\alpha/2}+Z_{\beta})^2 * (p_1(1-p_1) + p_2(1-p_2)) / (p_1-p_2)^2,$$

Where $Z_{\alpha/2}$ is the critical value of the Normal distribution at $\alpha/2$ (e.g., for a confidence level of 95%, α is 0.05, and the critical value is 1.96), Z_{β} is the critical value of the Normal distribution at β (e.g., for a power of 80%, β is 0.2, and the critical value is 0.84) and p_1 and p_2 are the expected sample proportions of the two groups (Wang and Chow, 2014)(Figure 3).

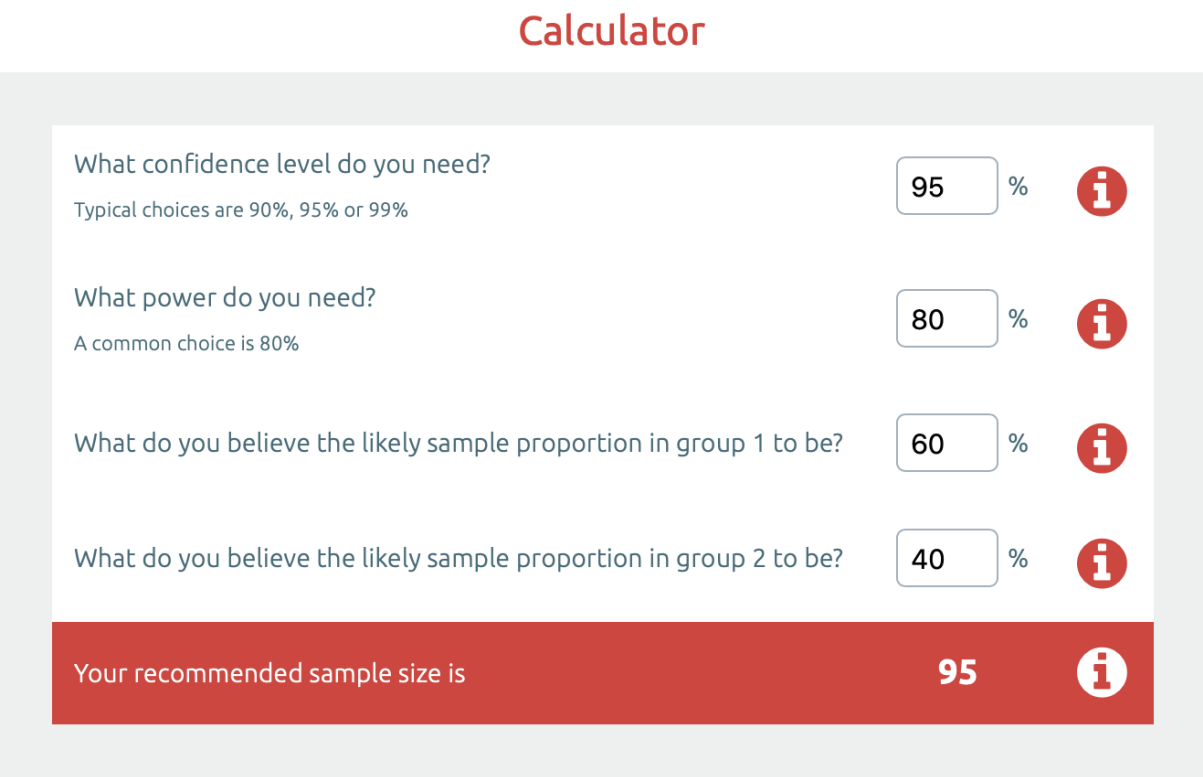

Figure 3: Comparing Two Proportions – Sample Size [Calculator] Retrieved from https://se-lect-statistics.co.uk.

Objective 1:

Location.

In a previous study by Surowiec et al. (2004), two out of five patients with stenosis at the superior vena cava who underwent central venoplasty failed in their initial treatment; the percentage success was 60%. However, only one of the fourteen patients with stenosis at the brachiocephalic vein failed in central venoplasty; the percentage success was 92%.

	P0(%)	P1(%)	n
Location	92	60	25

P0- Percentage of success central venoplasty in brachiocephalic vein.
P1- Expected percentage of success central venoplasty in superior vena cava.

Objective 2:

Clinical factor.

(Mohiuddin *et al.,* 2018), in their study, the percentage of a successful outcomes in the hypertension group was 48%.

	P0	P1	n
Demographic	48	72	62

Based on the sample size calculation for objectives 1 and 2, the highest sample size required is 62.

3.7 Research Tools

1. Patients' case notes for the demographic data.
2. Picture Archive And Communication System (PACS Universal Viewer Version 5.0 SP6)
3. Angio machine biplane

3.8 Variable Definition

1. **End-stage renal disease** is defined as kidney function no longer sufficient to sustain life (Ministry of Health Malaysia. 2018. National Action Plan for Healthy Kidney 2018-2025.
2. **Central venous stenosis (CVS)** is defined as 50% or more narrowing of the superior vena cava, brachiocephalic or subclavian veins (Cuthbert *et al.*, 2018).
3. **Central vein** includes axillary, subclavian, brachiocephalic, and superior vena cava (Dolmatch *et al.*, 2018).
4. **Location** is divided into axillary, subclavian, brachiocephalic, and superior vena cava (Dolmatch *et al.*, 2018)(Figure 1).
5. **The degree of stenosis** is identified as mild (<50%), moderate(50-75%), and severe (>75%) (Romann *et al.*, 2016).
6. **Length of stenosis**:

   Short segment stenosis is less than 5 cm.
   Long segment stenosis is more than 5 cm (Surgery and Washington, 1997).
7. **Successful central venoplasty** is defined as less than 30% residual stenosis per the Society of Interventional Radiology (SIR) guidelines immediately after the procedure (Sidhu *et al.*, 2016; Cuthbert *et al.*, 2018).
8. **Hypertension** is defined as the persistent elevation of systolic BP of 140mmhg or greater and/or diastolic BP of 90 mmHg or greater (Clinical Practice Guideline on Management of hypertension-4th edition, 2013)

9. **Diabetes Mellitus** is a chronic hyperglycemic state in conjunction with other metabolic derangements (CPG on Management of Diabetes Mellitus, 2015).

3.9 Data Collection

3.9.1 Subject recruitment

Angiography images of the patients who had undergone central venoplasty at Hospital Universiti Sains Malaysia were retrieved from the PACS system. Subject's information, i.e., age, gender, location, grading, and length of stenosis, were recorded in the data collection sheet.

3.9.2 Data Acquisition and Image Analysis

By using the Picture Archive and Communication System (PACS), Digital Subtraction Angiography (DSA) images of central venoplasty was reviewed. The demographics and radiological findings were recorded in the data collection sheet. Radiological variables assessed are location, grade, and length of stenosis before and after central venoplasty. The location of stenosis was identified as the axillary, subclavian, brachiocephalic, subclavian, brachiocephalic junction, or superior vena cava. The degree of stenosis was calculated from the initial DSA image. The grade of stenosis was measured against the diameter of the adjacent normal vein segment or graft. When stenosis was juxta-anastomotic, the vein segment preceding the stenosis or the size of the anastomosis was used. Stenosis is divided into mild (<50%), moderate(50-75%), and severe (>75%) Fields(Romann *et al.*, 2016).

Example:

Figure 4: Central venogram pre venoplasty

In this image, the grade of stenosis was calculated as 79% by 100 x (1-[26/127.77]); therefore, it is high-grade stenosis. (Figure 4)

The length of stenosis was measured using calipers in PACS. Length over 5 cm was considered long-segment stenosis, whereas less than 5cm was considered short-segment stenosis. Pre- and post-venoplasty venous stenosis was measured with electronic calipers from stored PACS images. Technical success is achieved when the residual stenosis is less than 30% compared to the preprocedural measurements per the Society of Interventional Radiology (SIR) guidelines (Sidhu *et al.*, 2016; Cuthbert *et al.*, 2018). Failure of treatment is defined as the presence of residual stenosis of more than 30% compared to the initial stenosis or lesion cannot be crossed or pass through (Surowiec *et al.*, no date)

Example:

Figure 5: Central venogram following venoplasty

Post venoplasty measurement 100 x (1-[97.65/124.17] =21%.

- The value of residual stenosis is 20 %; therefore, it is considered a successful procedure. (Figure 5)

All data were reviewed by two Interventional Radiologists with more than five years of experience who verified the findings.

By using case notes:

Patient demographics, including age, sex, ethnicity, and concurrent medical illness, were recorded. In addition, clinical signs and symptoms of central stenosis, such as ipsilateral limb edema, limb tenderness, and dilated collateral vein, were recorded. Clinical success was determined by the reduction of limb swelling or edema (Modabber and Kundu, 2013). However, these features were not assessed in this study.

3.10 Statistical Analysis and Hypothesis

I. All quantitative data were analyzed using Microsoft® Office Excel and Statistical Product and Service Solutions (SPSS) for Windows, SPSS Inc.© (version 26.0, SPSS Inc., Chicago, IL, USA).

II. Histogram and chart were used to present the numerical and categorical data. All categorical data were presented in frequency and percentage, while the numerical data were presented in mean and standard deviation.

III. The outcome was compared using the appropriate Chi-Square or Fisher's exact test.

IV. The P value of less than 0.05 was considered statistically significant.

3.11 Confidentiality and Privacy

All data were anonymous and entered into SPSS software. Only research team members can access the data. Data were presented as grouped data and did not identify the responders individually.

3.12 Ethical Consideration

I. Ethical approval

   a. The research has received ethical approval Human Research Ethics Committee of Universiti Sains Malaysia (JEPeM code: USM/JEPeM/21030252), which complies with the Declaration of Helsinki (Appendix E).

II. Informed Consent/Assent Process

   a. Approval to use the data taken from the hospital's director. The study utilizes secondary data. Additional Informed consent is not needed.

III. Subject vulnerability

a. Not applicable.

IV. Declaration of absence of conflict of interest

a. The investigators declare they have no conflict of interest.

V. Community sensitivities and benefits

i. There was no issue arose that affected the community sensitivities. The study result could help improve patient selection for future central veno-plasties.

VI. Publication policy

i. No personal information will be disclosed as the subjects will not be identified individually when the study findings are published.

3.13 Study Flowchart

Source population:
- Patients who are having central venous stenosis or occlusion in Hospital USM from PACS.

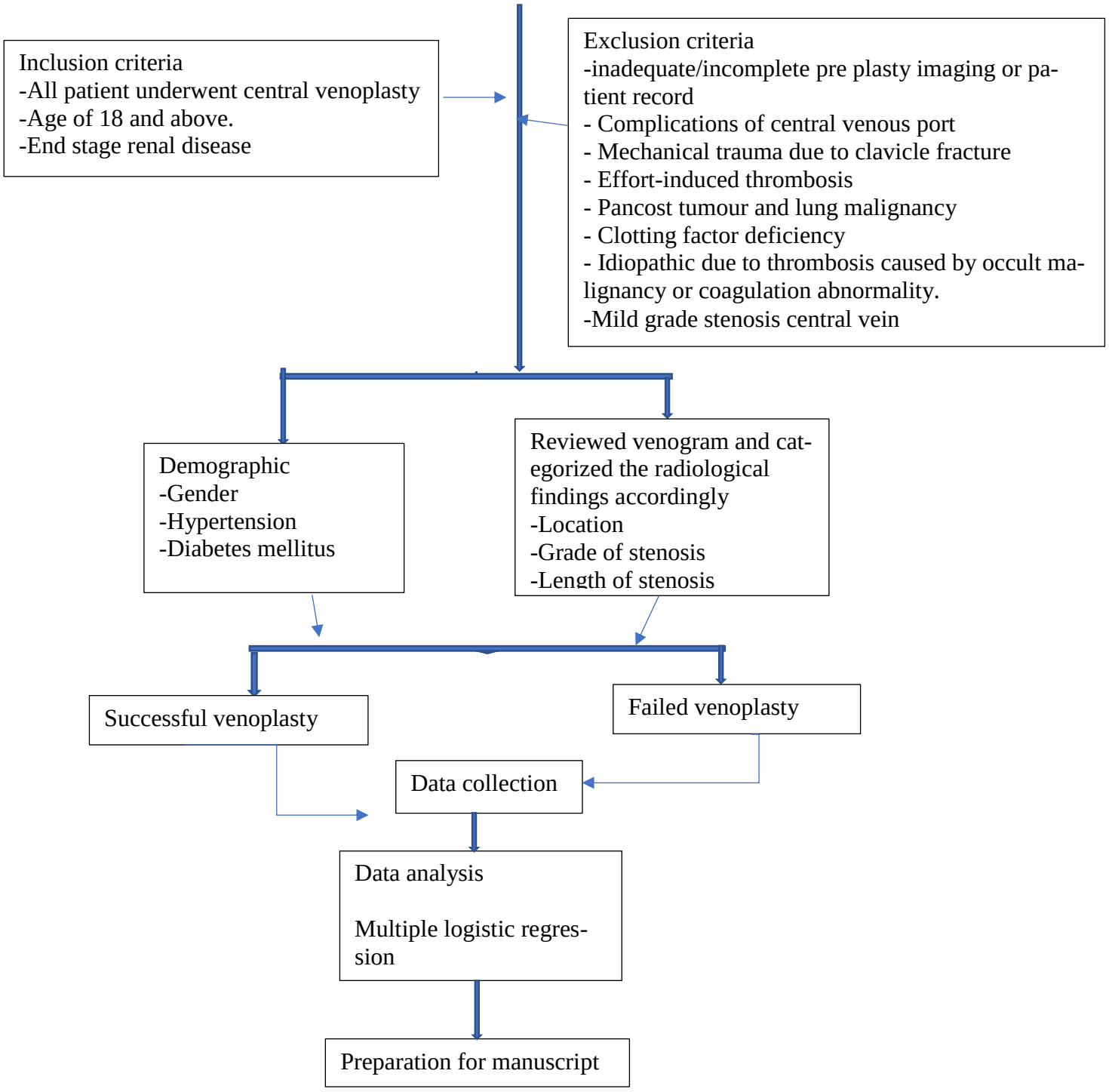

Figure 6: Study Flowchart

CHAPTER 4: MANUSCRIPT

Title: