UNIVERSITI PUTRA MALAYSIA

CHRONIC VENOUS DISEASE IN MALAYSIA POPULATION

MOHAMAD NIZAM ADHA BIN ILIAS
KEE KHAI SIEN
NUR AMYLIA BINTI MOHD ROSLI

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By

MOHAMAD NIZAM ADHA BIN ILIAS
KEE KHAI SIEN
NUR AMYLIA BINTI MOHD ROSLI

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Chronic Venous Disease in Malaysia Population

Mohamad Nizam Adha Bin Ilias [1], Kee Khai Sien [1], Nur Amylia Binti Mohd Rosli [1], Liew Ngoh Chin [2], Lee Limi [2]

[1] Second Year Medical Student
[2] Department of Surgery, Faculty of Medicine and Health Sciences, University Putra Malaysia

ABSTRACT

Backgorund: Chronic venous disease is a common condition with major socioeconomic impact due to its high prevalence. It manifest by a range of signs, the most obvious are varicose veins and venous ulceration. However, there is little literature on Chronic Venous Disease (CVD) in our country.From observational studies, many patients with CVD present late to the hospital when the disease is already in severe state (e.g eczema, ulcer), and there are no data if the symptoms and complications of CVD are amenable to treatment.

Objective: The aim of this study is to study the epidemiology (gender, age, ethnicity), etiology, presentation, results of management of ulcers and the association between epidemiology and etiology with the presentation of Chronic Venous Disease(CVD).

Methods: A retrospective cross-sectional study was performed in Hospital Pantai Ayer Keroh Melaka. All CVD patients' medical reports from 2010 to 2013 were extracted and reviewed. A total of 186 patients' medical reports were included after fulfilling the inclusive and exclusive criteria. Data were collected and entered in a proforma.

Results: Majority were female patients (71.5%) and aged between 40 to 59 years old (58.1%). Most of the etiology for the CVD is primary (90.9%) and 41.4% presented in C2 (varicose vein), while only 9.1% of patients have previous or current DVT. Of the patients that presented with venous ulcers, 52.8% underwent EVLT and have 89.3% of healing rate. On further analysis, there is a significant association between age and presentation of CVD ($p = 0.026$).

Conclusion: The presentation of CVD was significantly affected by age but not by gender, ethnicity and etiology. Majority of venous ulcers can be healed with proper intervention and EVLT improve healing of ulcer effectively.

Key words: chronic venous disease (CVD), varicose veins, endovenous laser therapy (EVLT), deep vein thrombosis (DVT).

PENYAKIT VENA KRONIK DALAM POPULASI MALAYSIA

Mohamad Nizam Adha Bin Ilias [1], Kee Khai Sien [1], Nur Amylia Binti Mohd Rosli [1], Liew Ngoh Chin [2], Lee Limi[2]

[1] Pelajar Perubatan Tahun Dua
[2] Jabatan Surgeri, Fakulti Perubatan dan Sains Kesihatan, Universiti Putra Malaysia

ABSTRAK

Latar belakang: Penyakit vena kronik adalah lazim dengan impaknya pada sosio ekonomi disebabkan oleh prevalens yang tinggi. Ia boleh dimanifestasi dengan pelbagai tanda, yang paling nyata adalah vena varicose dan vena ulser. Walaubagaimanapun, sedikit pembacaan terhadap penyakit vena kronik dalam negara kita. Daripada pemerhatian pembelajaran, ramai pesakit yang menghidap penyakit vena kronik hadir lambat ke hospital apabila penyakit sudah berada di tahap bahaya seperti ezema dan ulser dan tiada data yang menunjukkan bahawa simtom dan komplikasi penyakit vena kronik ini boleh dirawat.

Objektif: Tujuan kajian ini dijalankan adalah untuk menentukan epidemiologi (jantina, umur, etnik), etiologi, persembahan, keputusan rawatan ulser dan hubungan antara epidemiologi dan etiologi dengan persembahan penyakit vena yang kronik.

Methods: Satu kajian telah dijalankan di Hospital Pantai Ayer Keroh Melaka.
Kesemua rekod pesakit yang menghidapi penyakit vena kronik dari tahun 2010 hingga 2012 telah diambil dan dibaca. Seramai 186 rekod pesakit yang memenuhi kriteria yang ditetapkan (kriteria dalaman dan luaran) telah di rekodkan. Proforma digunakan untuk mengumpul kesemua data.

Keputusan: Majoriti pesakit adalah perempuan (71.5%) dan berumur di antara 40 hingga 59 tahun (58.1%). Kebanyakan mereka menpunyai etilogi yang prima (90.9) dan 41.4% mempersembahan (C2) vena varicos, manakala hanya 9.1% pesakit yang mempunyai pembekuan darah dalam vena dalaman yang lepas atau terbaru. 5.8% pesakit ulser menjalankan EVLT dan kadar pemulihan adalah 89.3%. Hubungan diantara umur dan persembahan penyakit vena kronik adalah ketara(p=0.026).

Conclusion: Persembahan penyakit vena kronik ialah signifikasi dipengaruhi oleh umur tetapi bukan jantina, etnik dan etiologi. Kebanyakan pesakit mempunyai etiologi pertama dan EVLT telah dibuktikan dapat memulihkan ulser dengan efektif.

Kata kunci: penyakit vena kronik, terapi laser dalaman vena, pembekuan darah dalam vena dalaman, vena varicos.

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LIST OF ABBREVIATIONS

CVD	Chronic Venous Disease
CVI	Chronic Venous Insufficiency
DVT	Deep Vein Thrombosis
CEAP	Clinical(C), Etiology(E), Anatomy(A), Pathophysiology(P) classification
AVF	American Venous Forum
GSV	Great Saphenous Vein
KTW	Klippel-Trénaunay-Weber
SSV	Small Saphenous Vein
EVLT	Endovenous Laser Therapy

CHAPTER 1: INTRODUCTION

1.1Background of Chronic Venous Disease (CVD)

Physiologically in healthy individuals, blood in the leg veins is pump by calf muscle pump. When calf muscles contract (calf muscle pump), the blood is returned to the heart and the venous valve prevents the blood from refluxing downwards. However, in CVD these processes are dysfunctional.

Chronic venous disease is a common condition with major socioeconomic impact due to its high prevalence. The cost of chronic venous disease includes its investigation, its treatment, and the loss of working days by the afflicted patients. Chronic venous disease of the lower limbs manifest by a range of signs, the most obvious are varicose veins and venous ulceration. However, the others signs also include oedema, venous eczema, hyperpigmentation of skin, atrophy blanch (white scar tissue), and lipodermatosclerosis.

Chronic venous disease can be graded based on clinical(C), etiology(E), anatomy(A), pathophysiology(P) classification or CEAP created by an international ad hoc committee of the American Venous Forum (AVF) in 1994(Rutherford et al,2000) . The clinical signs in the affected legs are categorized into seven classes designated C0 to C6 which are C0 (no clinical sign), C1(small varicose veins), C2(large varicose veins), C3(oedema), C4(skin changes without ulceration), C5(skin changes with healed ulceration), C6(skin changes with active ulceration). Leg symptoms associated with chronic venous disease include aching, heaviness, a sensation of swelling, pain, bleeding and skin irritation. For the etiology(E) it can be due to congenital, primary or secondary. Anatomically (A), the venous system of leg can be described by 3 parts which are superficial veins, deep veins or perforating veins. The pathophysiology of venous disease could be due to reflux, obstruction or both.

Chronic venous disease encompasses the full spectrum of signs and symptoms associated with classes C0 to C6, whereas the term "chronic venous insufficiency" is generally restricted to C4 to C6. Venous insufficiency is a chronic condition which means that the vein of leg cannot send blood back to the heart in an efficient manner. In contrast, the venous blood escapes from its normal ante grade path of flow and refluxes backward down the veins into an already congested leg. Complications of untreated venous insufficiency include recruitment of veins – high venous pressures may cause the recruitment of adjacent normal veins into refluxing circuits, DVT, pulmonary embolism (PE), venous ulceration and secondary lymphoedema.

1.1.1.**Epidemiology**

i. United States statistics

CVI is a significant public health problem in the United States. It has been estimated that 2-5% of all Americans have some changes associated with CVI. Published estimates of the prevalence of varicosities range from 7% to 60% in the adult population, with most studies demonstrating clinical varicose reflux in about 40% of the population. (Coon et al., 1973) Venous stasis ulcers affect approximately 500,000 people. The mean incidence of hospital admission for CVI is 92 per 100,000 admissions.

ii. International statistics

The frequency of venous insufficiency is believed to be higher in Westernized and industrialized nations than in developing nations, most likely because of differences in lifestyle and activity.

iii. CVI-dependence on age

All epidemiological studies confirm the relation between age and increased prevalence of CVI identically in both genders without dependence on other risk factors.(Preziosi rt al.,1999) (Canocino et al.,1998) The prevalence of varicose vein in men aged; a) 30-40 years old (3%), b) over 70 years old (40%) while in women aged; a) 30-40 years old (20%), b) over 70 years old (>50%).(Coon et al.,1973)(Kontosic I et al., 2000) In the other study, the prevalence of trunk varices increases from 11.5% in individual aged 18-24 years old to 55.7% in the population aged 55-64 years old.(Evans et al.,1999) The occurrence of skin changes in CVI depends on the patients age as well. In the Tecumseh Health Study, prevalence of skin changes in women aged 30-39 years was 1.8%, while in patients at age over 70 years old the prevalence of 20.7% was reported.

iv. Influence of sex

The incidence and prevalence of deep and superficial venous disease depend on the age and sex of the population, but at any age, such disease is more common in women than in men. In younger men, the incidence is lower than 10%, compared with 30% in similarly aged women. In men older than 50 years, the incidence is 20%, compared with 50% in similarly aged women.(Chiesa et al.,2005)

v. Pregnancy and CVI

Pregnancy and puerperium are critical periods for the venous system of lower limbs.(Zicot, 1999) Based on some statistics, up to 30% of varicose veins develop during this period. Preziosi in the Suvimax Cohort Study also confirm that there is positive correlation between pregnancy and varicose veins.(Zicot, 1999)This is because due to increase of the blood volume, increase compression of iliac veins that result to increase the venous pressure thus leading to CVI. However, nowadays the main influence on the development of varicose veins in pregnancy is thought to be the hormonal influence-estrogens cause a decrease in the smooth muscles tone of the venous wall.

vi. Occupation related (or the occupation condition)

According to the Kontosic's study, he divides occupation into 5 representative groups (waiters, salespersons, light and heavy industries, office workers). (Kontosic et al., 2000) A statistically significant difference was found in the prevalence of varicose veins in waiters and salesperson as compared to office workers. Women who were standing during work had a statistically higher prevalence of trunk varices in study group.

vii. Influence of genetic

In some cases, varicose vein can also occurred in childhood, especially to those who have a positive family history. Although heredity is an important risk factor, the familial incidence is reported only in about 50% of patents.(Lawrence et al., 1998)

viii. Geographical association

Most of the cases of CVD occurs in developed countries. The prevalence is very low in African and Asian or Australian population although immigrant subjects from these regions have the same risk as the population of their host country.(Coon et al., 1973) The changes in lifestyle and eating habits in industrialized countries, especially low fiber diet, which induce constipation and increased intra-abdominal pressure, are considered to be one of the main causes of this phenomenon.(Carpentier, 1994)

1.2 Problem Statement

1. There is little literature on Chronic Venous Disease (CVD) in our country, and there are few data among Asians.
2. From observational studies, many patients with CVD present late to the hospital when the disease is already in severe state (e.g eczema, ulcer).
3. There are no data if the symptoms and complications of CVD are amenable to treatment.

1.3 Objective

1.3.(a) General Objective

- To study the epidemiology (gender, age, ethnicity), etiology, presentation of Chronic Venous Disease (CVD) in the Malaysian population and the results of management of venous ulcers.

1.3(b) Specific Objective

i. To determine the epidemiology (gender, age, ethnicity) with presentation of patients with Chronic Venous Disease (CVD).

ii. To determine the etiology of Chronic Venous Disease (CVD).

iii. To determine the presentation of patients with Chronic Venous Disease (CVD).

iv. To review the results of management of ulcers.

v. To determine the associated factors of Chronic Venous Disease (CVD);

   i. Between epidemiology (gender, age, ethnicity) with the presentation of Chronic Venous Disease (CVD).

   ii. Between etiology with the presentation of Chronic Venous Disease (CVD).

1.4 Research Hypothesis

1. There is an association between epidemiology (gender, age, ethnicity) and etiology with the presentation of Chronic Venous Disease (CVD).

2. There is no difference in the etiology of Chronic Venous Disease (CVD) between Asian population and Western population.

3. Majority of venous ulcers can be healed with appropriate intervention.

CHAPTER 2: LITERATURE REVIEW

2.1 Risk Factor of CVD

If an individual has the risk factors for CVD, that person more likely than other people to develop the disease. The most important risk factors are:

- Deep vein thrombosis (DVT)
- Varicose veins or a family history of varicose veins
- Obesity
- Pregnancy
- Inactivity
- Smoking
- Extended periods of standing or sitting
- Female sex
- Age over 50

2.2 Classification of CVD

CVI classification is based on CEAP criteria, developed by an international consensus conference to provide a basis for uniformity in reporting, diagnosing and treating CVI.(Porter et al., 1995) This criteria is based on clinical class (C), etiology (E), anatomy (A) and pathophysiology (P) of chronic venous disease of the leg. It has been summarized as below;

- Clinical classification (C)
    - C0: no visible or palpable signs of venous disease
    - C1: telangiectasias or reticular veins
    - C2: varicose veins (distinguish from reticular veins by diameter 3mm or more)
    - C3: edema
    - C4: changes of skin (divided into 2 subclasses);
        - C4a: pigmentation or eczema
        - C4b: lipodermatosclerosis
    - C5: healed venous ulcer
    - C6: active venous ulcer

- Etiological classification
    - Ec : congenital
    - Ep: primary
    - Es: secondary
    - En: no venous cause identified

- Anatomical classification
    - As: superficial veins
    - Ap: perforating veins
    - Ad: deep veins
    - An: no venous location identified
- Pathophysiological classification
    - Pr: reflux
    - Po: obstruction
    - Pr,o: reflux and obstruction
    - Pn: no venous pathophysiology identified

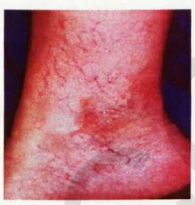


Fig 1.C1: reticular veins

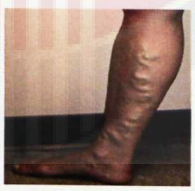


Fig 2. C2: Varicose veins

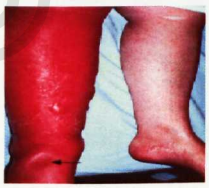


Fig3. C3: Edema

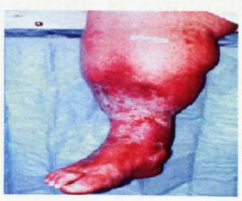


Fig4. C_{4B} - lipodermatosclerosis, atrophy blanche

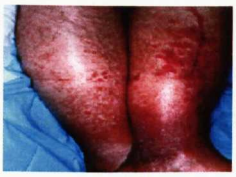


Fig5. C_{4A} - pigmentation, venous eczema

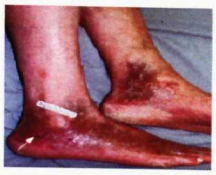


Fig6. C_5 - healed ulcer

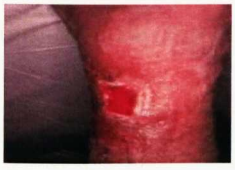


Fig7. C6 - active ulcer

2.3 **Clinical manifestation**

Manifestation of CVD varies which range from a simple telangiectasias or reticular veins to more advanced stages such as skin fibrosis and venous ulceration. The major clinical features of CVD are;

- Dilated veins or varicose veins (swollen and twisted superficial veins that are visible just under the surface of the skin)
- Edema (swelling)
  - Swelling may result from acute venous obstruction (as in deep venous thrombosis [DVT]) or deep or superficial venous reflux. Alternatively, swelling may be completely unrelated to the venous system. Lower-extremity pitting edema is common in patients with venous insufficiency. Hepatic insufficiency, renal failure, cardiac decompensation, infection, trauma, and environmental effects can also cause lower-extremity pitting edema that may be indistinguishable from edema due to venous obstruction or venous insufficiency.

- Leg pain or leg discomfort

  - Venous hypertension in muscles and fascial compartments of lower leg from exercise and prolonged standing results in the characteristics ache of CVD. The discomfort is described as pain, pressure, heaviness, itching, dull ache and burning.(Labropulous et al., 1994)

- Cutaneous or skin changes

- Stasis dermatitis

  - Darkened, discolored, and stained skin may be a sign of venous stasis, arterial insufficiency, chronic infection, prior injury, or various other conditions (see the image below). Such discoloration is particularly likely to be a sign of chronic venous stasis if it is localized along the medial part of the ankle or the medial aspect of the lower leg; these areas are especially prone to venous hypertension because their drainage largely depends on the competence and patency of the entire great saphenous vein (GSV) and all the attached perforating veins.

- Chronic cellulitis

- Venous ulceration

  - Venous ulceration accounts for 70-80% of lower limb ulceration; ischemic arterial ulcers, rheumatology disorder, local trophic effects, unrecognized cancer, and other exotic causes constitute the balance.(Abbade et al., 2005)(Weiss et al., 2001)

The manifestation can be viewed in term of well-established criteria, CEAP criteria. The clinical manifestation has 7 categories all together (from C0-C6) and is further categorized by presence or absence of the symptoms.

To complement the CEAP classification and further define the severity of CVD a venous severity

score was developed. The venous severity scoring provides a numeric score based on 3 components: the venous clinical severity score, the anatomic segment disease score, and the disability score. The venous clinical severity score consists of 10 attributes (pain, varicose veins, venous edema, skin pigmentation, inflammation, induration, number of ulcers, duration of ulcers, size of ulcers, and compressive therapy) with 4 grades (absent, mild, moderate, severe). The venous anatomic segmental score assigns a numerical value to segments of the venous system in the lower extremity that account for both reflux and obstruction. The venous disability score comes from the ability to perform normal activities of daily living with or without compressive stockings. The venous severity scoring has been shown to be useful to evaluate the response to treatment.(Rutherford et al., 2000)

2.4 Etiology of CVD

According to CEAP classification, etiology can be classified based on congenital, primary and secondary causes of dysfunction. Congenital disorders are those that are present at birth, although they may be recognized later in life, including the well recognized Klippel-Trenaunay and Parkes-Weber syndromes.

However, CVI is frequently categorized as primary or secondary. Primary CVI is the results of abnormalities of venous wall and the venous valves, usually congenital etiology and affecting the deep system in about 35% of symptomatic patients.(Ionnou et al., 2003) The cause of primary is usually uncertain in any individuals.

Secondary CVD is an acquired condition. It is usually resulted from injury to the venous valves due to vein thrombosis, which lead to reflux, obstruction of vein or both. All three venous systems are susceptible; however, deep vein insufficiency is 90% implicated for secondary CVI.(Araki et al., 2004)

CVD is more common among those who are obese, pregnant, or who have a family history of the problem. Individuals who have had trauma to the leg through injury, surgery, or previous blood clots are also more likely to develop the condition. Other causes of CVD include, but are not limited to, are;

- High blood pressure in the leg veins over a long time, due to sitting or standing for prolonged periods
- Lack of exercise
- Smoking
- Deep vein thrombosis (a blood clot in a deep vein, usually in the calf or thigh)
- Phlebitis (swelling and inflammation of a superficial vein, usually in the legs)

Although CVD can affect anyone, age and sex can also be the factors that may increase the tendency of getting CVD; women older than 50 years old most often get CVI.

Superficial venous insufficiency

In superficial venous insufficiency, the deep veins are normal, but venous blood escapes from a normal deep system and flows backwards through dilated superficial veins in which the valves have failed. More than 80% of varicose veins seen on the leg are caused by venous insufficiency or a leaky valve in the GSV, which terminates near the inguinal ligament as it joins the common femoral vein.

The initial valve failure may occur at any level between the groin and the ankle, but the saphenofemoral junction is the high point of reflux in most patients with severe superficial venous insufficiency. Valve

failure can be spontaneous in patients with congenitally weak valves. Congenitally normal valves can fail as a consequence of direct trauma, thrombosis, hormonal changes, or chronic environmental insult (eg, prolonged standing).

Deep venous insufficiency

Deep venous insufficiency can be due to congenital valve or vessel abnormalities, but it most commonly occurs when the valves of the deep veins are damaged as a result of DVT. With no valves to prevent deep system reflux, the hydrostatic venous pressure in the lower extremity increases dramatically.

Klippel-Trénaunay-Weber syndrome

A less common cause of venous insufficiency is Klippel-Trénaunay-Weber (KTW) syndrome, which involves port-wine stains, varicose veins, and bony or soft-tissue hypertrophy.(Preziosi et al., 1999) Patients with pure Klippel-Trénaunay syndrome have only venous involvement, whereas those with the Parkes Weber variant also have arteriovenous malformations.

The capillary hemangiomas (port-wine stains) of KTW syndrome, like those of other forms of venous insufficiency, can lead to local skin breakdown and ulceration, bleeding, and secondary infection. This can occur in any organ system of the body.

The sciatic vein is a large superficial vessel that is present during fetal development but usually does not persist. In patients with KTW syndrome, this vein may be noticed at birth, or it may become apparent

later in life. The vein extends along the posterolateral aspect of the leg from the foot to the gluteal region. When present, it is invariably a reflux pathway rather than a pathway for anti grade flow.

Patients with KTW syndrome may have atresia of the deep veins, as well as many abnormal venous pathways involving the deep and superficial venous systems. KTW syndrome can produce such severe venous insufficiency that the otherwise normal lymphatic system becomes overwhelmed by the amount of lymph production, which leads to secondary lymphoedema. Surgical attempts to treat the abnormal refluxing veins in KTW syndrome are fraught with peril because postoperative worsening of venous abnormalities is common.

2.5 Anatomy

The venous network in the lower extremities commonly affected by CVD is divided into the following 3 systems;(Preziosi et al., 1999)

- Superficial veins (including the great saphenous vein [GSV], the small saphenous vein [SSV], and their tributaries)
- Deep veins (including the anterior tibial, posterior tibial, peroneal, popliteal, deep femoral, superficial femoral, and iliac veins)
- Perforating or communicating veins

Normally, when in an upright position, the blood of leg veins will against the gravity (drain upwards) returns back to the heart. In order to return the blood back, the muscles of leg squeeze the deep veins of legs and feet. The leg valves, one-way flaps help to keep the blood flowing in the right direction. When the

muscles of leg relax, the valve will close and thus, preventing the blood to flow backwards, down the legs. This process (bringing the blood with poor oxygen back to heart) is called venous pump.

In venous insufficiency, after prolonged standing, the veins are completely filled, and all the venous valves float open. This cause the blood in leg veins can pool and increase the venous blood pressure. Usually, the deep and perforating veins could withstand the high pressure but only in short periods due to their flexibility of wall. But, incompetence valves cause the column of standing blood in the vein to remain high even during ambulation, thus resulting the wall of the veins become weak. This will lead to CVD.

2.6 Pathophysiology of CVD

The venous network in lower extremities composes of superficial veins, deep veins, and perforating veins which connecting the former two types of veins.

Large vein pathophysiology

When there is dysfunction or incompetence of the valves, the blood back flow and pooling in lower limbs, causing increase of blood pressure in veins, called venous hypertension. When the key valves that communicate the deep and superficial systems become incompetent, the high pressure blood from deep system can leak to the superficial system. There are two major sources of valve failure, which are junctional and perforator valve failure. The most common junctional valve failure occurs at the junction between the great saphenous vein and common femoral vein (saphenofemoral incompetency). A less common form results between small saphenous vein and the popliteal vein (saphenopopliteal

incompetency). The most common sites of perforator valve failure ae in the midproxial thigh (Hunterian perforator) and in the proximal calf (Boyd perforators). (Weiss , 2012) As blood pressure in veins stay elevated for long periods of time, leading to chronic venous insufficiency (CVD).

The microcirculation

The increased venous pressure impeding the blood flow and trapping leukocytes in capillaries. They release proteolytic enzymes, inflammatory mediators and free radicals, damage the capillary basement membranes. The leakage of plasma proteins and fibrinogen into surrounding dermis leading to edema. The fibrins build up around the vessels, forming fibrinous pericapillary cuff and decrease the delivery of oxygen, nutrient and growth factors to the affected tissue, causing hypoxic injury. The symptoms of chronic venous insufficiency include swelling in the lower legs and ankles, aching, varicose vein, leathery-looking skin or itching. If CVD is not treated, the increasing blood pressure result in capillaries burst and cause local tissue inflammation and internal tissue damage. At worse, this leads to ulcers and cellulitis if get infection. (Cleaveland clinic).

2.7 Management of CVD

2.7.1 Surgery

The patients with only superficial venous incompetence showed improvement in ulcer healing after superficial venous surgery. (O'Meara, 2009) But, it also has been reported that superficial venous surgery in patients with superficial insufficiency has not been proven to heal ulcer compared to compression alone. (Barwell, 2004)A randomised clinical trial, found that 87 patients with venous ulcers has complete healing by 31 days after superficial venous surgery, while patients that are on compression therapy alone, the ulcers heal in 63 days. The recurrence rates at 3 years were 9% and 38%. (Zamboni, 2002)

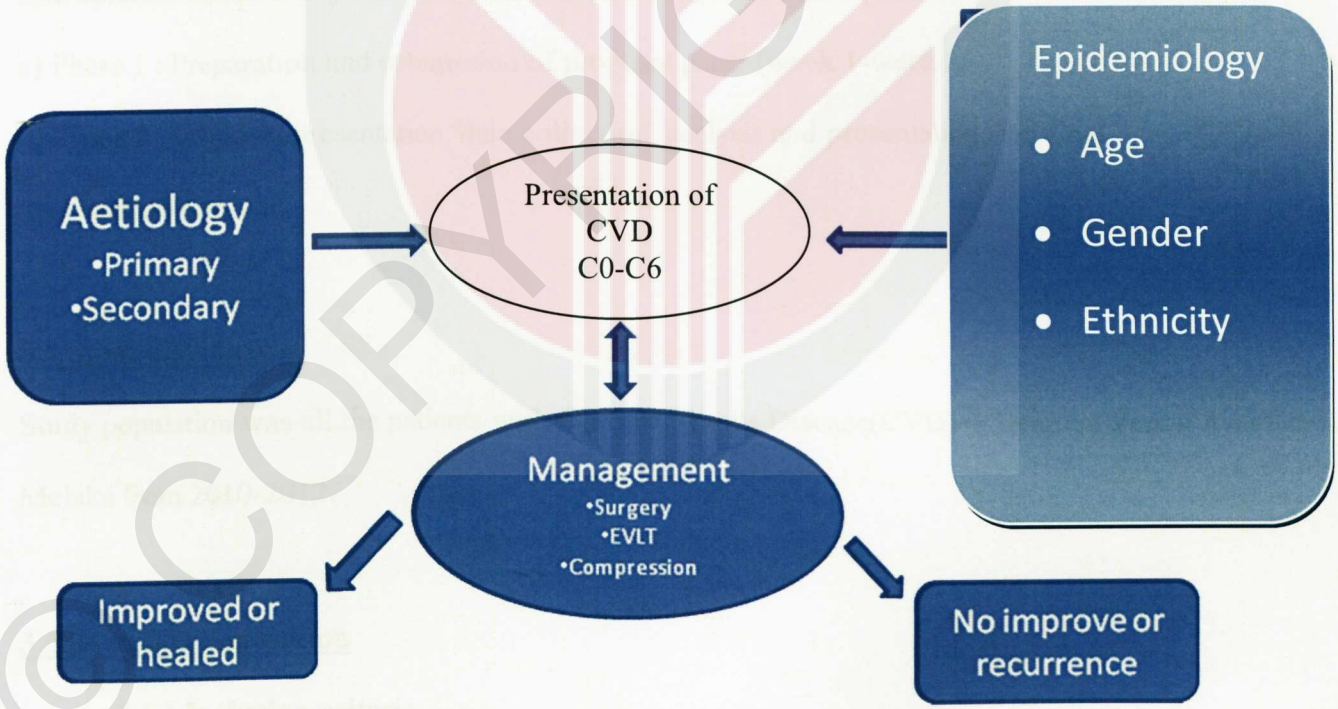
2.7.2 Compression therapy

Systematic review in 2009 showed the use of multilayered high compression is more effective than single layered low compression systems and it improved the healing rates of venous leg ulcers. (O'Meara, 2009) In 12-15 weeks more ulcers were healed with high compression systems compared to low compression systems. (Cullum , 2004) Although there is no significant different between the effectiveness of compression systems but mostly most ulcers were healed with four layer compression systems compared to one layer compression system at weeks 24. (Herrick , 1992)Up to 88% of patients with multilayered compression system are reported to have healed ulcers after 6 months of treatment. (Moffatt, 2003).Although the difference were non-significant by 24 weeks but it is found that patients with 4 layer long stretch systems had improved healing rates at 12 weeks compared to patient with 2 layer long stretch system. (Moffatt, 2003)

2.7.3Endovenous Laser Therapy

EVLT is a minimally invasive procedure that is popular in venous disease therapy. EVLT of the GSV has been compared with high ligation and stripping in randomized controlled trial. The results showed no significant difference in safety and efficacy in eliminating GSV reflux, alleviation symptoms and signs of GSV varicosities in the first 6 months after treatment. But, the patients in the surgical group might experience a slight increase in pain and bruising. In a cohort study, out of 44 patients from 139 patients from January 2004 to August 2007 had non healing ulcers is referred to EVLT and within 3 months mostly the ulcers healed with no recurrence. (Timperman, 2004).

Conceptual Framework



CHAPTER 3: METHODOLOGY

3.1 Study Location

This study was conducted at Hospital Pantai Ayer Keroh, Melaka.

3.2 Study Design

A retrospective cross sectional study was used in this study. Secondary data were extracted and reviewed. The patients were contacted for latest follow up.

3.3 Study Duration

The duration of this study was 12 weeks and can be divided into 2 phases :

a) Phase 1 : Preparation and submission of proposal paper (week 1-week 2)

b) Phase 2 : Proposal presentation, data collection, analysis and presentation, and final presentation/seminar.

3.4 Study population

Study population was all the patients with Chronic Venous Disease(CVD) in Hospital Pantai Ayer Keroh, Melaka from 2010-2012.

3.5 Sampling population

3.5.1 Inclusion criteria

The inclusion criteria was the patients above 18 years old.

3.5.2 Exclusion criteria

The exclusion criteria were the patients with congenital disorder, incomplete data and

pregnancy.

3.6 Sampling frame

The sampling frame was the list of patients with chronic venous disease in Hospital Pantai Ayer Keroh, Melaka which fulfilled the inclusion criteria.

3.7 Sampling unit

Sampling unit was the patient with chronic venous disease in Hospital Pantai Ayer Keroh, Melaka which fulfilled the inclusion criteria.

3.8 Sample size

Sample size was all the patients attending the venous clinic in Hospital Pantai Ayer Keroh from 2010-2012 which were 190 patients.

3.9 Sampling method

Convenience sampling method as we selected the samples from one particular hospital.

3.10 Parameters / variables

3.10.1 Dependent variable

The dependent variable in this study was the presentation of patients with CVD.

3.10.2 Independent variable

The independent variables were association factors which are age, gender, ethnicity and previous DVT.

3.11 Study instrument

The data were collected by using a proforma. There were two sections in the data sheet; Section A (patient's identification), and section B (history of disease).

3.12 Data collection

Secondary data was used in this study. It is based on the patients' medical history, proforma, and any insufficient data was completed through the phone interview or further follow up.

3.13 Quality control

In order to obtain accurate data, we had pretested the proforma by selecting few cases that fulfill the criteria, to standardize the proforma. All the data was collected and handled confidentially.

3.14 Data analysis

Data was analyzed by using Statistical Package for Social Sciences Program, SPSS version 2.0. We use cross –sectional study in both descriptive and analytic aspect. For descriptive study, the categorical data will be described by using frequency and percentage. In analytic study, we used chi-square for non-continuous data (eg. Age, gender, ethnicity and etiology).

Standard p-value of $p < 0.05$ was set for all significant levels.

3.15 Study ethics

Ethical forms was submitted to the following individuals/institutions .

a) The Ethical Committee of Faculty of Medicine and Health Sciences, UPM. (FPSK)

b) MREC, The Ministry of Health (MOH).

c) Director of Hospital Pantai Ayer Keroh , Melaka.

3.16 Limitation

Missing or not stated data as we carried out retrospective cross-sectional study.

CHAPTER 4.0 DATA ANALYSIS

4.1 Descriptive study of epidemiology, clinical presentation and treatment of patients.

Table 1 shows the epidemiology, clinical presentation of CVD patients in different aspects and figure 8 shows the ulcer treatment. In our study, there were 190 CVD patients' data collected from Hospital Pantai Ayer Keroh but 4 of them were excluded (total: 186).

4.1.1 Gender

Out of 186 patients, majority (71.5%) are females.

4.1.2 Age

In aspect of ages, highest percentage (58.1%) of patients aged between 40 to 59 years old. 28% of them aged older than 60 years old and the rest aged between 20 to 39 years old.

4.1.3 Ethnicity

For ethnicity, majority of patients (75.8%) are Chinese.

4.1.4 Etiology

In the aspect of etiology, majority of patients (90.9%) have primary causes of CVD while only 9.1% of patients having CVD which is secondary to other disease, for example DVT.

4.1.5 Classification

From the CEAP classification, CVD can be classified into 7 groups which are group C0 to C6. In our study, 41.4% of patients presented in group C2 (varicose veins), 24.7% of them are in C6 (active venous ulcer), 15.1 % in C4 (skin changes), 12.9% in C3 (edema), while only 4.3% of them are in C5 (healed venous ulcer) and 1.6% in C1 (telangiectasias) which is considered as very rare.

4.1.6 Clinical presentation

In clinical presentation, 21.5% of them presented with skin change or eczema, while 5.9% have Superficial Thrombophlebitis. And in overall, around 1/3 of patients which is 28.5 % have ulceration. 9.1% of patients have Deep Vein Thrombosis.

4.1.7 Treatment for ulcer

For the treatment to patients with ulceration, 28 (52.8%) out of 47 patients undergo EVLT and 25 (89.3 %) among them were healed, and 7.1 % of patients have improvement in the ulcer.
8 (15.1%) patients undergo 4-Layer Compression with 50% healed and other 50% were improved. Another 7 (13.2 %) patients undergo surgery, 5 (71.4%) of them with healed ulcer and the others got improvement. While the rest of 4 patients (7.5%) wear Graduated Compression Stocking, which have 3 among them got improvement in ulcer and 1 was healed.

Table I. Descriptive study of epidemiology, clinical presentation and treatment of patients.

	Frequency	Percentage (%)
Gender		
Males	53	28.5
Females	133	71.5
Age		
20-39	26	14
40-59	108	58.1
≥60	52	28
Ethnicity		
Malay	17	9.1
Chinese	141	75.8
Indian	28	15.1
Etiology		
Primary	169	90.9
Secondary	17	9.1
Classification		
C1	3	1.6
C2	77	41.4
C3	24	12.9
C4	28	15.1
C5	8	4.3
C6	46	24.7
Clinical Presentation		
Bleeding	7	3.8

Eczema / skin change	40	21.5
Superficial Thrombophlebitis	11	5.9
Ulceration	53	28.5
Previous DVT		
Yes	17	9.1
No	169	90.9

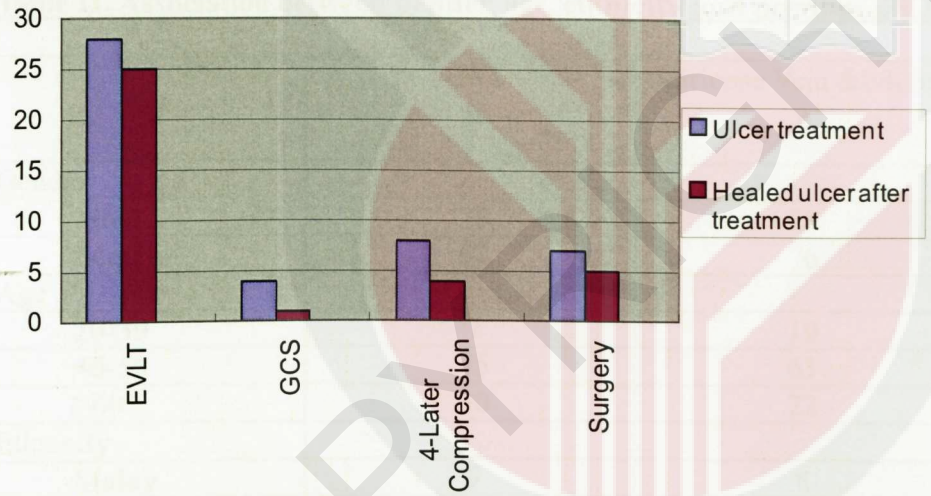


Figure 8. Ulcer treatment and healed ulcer after treatment.

4.2 Analytic study for the association between gender, age, ethnicity and previous DVT with presentation of CVD.

Table 2 shows the association between gender, age, ethnicity and etiology with presentation of CVD. Only the association between the age and the presentation of CVD is significant due to the p-value 0.026, which is < 0.05. There are no significant association between gender, ethnicity and etiology with presentation of CVD.

Table II. Association between gender, age, ethnicity and previous DVT with presentation of CVD.

	CVI n	Varicose Vein &Edema n	P-value
Gender			0.593
Male	25	28	
Female	57	76	
Age			0.026 *
20-39	7	19	
40-59	45	63	
≥60	30	22	
Ethnicity			0.621
Malay	9	8	
Chinese	77	64	
Indian	18	10	
Previous DVT			0.086
Yes	11	6	
No	70	93	

* Significant, p< 0.05.

CHAPTER 5. DISCUSSION AND CONCLUSION

5.1 Epidemiology, clinical presentation and treatment of patients.

5.1.1 Gender

Based on findings, majority were females patients (71.6%) but the association between gender and the presentation of CVD was not significant. As in previous study in Edinburgh, the estimated prevalence of varicose veins was 5% to 30% in the adult population, with a female to male predominance of 3 to 1. (Evans, 1999) However, it was reported that CVI was more common with increasing age, but there was no significant sex difference.(Brand et al.,1988) In Western Europe and the United States, reports of prevalence of chronic venous insufficiency vary from < 1% to 40% in females and from < 1% to 17% in males. Prevalence estimates for varicose veins are higher, <1% to 73% in females and 2% to 56% in males. (Jennifer et al., 2005) From here we can see that the prevalence of females in CVD might be higher than males, this may due to pregnancy but we had already excluded pregnant patients in our study, so the large difference of gender in our study might be due to the sample size inadequate which as only 186 patients included and the association was also not significant.

5.1.2 Age

There is an association between age and presentation of CVD and majority of patients aged between 40-59 years old. Based on the cohort study in Italy it shown that CVD increased with age; median age was 54 (range: 18–90) years for the women and 61.0 (range:18–89) years for the men ($t=14.35$, $p<0.0001$) and proof that presentation of CVD is affected by age (Chiesa, 2005). However, CVD are not restricted to adult: 27% of the school children between the ages of 10 and 16 years old in the Bochum study (from 11 German secondary schools) presented with varicose disease (Ruckley, 2002). But in our study we excluded the patients aged below 18 years old because it could be due to congenital disorders.

5.1.3Ethnicity

According to our finding, majority of patients were Chinese and the association between ethnicity and presentation of CVD was not significant. As in other studies, they stated that CVI is due to other risk factors such as family history, gender, increasing age, obesity and others. However, there are no well-supported by scientific evidence that mention about ethnicity affects the development of CVI. From here we can see that the high prevalence of Chinese in CVD might due to the selection bias as our study was performed in private hospital which normally will have higher percentage of Chinese patients.

5.1.4 Etiology

In our findings most of the patients have the primary disease. Previous study also showed that most of the patients have CVD due to primary cause. An analysis of cases of chronic venous disease indicated that primary valvular incompetence was present in 70 to 80 percent and a congenital anomaly in 1 to 3 percent; valvular incompetence was due to trauma or deep-vein thrombosis in 18 to 25 percent.(N, 2003)

5.1.5 Class

Most of the patients presented with varicose vein or C2. Previous study,_The Framingham Study was a longitudinal study that followed up men and women living in Framingham, USA, over a 16-year period from 1966 (Brand , 1988). Every second year over this period, subjects were examined for varicose veins, defined as "the presence of distended and tortuous veins, clearly visible on the lower limbs with the subject standing." Over the 16-year period, 396 out of the 1720 men and 629 out of the 2012 women who were free from venous disease in 1966 developed varicose veins. Telangiectases are more frequent in women and occur in over 80% of those living in Southern Italy (Chiesa, 2005). However, from our study, up to 50% of patients developed C4, C5 and C6 which are Chronic Venous

Insufficiency (CVI). This tells that Malaysian population presented late to the hospital compared to Western population.

5.1.6 Clinical presentation / manifestation

A previous study that has been carried out by Browse NL, Burnard KN (2011) stated that skin changes/eczema is the most common skin manifestation of CVI of lower limbs occurring among the first symptoms of the disease. Most times, it is preceded by edema for months and years, but also can be occurred in their absence. It can be coexist with varicose ulcer (most often) complicates this manifestation. While varicose ulcer represents a loss in the demo-hypodermic favorite location in the lower half of calf with long development and without a tendency to spontaneous healing.(Carpentier PH et al., 2004).Leg ulcers are debilitating and greatly reduce patients' quality of life. Based on our finding, many patients presented to hospital with eczema/skin change and ulceration. This tells that many patients with CVD present late to seek help when the disease is already in severe state (e.g eczema, ulcer). That could be due to a lack of awareness on CVD or cultural factors that affect in late presentation.

5.1.7 DVT

Our study showed that there was no significant association between DVT and presentation of CVD. However, from the previous study that had been done by Walker N et al. (2003) showed that, people who had a diagnosed thromboembolism were at almost three times higher risk of having a leg ulcer. In addition, people who had been at high risk of a venous thrombosis but were not diagnosed with this condition (eg, people with a history of major leg surgery) were also at increased risk of ulceration. The insignificant of result in our study might because of the inadequacy of sample size which was only 186 patients were included.

5.1.8 Treatment

Based on finding, more than half(52.8%) of ulcer patients had undergone EVLT and 89.3 % among them were healed, and 7.1 % of patients have improvement. Compare to the study done by Teo TK et al. (2010), the ulcer healing occurred as early as 1 week after the EVLT procedure in some patients, and the cumulative healing rates at 1, 3, 6, and 12 months were 82.1%, 92.5%, 92.5%, and 97.4%, respectively. Another study carried out by Dumantepe M et al. (2012) also concluded that : "Especially in the case of liposclerotic or ulcerated skin in the affected region, EVLA of incompetent perforator veins with 1470□nm diode laser is highly effective and safe, and appears to be feasible". From here we can see that, EVLT is an effective treatment for ulceration.

In our study, the ulcer healing occurred in 50% of patients after wearing 4-Layer Compression and 25% of patients with Graduated Compression Stocking. This proof the report from Laurie Barclay (2011), stated that compression therapy is the standard of care for treatment of venous ulcers and has been proven beneficial. Another study from Cullum N et al. (2004) also showed that compression encouraged healing of ulcers. More ulcers were healed at 12-15 weeks with high compression systems than with low compression systems. No significant difference was found between the effectiveness of different high compression systems, but more ulcers healed at 24 weeks with four layer bandages than with a single layer.

From aspect of surgery, 71.4% of patients with healed ulcer after the procedure. Previous study showed that surgical management led to an ulcer healing rate of 88 %, with only a13% recurrence rate over 10 months.(Barwell et al.,2004) When superficial venous surgery was compared with compression alone in 87 patients with venous ulcers, surgery achieved complete healing at a mean of 31 days compared with 63 days with compression; recurrence rates at three years were 9% and 38%.(Zamboni et

al.,2002) This showed that surgery improve healing of ulceration.

5.2 Conclusion

Epidemiological studies are used to assess the prevalence (occurrence) of diseases or disorders within populations in order to establish the magnitude of a certain problem. Basically, we have achieved all of our objectives in this study. There are three important things that we can conclude of. Firstly, we can conclude that increasing in age has the higher risk to develop CVD since there is clear association between age and presentation of CVD. Secondly is we can conclude that in our population, Malaysian tends to present late to the hospital with already in severe state of this disease which are up to 50% develops C4-C6. Last but not least, we conclude that proper intervention can heal this disease and it was been proven that EVLT is highly efficient to treat the venous ulceration.

5.3 Limitation

The limitation we faced was that the sample size in this study was small because we only conducted our study in one particular hospital which was Hospital Pantai Ayer Keroh, Melaka. Besides that, our study was based on retrospective observational study, thus some incomplete or missing data had occurred. There was also selection bias in our study. This is because the study location was in private hospital in Melaka that the Chinese population is more predominant compared to Malay and Indian.

5.4 Recommendation

For further studies, we would like to recommend doing the study in the several hospital and a large sample with high file retrieval rate. It can include the entire population and produce an accurate result by avoiding the selection bias. With the study, we recommend that patients with symptoms such as oedema, pain or varicose vein should present earlier to seek help from hospital instead of waiting until the disease is already in severe state (e.g eczema, ulcer). The awareness of CVD should be enhanced by conducting more public education via forums or media. Due to high association of age to CVD, more public screening should be done for the elderly and advices of exercise, weight loss, and appropriate care for CVD should be provided. EVLT was proven to be highly effective and safe to treat ulceration. However different pathophysiology requires different types of treatment, we suggest that future study should focus on pathophysiology of the CVD in order to approach the appropriate treatment.

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APPENDIX

Proforma

Chronic venous insufficiency study- Proforma

Profile:

Name of Patient :

Sex/ Age :

Date first seen :

Telephone number- Home/ Handphone:

Employment : ☐ **Yes** ☐ **No**

Etiology : ☐ Primary ☐ Secondary

Anatomy:

☐ **SFI** ☐ **SPI** ☐ **Thigh Perforator I**

☐ **Calf Perforator I** ☐ **DVI** ☐ **SVI**

Presentation:

Class: ☐ C0 ☐ C1 ☐ C2 ☐ C3 ☐ C4 ☐ C5 ☐ C6

☐ Bleeding ☐ Eczema /skin change ☐ STP

Ulceration : ☐ No ☐ Yes

Ulcer site: ☐ Left ☐ Right

Location: ☐ Medial ☐ Lateral ☐ Others

Ulcer size (cm):

Duration of ulcers before clinic visit (months): ☐ **1** ☐ **3** ☐ **6** ☐ **12** ☐ **>12**

Co-morbidity:

☐ DVT ☐ Hypertension ☐ Bronchial asthma ☐ Renal failure/ on dialysis

☐ IHD ☐ Stroke ☐ PAD ☐ Diabetes ☐ Peripheral neuropathy ☐ Others _____

Duplex scan finding:

☐ Superficial vein incompetenc ☐ LSV ☐ SSV

☐ Thigh & calf perforators:

☐ Deep Vein incompetence:

☐ Deep Vein Thrombosis:

Other imaging done: ☐ No ☐ Yes (state)_____

Treatment given after visit to vein clinic and date:

☐ Injection sclerotherapy Date _____

☐ GCS Date _____

☐ 4-Layer compression Date _____

☐ Surgery Procedure _____ Date_____

☐ EVLT Procedure _____ Date_____

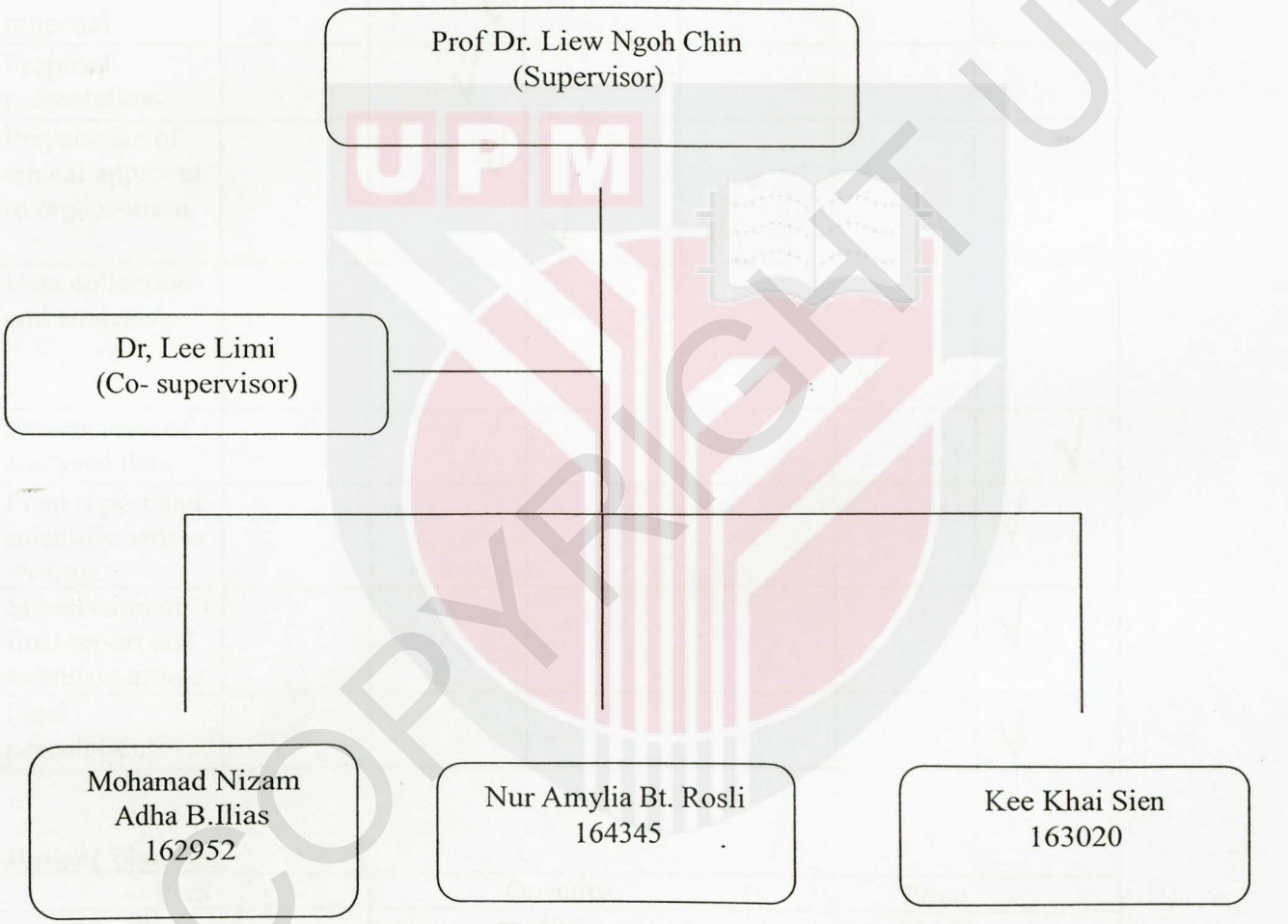
☐ RFA Procedure _____ Date_____

Date last seen: _____

Present state of ulcer :

☐ Healed ☐ Improve ☐ Non-healing ☐ Recurred ☐ Not relevant

Research Team



Gantt Chart

	March	April	May	June	July	August
Proposal presentation	√					
Submission of proposal		√				
Proposal presentation		√				
Preparation of ethical approval to organization		√	√	√		
Data collection and analysis					√	
Presentation of analysed data						√
Final report and scientific article writing						√
Submission of final report and scientific article						√
Final pesentation						√

Budget Planning

Item	Quantity	Price
Photostat	400	RM40
Printing	50	RM50
Hard covers for final report	4 sets	RM200
Fuel	4 times	RM240
Tol	4 times	RM120
Total		RM650

Attachment 2

JKEUPM Ref No. : FPSK_Mei (13)17(undergaraduate)

Members of the JKEUPM who reviewed the documents:

Prof. Madya Dr. Johnson Stanslas

Date of approval: 31/5/2013

Endorsed at JKEUPM Meeting on **7/6/2013**, attended by:

NAME	DESIGNATION	GENDER	TICK IF PRESENT
Prof. Dr. Norlijah Othman	Paediatrics& Dean, Faculty of Medicine and Health Sciences	Female	√
Prof. DrZamberiSekawi	Medical Microbiologist & Deputy Dean of Research and Internationalization, Faculty of Medicine and Health Sciences	Male	
Prof. Dato' Dr. Lye Munn Sann	Medical Statistician, Dept of Community Health, Faculty of Medicine and Health Sciences	Male	√
Prof. Dr. TengkuAizanAbd Hamid	Gerontologist & Director, Institute of Gerontology	Female	
Prof. Dr. LekhrajRampal	Medical Statistician, Dept of Community Health, Faculty of Medicine and Health Sciences	Male	√
Prof. Dr. Elizabeth George	Pathologist, Dept of Pathology, Faculty of Medicine and Health Sciences	Female	
Prof. Dr. Lim ThiamAun	Anesthesiologist, Dept of Surgery, Faculty of Medicine and Health Sciences	Male	
Prof. Dr. Wan Omar Abdullah	Medical Parasitologist, Dept of Medical Microbiology and Parasitology, Faculty of Medicine and Health Sciences	Male	√
Prof. Dr. Patimah Ismail	Professor of Biomedicine, Dept of Biomedical Sciences, Faculty of Medicine and Health Sciences	Female	√
Prof. Dr. Azali Mohamed	Professor of Macroeconomics, Dept of Economics, Faculty of Economics and Management	Female	
Assoc. Prof. Dr. Johnson Stanslas	Pharmacologist, Dept of Medicine, Faculty of Medicine and Health Sciences	Male	√
Assoc. Prof Dr. Mansor Abu Talib	Assoc. Professor of Guidance and Counselling, Dept of Human Development and Family Studies, Faculty of Human Ecology	Male	
Assoc. Prof. Dr. Noritah Omar (Lay Person)	Assoc. Professor of English Language, Dept of English Language, Faculty of Communication and Modern Languages	Female	√
Dr. RojanahKahar (Lay Person)	Lecturer of Dept of Human Development and Family Studies, Faculty of Human Ecology	Female	√
Tan Sri Dato' Napsiah Omar (Lay Person)	Chairman, National Population and Family Development Board	Female	√