THE OPTIMAL TIME FOR BLOOD PRESSURE MEASUREMENT IN END-STAGE RENAL FAILURE PATIENTS ON REGULAR HEMODIALYSIS IN HOSPITAL UNIVERSITY SAINS MALAYSIA

KURNIA PRIMA SAWAI BIN SUARDI

MBBS (IIUM)

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LIST OF ABBREVIATIONS

ABPM	Ambulatory Blood Pressure Monitoring
CKD	Chronic Kidney Disease
ESRF	End Stage Renal Failure
HD	Hemodialysis
HUSM	Hospital University Sains Malaysia
IVC	Inferior Vena Cava
RRT	Renal Replacement Therapy

ABSTRAK

Pengenalan: Masa dan kaedah yang terbaik untuk mengambil bacaan tekanan darah dalam kalangan pesakit kegagalan buah pinggang peringkat akhir yang sedang menjalani rawatan haemodialisis masih belum dapat ditentukan. Selepas prosedur haemodialisis, plasma dari interstitium akan kembali ke dalam salur darah. Masa sebenar proses keseimbangan berlaku tidak diketahui. Diameter "inferior vena cava" mencapai ukuran normal apabila pesakit dalam keadaan "euvolemia". Kaedah ukuran ultrasonografi secara langsung boleh digunakan unutk mengetahui samaada pesakit telah mencapai "euvolemia". Masa apabila diameter "inferior vena cava" normal adalah waktu terbaik untuk mengambil tekanan darah memandangkan pada saat ini paras air dalam badan adalah normal.

Objektif: Mengenalpasti waktu yang paling tepat untuk mengambil tekanan darah selepas rawatan haemodialisis. Mengenalpasti variabiliti tekanan darah dalam tempoh 24 jam termasuk 4 jam selepas dialisis.

Kaedah: Ini adalah satu kajian keratan rentas melibatkan 14 pesakit buah pinggang yang menjalani rawatan hemodialisis secara berkala di pusat hemodialisis, HUSM. Pesakit diminta memakai alat tekanan darah 24 jam yang akan mengambil tekanan darah setiap jam selama 24 jam bermula hari sebelum hemodialisis sehingga 4 jam selepas hemodialysis. Selepas hemodialisis, diameter "inferior vena cava" dan tekanan darah akan diukur pada 10, 30 dan 60 minit selepas tamat rawatan hemodialisis. Keputusan dipersembahkan dalam bentuk median untuk data yang taburannya tidak normal dan purata untuk data yang taburannya normal.

Keputusan: Diameter vena cava inferior pada 10 minit selepas hemodialisis adalah kecil, kemudian menjadi normal pada 30 minit dan tiada perubahan pada 60 minit. Tekanan darah selepas hemodialisis lebih menghampiri nilai purata pada waktu 60 minit selepas dialisis. Kajian ini juga mendapati tiada perbezaan ketara dari segi perubahan purata tekanan darah 24 jam.

Kesimpulan: Waktu yang paling tepat untuk mengambil bacaan tekanan darah selepas rawatan haemodialisis adalah selepas 60 minit. Kajian ini juga mendapati tiada perbezaan ketara dari segi perubahan purata tekanan darah.

Kata kunci: kegagalan buah pinggang peringkat akhir, hemodialisis, diameter "inferior vena cava"

ABSTRACT

Introduction: The appropriate time and method of blood pressure measurement in end stage renal failure (ESRF) patients on regular hemodialysis is still uncertain. During post-hemodialysis, refilling of plasma volume from the interstitium took place. Therefore, the exact timing of when blood volume reaches equilibrates is uncertain. The inferior vena cava diameter normalizes when patient is euvolemic. Therefore, ultrasonographic direct measurement of inferior vena cava can be used to reflect the euvolemic state.

Objectives: To determine the best time to measure post-hemodialysis blood pressure in ESRF patients on regular hemodialysis. To determine the variability of 24 hours blood pressure readings.

Method: This is a cross sectional study involving 14 ESRF patients on regular hemodialysis in the HUSM outpatient hemodialysis unit. Hourly blood pressure reading was taken using ambulatory blood pressure monitoring device, starting from a day before hemodialysis session and 4 hours of post-hemodialysis, total duration of 24 hours. Upon completion of the hemodialysis treatment, serial ultrasonographic inferior vena cava diameter measurements were performed at 10, 30 and 60 minutes post-hemodialysis. Simultaneously, blood pressure readings were also taken at 10, 30 and 60 minutes post-hemodialysis. Results were expressed as median (interquartile range) for data that was not normally distributed and described as mean (standard deviation) for normally distributed data. Repeated measure ANOVA was used to test for significance of blood pressure variability.

Results: The inferior vena cava diameter was small at 10 minutes post-hemodialysis but it become normalize at 30 minutes and not much difference at 60 minutes. Blood pressure at 10, 30 and 60 minutes was found to be closer to average value at 60 minutes. Variability of the average blood pressure was not significant.

Conclusions: The optimal time for blood pressure measurement in end stage renal failure patients on regular hemodialysis was found to be at 60 minutes post-hemodialysis based on euvolemic state reflected by IVC diameter. This study also found that there was no significant difference in blood pressure variability from one person to another.

Keywords: end stage renal failure, hemodialysis, inferior vena cava diameter

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Dr Kurnia Prima Sawai bin Suardi

MMed Internal Medicine

Department of Internal Medicine

School of Medical Sciences, University Sains Malaysia

Health Campus, 16150 Kelantan, Malaysia

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Dr Azreen Syazril Adnan: Supervisor

CHAPTER 1

INTRODUCTION

1.1 Background of the Study

1.1.1 End Stage Renal Failure (ESRF)

The prevalence of chronic kidney disease (CKD) and end-stage renal failure (ESRF) is increasing worldwide. The overall prevalence of chronic kidney disease in West Malaysia was 9.07% (Hooi *et al.*, 2013). In 2013, there were 31,637 patients receiving dialysis in Malaysia, significantly increased from 11,842 in 2004. The new intake of dialysis patients had doubled from only 2,901 in 2004, to 6,222 in 2013 (BL Goh *et al.*, 2014).

There are many causes of chronic kidney diseases. In Malaysia, diabetic kidney disease (DKD) is the main cause of ESRF, contributing to 61% of new patients accepted for hemodialysis (BL Goh *et al.*, 2014). Other causes of ESRF include hypertension, glomerulonephritis, drug-induced, obstructive uropathy, polycystic kidney disease and bilateral renal artery stenosis (Li PKT *et al.*, 2011).

Patients who suffered from ESRF require RRT to sustain life. The modalities available for RRT include hemodialysis, hemodiafiltration, peritoneal hemodialysis and renal transplantation. Mode of RRT depends on several factors, including the primary need (e.g. solute or water removal or both), hemodynamic stability, vascular access, local expertise, availability, and patient preference and capability (e.g. for home dialysis). A survey in 2005 which utilized the Fresenius medical care network, has estimated 1.3 million patients received RRT worldwide, of which 89% received hemodialysis and 11% received peritoneal dialysis (Grassmann *et al.*, 2005). In Malaysia, the incidence and prevalence of patients on dialysis were 210 and 1,065 per million populations in 2013. Most (90%) of these patients were on hemodialysis, with only a small percentage (10%) were on peritoneal dialysis (BL Goh *et al.*, 2014).

1.1.2 Burden of ESRF

The increasing number of ESRF places significant burden on the health care system in terms of human and socioeconomic burden. Patient with ESRF has a significantly reduced life span; many amongst them would meet with an untimely demise mainly due to cardiovascular complication.

ESRF is considered as the most expensive chronic disease. This is due to the high costs of the treatment modalities (i.e. hemodialysis and kidney transplant). The costs of dialysis and transplantation consume disproportionate amounts within the health-care budgets in all jurisdictions which is 5% of annual budgets consumed by less than 1% of the population (Ministry of Health, 2011). In an economic evaluation among Ministry of Health hemodialysis centres in Malaysia, it was found that the cost of hemodialysis and erythropoietin was RM2500 per month. A study in the United States has found that the cost of medical care was 1.7 times higher in patients with CKD stage 3 and 2.6 times higher in those with stage 4 CKD compared with control (Smith DH *et al.*, 2004).

ESRF also place a significant social burden as illustrated in the paper by Tan *et al*, “Why patients say, ‘No’ to RRT” (Tan L *et al.*, 2013). Their analysis of 24 patients showed that the most common reason why patient did not undergo RRT was because the family members or caregivers who refused and not patient themselves refused. Such patients did not have a good family or social support. Their relatives are not keen to take them home after discharge, meaning they usually have no home to go to. If they do bring patients home, they opt for conservative treatment at home without any form of RRT, because either very few caregivers are willing to bring these patients to and from the hemodialysis centres for hemodialysis thrice weekly or not many caregivers can help to perform the peritoneal dialysis exchanges 4 times a day at home.

1.2 Hypertension in ESRF patients

1.2.1 Prevalence of hypertension in ESRF patients

According to Malaysia Clinical Practice Guidelines for Management of Hypertension 2013, hypertension is defined as persistent elevation of systolic BLOOD PRESSURE of 140 mmHg or greater and/or diastolic BLOOD PRESSURE of 90 mmHg or greater (Ministry of Health 2013). The prevalence of hypertension in hemodialysis patients and those with ESRF is much higher than in the general population, reaching 70%–80% (Charra *et al.*, 2004; Kiss *et al.*, 2005). Despite its high prevalence, there is limited knowledge on optimal control and hypertension management in hemodialysis patients (Peixoto and Santos, 2010).

1.2.2 Control of hypertension in ESRF patients

Hypertension management is difficult in hemodialysis patients because of the significant variation in blood pressure between pre-, post- and inter-dialytic period (Ekart *et al.*, 2011). According to 19th Report of the Malaysian Dialysis and Transplant Registry 2011, “The difficulty in controlling pre-hemodialysis systolic blood pressure in hemodialysis patients persisted in 2011 with only 26% of hemodialysis patients achieving systolic blood pressure <140 mmHg in 2011” (Lim YN *et al.*, 2012).

1.2.3 Complication of hypertension in ESRF patient

Uncontrolled hypertension in pre-dialysis patients has been identified as a major risk factor for progressive kidney dysfunction and also increased rate of cardiovascular complications. At the stage of, this hemodynamic abnormality can increase cardiovascular mortality by 3-fold (Lucas *et al.*, 2003). It is also associated with an annual mortality of 43% higher compared to person without renal disease (USRDS, 2012) and the mortality is contributed mainly from cardiovascular disease (Locatelli *et al.*, 2004).

1.3 Justification and Rationale of Study

Post-hemodialysis blood pressure measurement of ESRF patients is not accurate if taken immediately after hemodialysis. This is due to the nature of the hemodynamic instability that occurs prior to the equilibration between the intravascular and extravascular space. In the euvolemic state, evidenced by normalized inferior vena cava diameter, blood pressure recordings can be considered near to the accuracy. Therefore, determination of the right time to measure blood pressure post-hemodialysis will assist clinician in the hypertension management.

The rationale of carrying out this study is to identify the best possible time for blood pressure measurement in ESRF.

CHAPTER 2

LITERATURE REVIEW

2.1 Blood pressure measurement in hemodialysis patients

2.1.1 Options of blood pressure measurement

There are several options at which blood pressure are being measured in hemodialysis patients. These include pre- or post-dialysis blood pressure, ambulatory blood pressure monitoring (ABPM), and inter-dialytic home blood pressure. However the most appropriate time of blood pressure measurement in hemodialysis patients is still uncertain. There is no consensus of what is the best option to measure blood pressure (Levin *et al.*, 2010; Ekart *et al.*, 2011).

National Kidney Foundation Kidney Disease Outcomes Quality Initiative guidelines suggest that pre-hemodialysis and post-hemodialysis blood pressure should be 140/90 and 130/80 mmHg, respectively (Stidley *et al.*, 2006).

It is unclear as to which time of blood pressure measurement best reflects the burden of hypertension and correlates best with cardiovascular outcomes (Rahman *et al.*, 2002). Management decisions were confounded by the variability of these blood pressure measurements. This variability contributes to its difficulty to ascertain the optimum timing and method of blood pressure measurement (Levin *et al.*, 2010).

2.1.2 Pre- and post-hemodialysis blood pressure measurement

Agarwal (2003) found that the blood pressure is often extraordinarily elevated prior to hemodialysis and changed to hypotensive levels during hemodialysis. These changes in blood pressure within a short duration of time make the application of the traditional definitions of hypertension problematic. In fact, blood pressure fluctuates so much that the variability within patients from one visit to the next is about the same as between patients (Rohrscheib *et al.*, 2008). He found that the standard deviation of pre-hemodialysis systolic blood pressure between patients is 17.9 mmHg whereas visit-to-visit standard deviation within patient is 18.0 mmHg whereas the standard deviation for post-hemodialysis BP between patients is 17.4 mmHg and within patient 18.4 mmHg (Rohrscheib *et al.*, 2008).

Routine peri-hemodialytic blood pressure recordings performed by a hemodialysis unit staff shortly before and after the hemodialysis session are highly variable and poorly reproducible (Agarwal *et al.*, 2006a; Rohrscheib *et al.*, 2008) and do not correlate well with end-organ damage (Agarwal *et al.*, 2006b; Alborzi *et al.*, 2007). Nevertheless, peri-hemodialysis blood pressure measurements are used for management of hypertension in the majority of hemodialysis patients today (Sinha and Agarwal, 2009).

2.1.2.1 Pre-hemodialysis blood pressure measurement

According to Zoccali (2003), pre-hemodialysis blood pressure was a better predictor of left ventricular mass index than post-hemodialysis blood pressure. Pre-hemodialysis blood pressure also generally overestimate the ambulatory blood pressure with wide agreement limits (23.7 to 18.9 mmHg) (Agarwal *et al.*, 2006c).

2.1.2.2 Post-hemodialysis blood pressure measurement

Post-hemodialysis blood pressure underestimate average ambulatory blood pressure with wide agreement limits for both post-hemodialysis systolic blood pressure (33.1 to 36.3mmHg) and diastolic blood pressure (19.3 to 23.9 mmHg) (Agarwal *et al.*, 2006c).

Another option exists, that is the inter-hemodialytic period. Even when blood pressure is recorded in the inter-hemodialytic period, the timing is critically important. Other studies found large variations of blood pressure readings when it is recorded 12 hours versus 36 hours after termination of hemodialysis (Kelley *et al.*, 2007; Agarwal and Light, 2009). Furthermore, the inter-hemodialysis weight gain affects the rate of rise in inter-hemodialysis blood pressure. The rate of change in both the systolic and diastolic blood pressure are more abrupt when the inter-dialytic weight gain is excessive (Kelley *et al.*, 2007; Agarwal and Light, 2008). In contrary, the decline in blood pressure is more marked when more ultrafiltration is performed during hemodialysis.

2.1.3 Ambulatory blood pressure monitoring (ABPM)

ABPM remains the gold standard to quantify the integrated blood pressure load applied to the cardiovascular system (Saint-Remy and Krzesinski, 2005; Pickering *et al.*, 2006; Agarwal, 2012). Out-of-office blood pressure measurements (home blood pressure or ambulatory blood pressure monitoring) are better predictors of target organ damage and mortality in patients with essential hypertension and in patients with kidney disease (Peixoto and Santos, 2010). ABPM has been generally considered as the most accurate method for evaluating blood pressure load in the general population as well as in hemodialysis patients (Peixoto *et al.*, 2000; Pickering *et al.*, 2006).

ABPM has been shown to predict cardiovascular events better than conventional blood pressure measurement in patients with essential hypertension. Although measurement of ABPM nor self-measured home blood pressure better than peri-dialysis blood pressure measurement, they may not be feasible or practical for most patients throughout the world, leaving pre-hemodialysis and post-hemodialysis blood pressure measurements to be used, but with caution and with the knowledge that these are inferior (Levin *et al.*, 2010).

2.2 Relationship between blood pressure and volume

A direct relationship between volume status and blood pressure in patients with ESRF treated with hemodialysis has long been recognized. An increase in pre-hemodialysis systolic blood pressure may reflect hypervolemia. Data from the CRIT-Line Intra-dialytic Monitor Benefit (CLIMB) Study obtained during 32 295 sessions of 442 subjects followed up for 6 months confirmed that an increasing percentage of inter-hemodialysis weight gain is associated with a higher pre-hemodialysis blood pressure and a greater decrease in blood pressure associated with hemodialysis. However, the magnitude of the relationship between blood pressure and inter-dialytic weight gain, was found to be modest and modified by other clinical factors such as malnutrition or inflammation (Inrig *et al.*, 2007). Nevertheless, hemodialysis patients with a 15% or greater extracellular volume increase over the normal were at an increased risk of mortality (Wizemann *et al.*, 2009).

Salt and water overload is a key component of high blood pressure in dialysis patients. Therefore, controlling the body sodium content and the extracellular volume is the essential in controlling blood pressure and reducing the cardiovascular mortality in this patient population (Charra, 2007). If volume is strictly under control, antihypertensive drug treatment may be unnecessary and may even be dangerous (Tomson, 2009). Antihypertensive drugs may interfere with the compensatory vasoconstriction in blood pressure maintenance in the face of rapid changes in intravascular volume during conventional hemodialysis (Tomson, 2009).

Volume status of ESRF patients influences both pre- and post-hemodialysis blood pressure. Volume status is perhaps the most important factor in the development and maintenance of hypertension in dialysis patients (Mailloux and Haley, 1998). It has been shown that normotensive patients have significantly less total body water than hypertensive hemodialysis patients, demonstrating the importance of intravascular volume in the pathogenesis of hypertension in patients with ESRF (Lins *et al.*, 1997)

Even though volume plays an important part in high blood pressure in this population, not all hypertensive patients are volume overloaded. This is shown by study by Wabel *et al.* (2008) who illustrated the wide variability in systolic blood pressure regardless of the degree of change in hydration status from normal ranges. In this study of 500 hemodialysis patients, a new bio-impedance spectroscopy device was selected that allows quantitative determination of the deviation in hydration status from normal ranges and a graphical tool (hydration reference plot) was devised allowing deviation of hydration status to be combined with measurements of systolic blood pressure enabling comparison with a matched healthy population (1244 healthy participant). They have found that in only 15% of patients (n = 74) was hypertensive, observed blood pressure (systolic blood pressure >150 mmHg) with a concomitant deviation from hydration status >2.5 L (possible volume-dependent hypertension). In contrast, 13% of patients (n = 69) were hypertensive with deviation from hydration status <1.1 L (possible essential hypertension). In 10% of patients (n = 52), systolic blood pressure <140 mmHg was recorded despite deviation from hydration status exceeding 2.5 L (Wabel *et al.*, 2008).

2.3 Inferior vena cava (IVC) diameter

2.3.1 Relationship between inferior vena cava and volume

Inferior vena cava is a highly collapsible vein. Its diameter and collapsibility on deep inspiration allow evaluation of the intravascular volume. It correlates well with central venous pressure, and it can detect intravascular overload and depletion in hemodialysis patients. Non-invasive and fast, it reflects well the plasma but not the interstitial volume, and it varies widely as a function of heart function. Agarwal *et. al.* found that IVC diameter is modifiable with dry weight reduction, thus, it reflects in part intravascular volume (Agarwal *et al.*, 2011).

The IVC diameter is not affected by body's compensatory vasoconstrictor response to volume loss (Nette *et al.*, 2006). Therefore, IVC diameters reflect volume status more accurately compared to other parameters based on arterial system such as blood pressure and pulse rate. Studies have shown that IVC diameter is useful in monitoring volume status in patients undergoing hemodialysis and in patients under mechanical ventilation in intensive care units (Feissel *et al.*, 2004).

The IVC size varies with changes with intravascular pressure. Consequently, the IVC collapses with inspiration as the blood is pumped out of the IVC due to the negative pressure created by chest expansion. In healthy subjects breathing spontaneously, cyclic changes in thoracic pressure, result in collapse of the IVC diameter of approximately 50% (Pinsky *et al.*, 2006).

The pioneering study by Cheriex *et al.* (1989) in 18 hemodialysis patients suggested the usefulness of IVC diameter and its collapse with inspiration as a marker of volume. These authors reported a good relationship between IVC diameter and right atrial pressure and between collapse index and right atrial pressure; right atrial pressure was measured invasively. Collapse index was found not to correlate with changes in blood volume. Another recent study by Agarwal also concluded that collapse index was found to be of limited value (Agarwal *et al.*, 2011).

2.3.2 Inferior vena cava relationship with blood pressure

IVC diameter in expiration and inspiration and the left atrial diameter are volume responsive. Hence, they are at least partly markers of volume. However, as reported by Agarwal *et al.* (2011), echocardiographic volume parameters at baseline are poor determinants of inter-dialytic blood pressure. The author gave three possible explanations for these apparently discrepant findings.

First, echocardiographic parameters did not reflect the expanded extracellular fluid volume that is more closely related to hypertension, it only reflect intravascular volume. In the post-hemodialysis state, even when patients are volume expanded, an increased rate of ultrafiltration may shrink echocardiographic volume and falsely classify these patients as under-volume when they are actually volume overload. In fact, IVC expands because of vascular refilling; this rate of refilling is more rapid in patients who has more aggressive ultrafiltration such as in shorter hemodialysis (Agarwal, 2012)

Second, different patients may have different sensitivities to volume. For some patients, a small reduction of IVC or left atrial diameter may lead to a large change in blood pressure, whereas for others, a large change may be needed to affect a drop in blood pressure. Thus, this may affect the overall relationship between echocardiographic volume and change in blood pressure.

Third, the diameter of IVC and atrial diameter may be affected by venous compliance. For example, a small change in volume may lead to large changes in diameter in those with low venous compliance. Thus, venous compliance can confound the measurement of intravascular volume (Agarwal *et al.*, 2011).

2.3.3 IVC diameter post-hemodialysis

The timing of measurement is very important, because of the refill of plasma volume from the interstitium after hemodialysis. Especially when measured directly after hemodialysis, IVC echography may inappropriately suggest a hypovolemic state, because of the fact that refill of plasma volume from the interstitium is not yet complete. However, performing vena cava echography is operator dependent and not widely available (Charra, 2007).

2.3.3 Normal range of IVC diameter

Although there is a lack of universally accepted cut-offs, in healthy individuals, IVC diameter at inspiration ranges from 0 to 14mm at rest, and expiratory diameter of 15 to 20mm at rest (Field *et al.*, 2012).

2.3.4 Factors affecting IVC diameter

Inferior vena cava diameters are not exclusively influenced by the fluid status of a given patient. It may be influenced by the presence of tricuspid regurgitation and diastolic dysfunction. The IVC may also be dilated in normal young athletes, and in this population, it may not reflect elevated right atrial pressure (Lang *et al.*, 2005). However, hemodialysis patient are not usually young athletes. Since IVC diameter is measured by using ultrasound, it is operator dependent.

2.3.5 Measurement of IVC diameter

In this study, measurement of inferior vena cava diameter follows the guideline from American Society of Echocardiography. According to the guideline, the subcostal view is most useful for imaging the IVC, with the IVC viewed in its long axis. The guideline further states that diameter of the IVC should be measured with the patient in the left decubitus position at 1.0 to 2.0 cm from the junction with the right atrium and to accurately assess IVC collapse, the change in diameter of the IVC with a sniff and also with quiet respiration should be measured, ensuring that the change in diameter does not reflect a translation of the IVC into another plane (Lang *et al.*, 2005).

CHAPTER 3

OBJECTIVES, RESEARCH QUESTIONS, HYPOTHESIS

3.1 Objectives

3.1.1 General

To determine the optimal time to measure post-hemodialysis blood pressure in ESRF patients at euvolemic state evident by normalization of IVC diameter.

3.1.2 Specific

1. To measure inferior vena cava diameter 10 minutes, 30 minutes and 1 hour after completed hemodialysis.
2. To measure post-hemodialysis blood pressure 10 minutes, 30 minutes and 1 hour after completed hemodialysis.
3. To assess the variability of blood pressure among ESRF patients on regular hemodialysis by using ambulatory blood pressure measurement device to record hourly blood pressure for 24 hours.

3.2 Research Question

1. To assess when will IVC diameter normalize after hemodialysis
2. To assess when is the near accurate time to measure post-hemodialysis blood pressure in ESRF patients

3. To assess what is the variability of blood pressure in ESRF patients on regular hemodialysis

3.3 Hypothesis

1. The earliest time IVC diameter start to normalize can either be at 30 minutes or 60 minutes post hemodialysis.
2. Post-hemodialysis blood pressure readings when the IVC diameter normalizes will be the near accurate blood pressure readings for ESRF patients

CHAPTER 4

METHODOLOGY

4.1 Study Design

Cross sectional study

4.2 Study Period

January 2014 to May 2014

4.3 Reference Population

ESRF patients on regular hemodialysis in Kelantan

4.4 Source population

ESRF patients on regular hemodialysis, at outpatient Hemodialysis Unit, Hospital University Sains Malaysia

4.5 Inclusion criteria

1. Age $\geq$ 18 years
2. On regular hemodialysis therapy three times per week for at least more than 3 months

4.6 Exclusion Criteria

1. Recent adverse cardiovascular events
2. Signs of current infection
3. Active auto-immune disease
4. Advanced or severe liver disease

4.7 Sampling Frame

Patient registry at outpatient Hemodialysis Unit, Hospital University Sains Malaysia

4.8 Sample Size Calculation

Sample size was calculated using the following formula for single mean:

$$n = \left(\frac{Z\ x\ SD}{\Delta}\right)^2$$

Where:

n= sample size

Z= value from the standard normal distribution reflecting the confidence level that will be used. Thus, for confidence interval of 95%, Z = 1.96

SD= standard deviation

Δ= detectable differences

Based on the above formula,

1. The sample size calculation for objective 1 is as follows: (reference for standard deviation was taken from (Brennan *et al.*, 2006)

$$n = \left(\frac{1.96\ x\ SD}{\Delta}\right)^2$$

$$n = \left(\frac{1.96\ x\ 6}{4}\right)^2 = 8.6$$

2. For objective 2, the calculated sample size is shown below: (standard deviation taken from (Agarwal *et al.*, 2011))

    a. systolic blood pressure

$$n = \left(\frac{1.96 \ x \ SD}{\Delta}\right)^2$$

$$n = \left(\frac{1.96 \ x \ 18.3}{11}\right)^2$$

$$n = 10.6$$

    a. diastolic blood pressure

$$n = \left(\frac{1.96 \ x \ SD}{\Delta}\right)^2$$

$$n = \left(\frac{1.96 \ x \ 11.2}{7}\right)^2 = 9.8$$

3. The calculation of sample size for objective 3 is described below (standard deviation taken from (Rossignol *et al.*, 2012)):

    b. systolic blood pressure

$$n = \left(\frac{1.96 \ x \ SD}{\Delta}\right)^2$$

$$n = \left(\frac{1.96 \ x \ 16.37}{10}\right)^2 = 10.3$$

c. diastolic blood pressure

$$n = \left(\frac{1.96\ x\ SD}{\Delta}\right)^2$$

$$n = \left(\frac{1.96\ x\ 8.61}{5}\right)^2$$

$$n = 11.4$$

Thus, the largest calculated sample size is 11.4. Assuming 20% drop rate, the final sample size would be 11.4 + 2.3= 13.7, rounded to 14.

4.9 Sampling Method

All eligible respondents were included in the study via convenient sampling

4.10 Research Tool

4.10.1 Echocardiogram machine

Brand:	Philips
Type:	Sonos 5500
Model no:	MCMD02AA,
Manufactured:	Massasschusets, USA, year 2003.

4.10.2 Ambulatory blood pressure measurement set

Brand :	Spacelabs healthcare
Model no:	040-1546-00,
Manufactured :	Hertford, UK,_year 2010,

**calibration was done before each recordings.

4.11 Data Collection

4.11.1 Recruitment of research participant

Patients that are listed in the hemodialysis unit patient registry that underwent hemodialysis at HUSM outpatient Hemodialysis Unit, were included in the study if they fulfilled the inclusion and exclusion criteria. Sampling method is based on convenient sampling.

Eligible patient were invited to join the study and preliminary information on the research were given. Agreed volunteers were given specific date for appointment in CKD Resource Center, Hospital USM

4.11.2 Ambulatory blood pressure monitoring (ABPM)

Selected patient were given a detailed explanation regarding the study and informed consent were recorded. Patients were asked to wear the ambulatory blood pressure monitoring device in their non-access arm in the evening before their next hemodialysis session. The ABPM was applied for 24 hours, inclusive the 4 hours post hemodialysis.

The device was calibrated by the researcher and a dedicated medical assistant before applying to the patient. Device application was explained by the researcher to the patient. It is compulsory for the patient to wear the device for 24 hours.

4.11.3 Serial IVC and blood pressure measurement

Patients presented for hemodialysis via arterio-venous fistula. None of them had hemodialysis via catheter. Upon completion, blood pressure and IVC diameter were measured at 10, 30 and 60 minutes post-hemodialysis. All patients received normal sodium dialysate concentration 1.25mmol/L.

Blood pressure at 10, 30 and 60 minutes post- measurements were performed by trained hemodialysis nurses according to the American heart Association guidelines, using a mercury sphygmomanometer with an appropriate cuff at the arm without arterio-venous fistula. Measurements were systematically performed post-dialysis after a 10-minute rest, with the patient relaxed and seated with legs uncrossed and back and arm supported, and the cuff and the mercury reservoir at the level of the heart. Three consecutive measurements were performed 2 minutes apart, in the same arm with the patient in the same position, and the mean value was recorded by the researcher.

The IVC diameter measurement was performed by a single experienced and trained echocardiography technician. The measurement procedure were as follows: The IVC was visualized in two dimensions, subcostal view for the IVC imaging, viewed in its long axis. The measurement of the IVC diameter was made at both end-expiration and inspiration, diameter of the IVC was measured with the patient in the left decubitus position at 1.0 to 2.0mcm from the junction with the right atrium and to accurately assess IVC collapse, the change in diameter of the IVC with a sniff and also with quiet respiration were measured, ensuring that the change in diameter does not reflect a translation of the IVC into another plane. Valsalva manoeuver was avoided.

4.12 Data Entry and Statistical Analysis

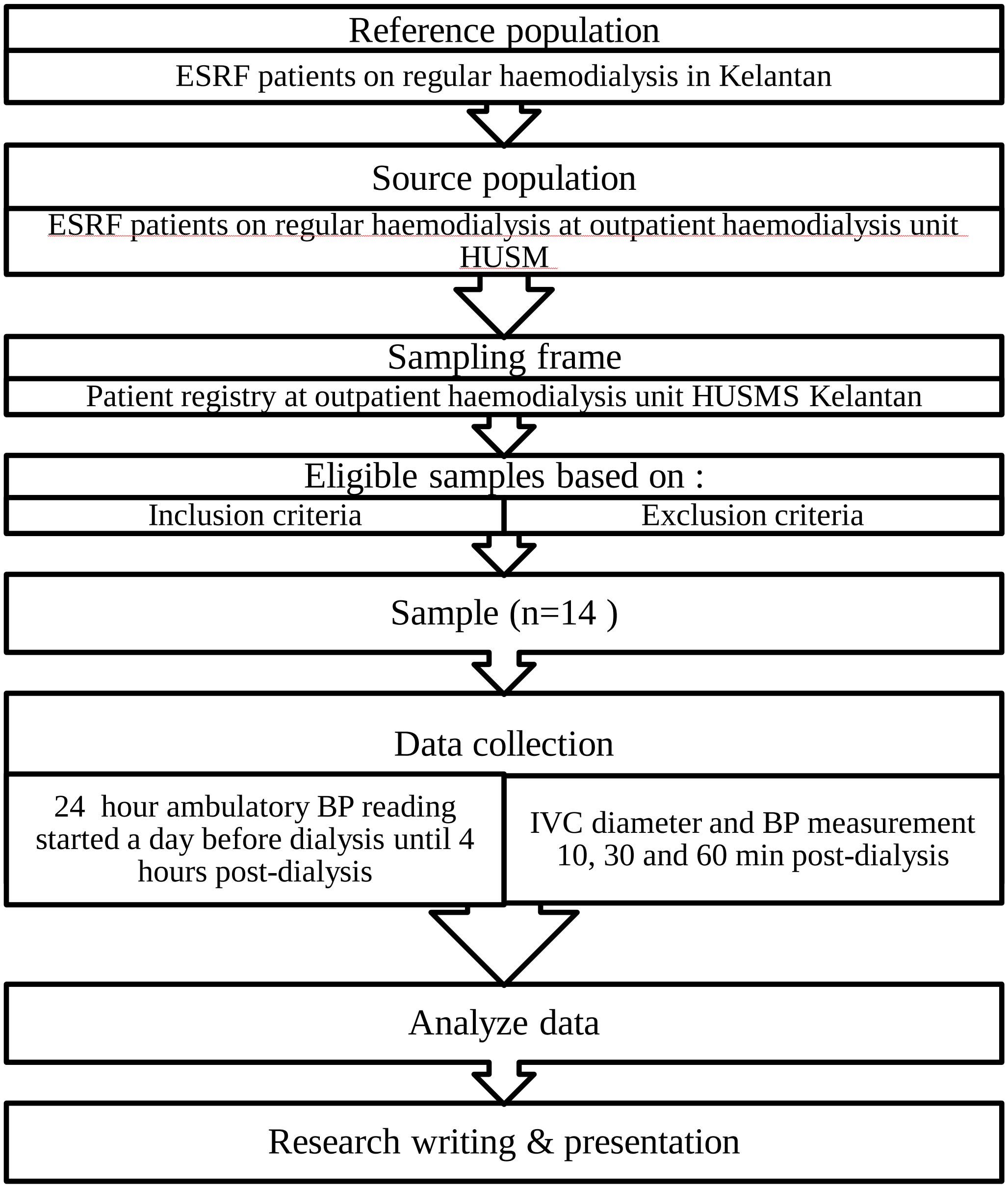
Data was entered into SPSS version 20 and was analyzed. Data were expressed as median ± interquartile range (IQR) for IVC diameter and diastolic blood pressure since the data was not normally distributed while for systolic blood pressure readings data was expressed as mean ± standard deviation (SD). Repeated measure ANOVA was used to test for significance of blood pressure variability.

4.13 Ethical issues

The main ethical issue in this study is regarding the use of ambulatory blood pressure device. Since patient need to wear it for 24 hours with hourly blood pressure measurement, patient’s daily activity especially sleep maybe interrupted.

This study was approved by the local research ethical committee, University Sains Malaysia (ref: USM/JePeM/278.3. (1) on 28th January 2014.

4.14 Flow chart of study



CHAPTER 5

RESULTS

5.1 Profiles of hemodialysis patients participating in the study

A total of 14 ESRF patients consented and volunteered to participate in this study. They regularly underwent three times-per-week hemodialysis sessions in Hospital University Sains Malaysia. All respondents were Malays.

5.1.1 Socio-demographic characteristic

The socio-demographic characteristics of the study subjects as shown in Table 5.1. The mean (SD) age of patients participated were 50 (17.69) years. Their age ranging was from 17 to 77 years old. Eleven of them were male participants. The mean (SD) of their BMI was 22.74 (3.26), corresponding within the normal range. None of them smoke, however 42.9% had history of smoking before.

Table 5.1: Socio demographic characteristic of hemodialysis patients (n=14)

Characteristics	**n (%)**
Age (year)	50 (17.69)[a]
Gender	
Male	11 (78.6%)
Female	3 (21.4%)
BMI (kg/m^2)	22.74 (3.26)[a]
Smoking history	
Previous	6 (42.9)
Never	8 (57.1)

[a] mean (SD)