

ผลเปรียบเทียบระหว่างการเดินจงกรมและการนวดต่อการไหลเวียนเลือดส่วนปลาย และอาการเส้นประสาทส่วนปลายเสื่อมในผู้ที่มีภาวะเส้นประสาทส่วนปลายเสื่อมจากเบาหวานชนิดที่ 2

COMPARATIVE EFFECTS BETWEEN WALKING MEDITATION AND MASSAGE ON PERIPHERAL BLOOD CIRCULATION AND NEUROPATHIC SYMPTOMS IN PERSONS WITH TYPE-2 DIABETIC PERIPHERAL NEUROPATHY

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2019

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พิชญา สุขไพบูลย์

ปริญญานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตร
วิทยาศาสตรมหาบัณฑิต สาขาวิชากายภาพบาบัด
คณะกายภาพบำบัด มหาวิทยาลัยศรีนครินทรวิโรฒ
ปีการศึกษา 2562
ลิขสิทธิ์ของมหาวิทยาลัยศรีนครินทรวิโรฒ

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PICHAYA SUKPHAIBOOL

A Thesis Submitted in partial Fulfillment of Requirements

for MASTER OF SCIENCE (Physical Therapy)

Faculty of Physical Therapy Srinakharinwirot University

2019

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THE THESIS TITLED

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HAS BEEN APPROVED BY THE GRADUATE SCHOOL IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE MASTER OF SCIENCE IN PHYSICAL THERAPY AT SRINAKHARINWIROT UNIVERSITY

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Author	PICHAYA SUKPHAIBOOL
Degree	MASTER OF SCIENCE
Academic Year	2019
Thesis Advisor	Assistant Professor Saitida Lapanantasin

Peripheral neuropathy are common complications causing foot ulcers and amputation risk in type-2 diabetes (DM). This study aimed to compare the effects of walking meditation (WM) and massage (M) on peripheral blood flow, neuropathic symptoms and quality of life (QoL) in persons with type-2 DM. Twenty-six participants, both men and women with type-2 DM aged between 42-69 years were randomized into WM (n=8), M (n=9) and control (n=9) groups. WM and M groups engaged in 4 weeks of practice (30 min/day, 3 days/week). Peripheral blood flow was assessed by doppler ultrasound. Neuropathic symptoms represented by the perception of pressure and vibration senses. The QoL was assessed by WHOQOL-BREF-THAI. Data were analyzed using nonparametric statistics. The results showed that, at post-intervention, WM and M groups showed improvement of peripheral blood flow when compared to baseline and also higher than the control group significantly ($p<0.05$). As neuropathic symptoms, after 4 week, WM and M groups presented significantly better pressure sense perception than baseline ($p=.012$) and also than the control group (WM: $p=.001$, M: $p=.014$). As the vibration sense outcome, only the WM and M groups showed statistically significant improvement of vibration sense when compared to their baseline ($p=.012$). In conclusion, this study supported that either WM or M can improve peripheral blood flow and also reduce the neuropathic symptoms of a diabetic foot in persons with type-2 DM.

Keyword : Walking Meditation, Massage, Neuropathy, Diabetes Mellitus, Pressure Sense, Vibration Sense, Monofilament, Tuning Fork

ACKNOWLEDGEMENTS

I would like to express my deep gratitude to Asst. Professor Saitida Lapanantasin and Asst. Prof. Witid Mitranun, my research supervisors, for their patient guidance, enthusiastic encouragement and useful critiques of this research work. I would also like to thank Faculty of Physical Education, Srinakharinwirot University where lent me an important equipment as Doppler Ultrasound for this research and I am thankful to the National Research Council for the research grant. In addition, I would like to express my deepest thank to the authorities at That Phanom Community Health Center, Nakorn Panom, Thailand for every assistance in research coordination. My grateful thanks are also extended to Thanapun Farmcare Company Limited for their help and support my accommodation during I lived in Nakorn Panom.

Finally, I wish to thank my beloved family for their supports and encouragement throughout my study.

PICHAYA SUKPHAIBOOL

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CHAPTER 1
INTRODUCTION

Background

World Health Organization reported that there were approximately 422 million adults with diabetes in 2014 compared to 108 million in 1980. The global prevalence of diabetes had been rising from 4.7% to 8.5% in the adult population and had risen faster in the low and middle income countries than in the high income countries.(1) Since 2005 to 2013, incidence of diabetes in Thailand was 177 per 1000 and it significantly increased in both male and female.(2) Moreover, the age and body mass index had a positive relation with increased Diabetes prevalence.(2)

Type-2 diabetes, caused by insulin resistance, was mostly affecting on people with diabetes.(3) People with diabetes were risky to a premature death because of the complications(4) such as diabetic retinopathy, diabetic nephropathy, cardiovascular and cerebrovascular problems. Most of these complications in people with diabetes were usually caused by a chronic uncontrolled hyperglycemia inducing arterial blood vessel damage. The damaged arterial vessels became stiff and increased in vascular resistance which dued to poor blood circulation to the organs that they supplied. Therefore, diabetic patients who had peripheral arterial complications with diabetic foot ulcers were likely to have a high risk of lower limb amputation.(5)

Moreover, chronic uncontrolled hyperglycemia was one of the factors that resulted in peripheral neuropathic symptoms which called diabetic peripheral neuropathy, DPN.(6) The hyperglycemia condition produced micro and macro vascular alterations(7-10) which caused poor blood supply to peripheral nerves and then the nerves had been damaged(11, 12) or demyelination from hypoxia.(13) Impaired sensations and muscle weakness of lower limbs from the DPN could disturb balance during walking, increased risk of fall and reduced individual's daily activity performance.(14) Moreover, sensory impairment from DPN could cause incurable foot ulcer which leaded to amputation.(9, 14) The vascular and peripheral nerve complications in diabetes adversely affected patient's

quality of life(9) and would bring a high expenditure to diabetic patients if they got an improper management.(15) Therefore, the assessment and treatment for vascular and peripheral neuropathic problems were very important in diabetes.

Glycemic control was the major treatment, but it was difficult to achieve for many patients.(14) Using drug could help patient to get better but sometimes it also had side effects.(16) Exercise program in physical therapy was another way to improve quality of life in diabetic people who had micro-vascular disease because it was not only to decrease risk of vascular disease, enhance glycemic control but also improved physical function.(17-20) In addition exercise could reduce psychological responses to stress as well.(21)

In 2001, Ezzo et al had found that massage not only improved Hemoglobin A1c from baseline, decreased depression level, and sleep better(22) but also relieved diabetic neuropathic symptoms.(22, 23) On the other hand, massage also had adverse effects in diabetic patients such as the following. The patient who used insulin, massage could induce hypoglycemia and the patients who had vascular problem should avoid do friction because it could induce vascular damage.(22)

In a Buddhist society, meditation was a widespread practice. Many evidences supported and adviced that meditation and walking meditation had benefit to type-2 diabetes patients(24-27) same as weight bearing exercise. Both was useful to type-2 diabetes in many ways such as improved cardiovascular fitness, physical activity, exercise capacity, glycemic control, muscle strength, fatigue, balance, arterial stiffness, blood flow, quality of life or general well-being and decreased triglyceride, blood pressure, and body mass index.(17-21, 25, 28-32) In 2014, Prakhinkit et al investigated in depressed elderly and found that walking meditation had tendency to decrease depression, low-density lipoprotein cholesterol, cortisol, and interleukin-6concentrations more than traditional walking.(33) Similarly, Gainey et al, in 2016, had found that blood cortisol level of type-2 Diabetic patients would reduce only in walking meditation group and also arterial stiffness would decrease after the patients performed walking meditation 12 week.(25)

Base on the evidences, it couldn't deny that people with diabetes and diabetic peripheral neuropathy had resistance in blood flow.(34, 35) Several studies in diabetic patients discovered that meditation could help blood flow and improved by increasing in a flow-mediated dilation at right brachial artery of the patients.(25, 33) However, it was lack of a study finding an effect of walking meditation on neuropathic symptoms, peripheral blood flow of foot in individuals with type-2 diabetic peripheral neuropathy and also lack of comparative research between the effects of walking meditation and massage on peripheral blood circulation and neuropathic symptoms in person with type-2 Diabetic peripheral neuropathy.

Accordingly, the purpose of this study was for comparison between walking meditation and massage effects on peripheral blood circulation and neuropathic symptoms in individuals with type-2 Diabetic peripheral neuropathy.

Conceptual framework

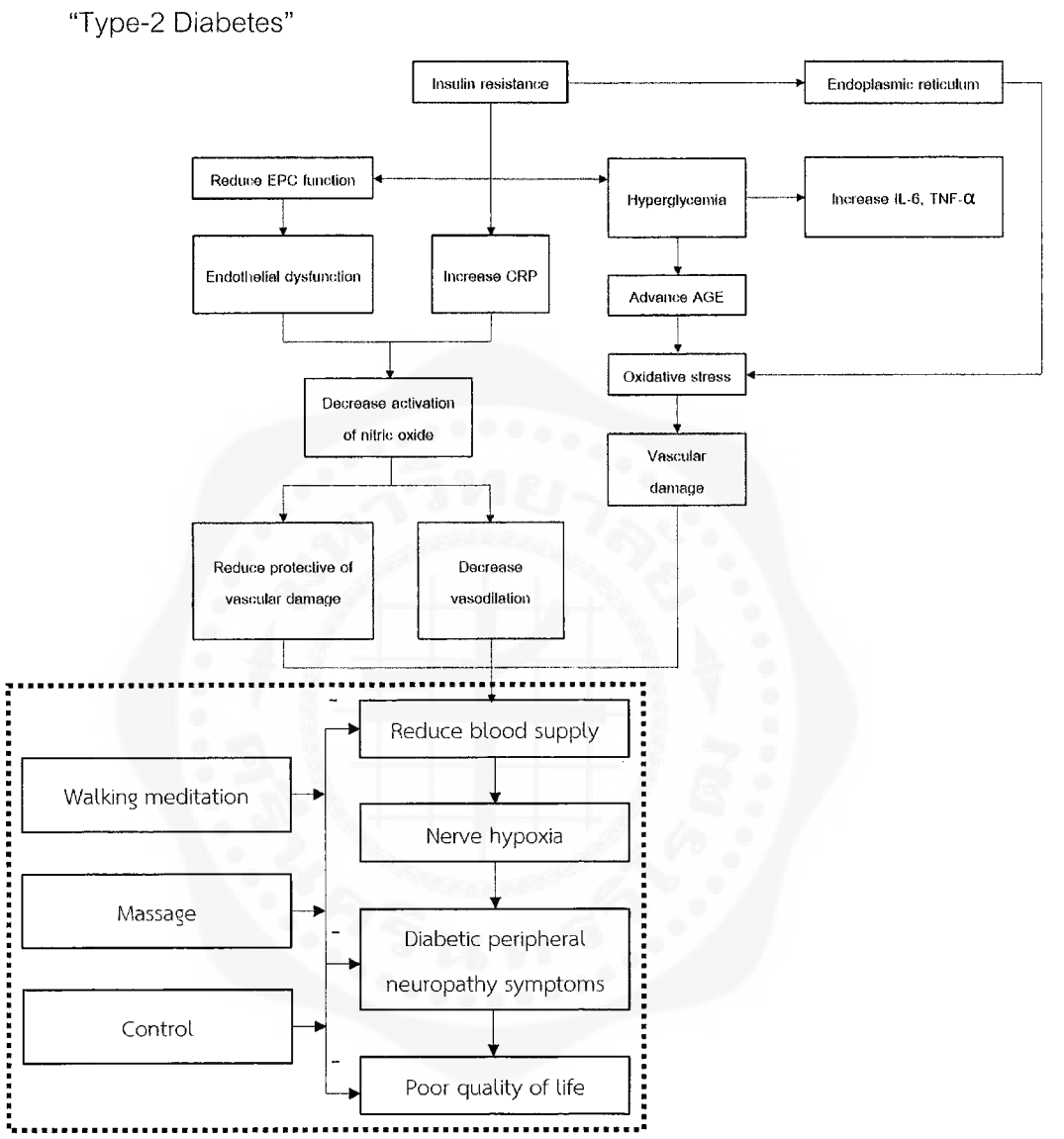


Figure 1 Conceptual framework

EPC: Endothelial Progenitor Cells

CRP: C-reactive protein (CRP)

AGE: Advanced Glycation End Products

IL-6: Interleukin-6

TNF-α: Tumor Necrosis Factor-Alpha

Research questions

Primary question

Does walking meditation improve peripheral blood flow and reduce neuropathic symptoms in persons with type-2 diabetic peripheral neuropathy better than massage?

Secondary question

Does walking meditation improve quality of life in persons with type-2 diabetic peripheral neuropathy better than massage?

Purposes

Primary objective

To determine effects of walking meditation compared with that of massage on peripheral blood flow and neuropathic symptoms in persons with type-2 diabetic peripheral neuropathy.

Secondary objective

To determine effects of walking meditation compared with that of massage on a quality of life in persons with type-2 diabetic peripheral neuropathy.

Research hypothesis

Primary hypothesis

Walking meditation could improve peripheral blood flow and reduced neuropathic symptoms in persons with type-2 diabetic peripheral neuropathy better than massage.

Secondary hypothesis

Walking meditation could improve quality of life in persons with type-2 diabetic peripheral neuropathy better than massage

Study variables

Independent variables

1. Walking meditation
2. Massage

Dependent variables

1. Peripheral blood flow
2. Neuropathic symptoms
3. Quality of life

Confounding factors

1. Diabetes Duration
2. Age
3. Gender
4. Ever smoked
5. Drinking caffeine
6. Body mass index
7. Frequency of exercise

Abbreviations

DPN: Diabetic Peripheral Neuropathy

MNSI: Michigan neuropathy screening instrument (It is a tool to detect peripheral neuropathic symptoms)

ABI: Ankle brachial index (It is a tool for detecting arterial stiffening, lower extremity ischemia or Peripheral arterial disease)

PAD: Peripheral arterial disease

Clinical applications

Either walking meditation or massage might apply as an additional alternative treatment for diabetic patients who had poor blood circulation of foot, neuropathic symptoms and poor quality of life.

Walking meditation, which was effective, safe and easy to use by themselves either at home or in the community, might apply as an exercise protocol for promoting peripheral blood flow of foot in persons with diabetes.

Either walking meditation or massage was an incentive for individuals with diabetes to look after themselves because it is easy to follow

CHAPTER 2

LITERATURE REVIEW

The review of literature included the following categories

1. Prevalence and incidence of diabetes
2. Characteristic of type-2 diabetes
3. Peripheral arterial disease
4. Assessment tools for peripheral arterial disease
5. Peripheral neuropathy in type-2 diabetes
6. Pathophysiology of diabetic peripheral neuropathy
   6.1 Risk factors of peripheral neuropathy
7. Assessment tools for peripheral neuropathy
8. Peripheral blood circulation
9. Factors affect blood circulation
10. Assessment tools of peripheral blood flow
11. Quality of life in diabetes
12. Assessment tools of quality of life in diabetes
13. Effects of massage in diabetes
14. Effects of exercise in diabetes
15. Effects of meditation in diabetes

Prevalence and incidence of diabetes

World Health Organization reported that there were approximately 422 million adults with diabetes in 2014 compared to 108 million in 1980. The global prevalence of diabetes increased from 4.7% to 8.5% in the adult population and has risen faster in low and middle income countries than in high income countries.(1) Since 2005 to 2013, the incidence of diabetes in Thailand was 177 per 1000 and it significantly increased in both male and female.(2) Moreover, age and body mass index had a positive relation with an increase in diabetes population.(2)

Age, duration of disease, the level of fasting blood glucose and number of co-morbidities were variable which increased cost of treatment in Diabetes. Complication from Diabetes was a major impact on the cost. Patients with complications had median cost more than who didn't have complications about USD$ 364.81. Common diabetes complications were nephropathy, retinopathy, cardiovascular problem and neuropathy.(5, 36) International Diabetes Federation predicted that in 2040, population about 642 million will have diabetes and about 2.2 million people could be death from diabetes and its complications such as cardiovascular problems and other diseases.(37) So diabetes complication screening was an important for manage patients.

In 2014, Sobhani et al found that most of diabetic patients had neuropathy and the symptoms disturbed their life.(37) In 2011,Jambart et al reported that more than half, type 1 and type 2 diabetic patients in the middle east region felt numbness and burning pain.(38) In 2012, Katulanda et al surveyed in developed country and found that at least 19.7% of persons with diabetes had diabetic peripheral neuropathy.(39)

Characteristic of type 2 diabetes

Type-2 diabetes was the most affect in people with diabetes. The body of person with type-2 diabetes was able to produce insulin but the insulin was ineffective.(1, 40) The type-2 diabetes showed an increased circulating level of insulin but it had insulin resistance.(3) Therefore, the blood sugar level was still high and would result in further complications.(1, 40) Hyperinsulinaemia was a compensatory condition which found in type-2 diabetes to maintain blood glucose level.(41) Diabetes often found in people who

was above 30 years old with hypersthenic body build (body mass index ≥ 23 kg/m2).(5) Actually, diabetes did not happen only in adults but also in children. Especially, the children who were girls living in low income families and also had family history of diabetes.(5) In young adult, decreased action of beta cell was major cause of type-2 Diabetes and it induced complication as same as adults.(5)

Type-2 diabetes was a part of metabolic syndrome. It mostly caused by a defect of beta cells in pancreas and insulin resistance.(3) The beta cells released an insulin which was a peptide hormone, its role was maintaining of a normal level of blood glucose by facilitating muscle cells to uptake glucose from blood plasma into the cells, and by facilitating adipose and liver cells to change the excess glucose to be lipid and glycogen keeping in the cells respectively.(41) The defect of beta cell leaded to less insulin production or inactivity which resulted in insulin resistance and hyperglycemic conditions. The people with chronic hyperglycemia were likely risked to the premature death because of the complications.(4) Although it severely affected to patients, it still had solution such as taking some medicine and changing lifestyle.(4)

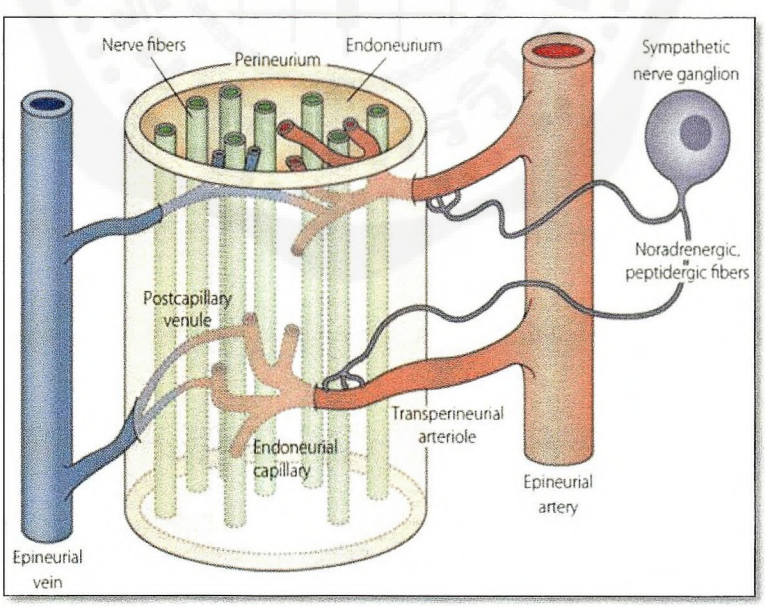


Figure 2 Peripheral nerve and vessel, figure from the study of Yagihashi et al, 2011.(42)

Peripheral arterial disease

In 2014, Leoniuk et al studied in 37 diabetes patients and 36 non-diabetes patients and found that both sides of dorsalispedis and posterior tibial arteries had overall vascular diameter and wall thickness in early stage of type-2 diabetic patients. In addition, they found that a high level of blood glucose correlated with a flow resistance index in the right dorsalispedis and both posterior tibial arteries and also with the decreasing in pulsatility index within dorsalispedis artery. Moreover, the high level of blood glucose correlated with having a trophic skin.(1)

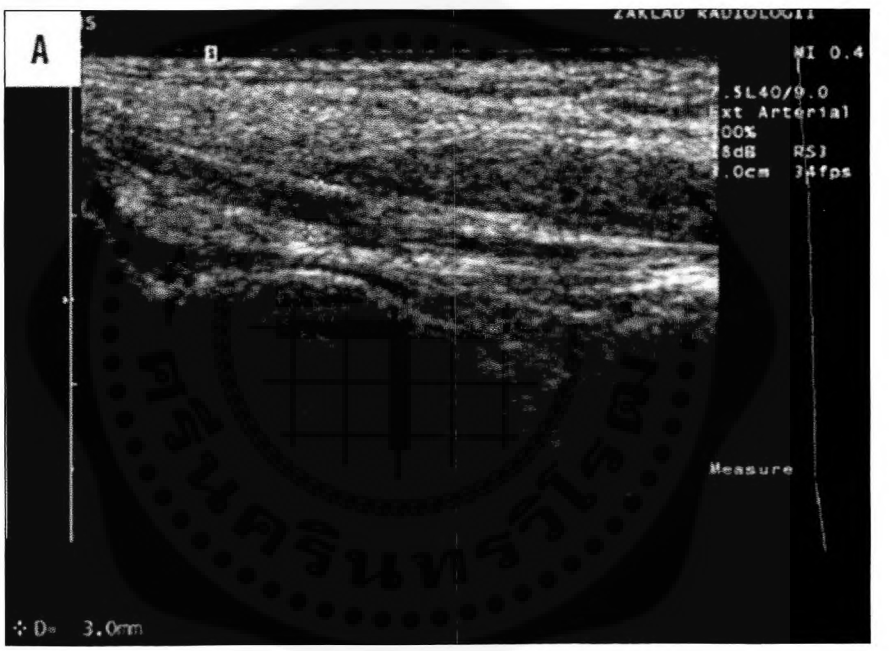


Figure 3 Blood vessel detected by ultrasound Doppler, figure from the study of Leoniuk et al, 2014(34)

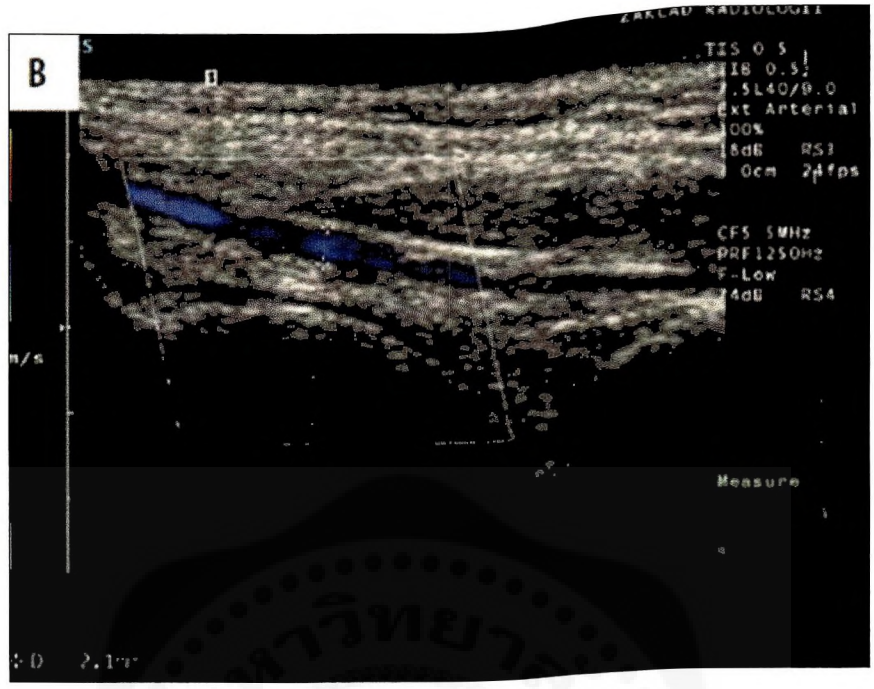


Figure 4 Used color imaging blood vessel, figure from the study of Leoniuk et al, 2014(34)

Assessment tools for peripheral arterial disease

Ankle brachial index(ABI)(6)

ABI has also been called the ankle-arm index, the ankle brachial blood pressure index, the ankle arm ratio or the Winsor index.(8) It was simple instrument, with affordable price to detect arterial stiffening, detected lower extremity ischemia or peripheral arterial disease.(2) and it demonstrated a relationship with diabetes duration as If diabetes duration less than 10 years, a mild to moderate peripheral arterial disease (PAD) would show (ankle brachial index value approximately 1.00-1.30). On the others hand, if diabetes duration 10-20 years, a moderate to severe PAD would showed (ankle brachial index value approximately 0.00-0.90).(43)

Table 1 Peripheral arterial disease severity in each leg are according to the levels of ABI(44)

Level of ABI	Results
More than 1.30	Poorly compressible vessel
0.91-1.30	Normal
0.7-0.9	Mild occlusion
0.4-0.69	Moderate occlusion
Less than 0.40	Severe occlusion

Actually, we often found a high ABI in patient who had neuropathy.(44) Many people who were diabetes had ABI values >1.3(45) and it always followed by calcification.(44) In 2005, Williams found that peripheral neuropathic patients had lighter foot pulses by sensitivity and specificity of ABI had changed when detected in pure Diabetes patient versus patients with DPN. They had found that the sensitivity changed from 100% to 53%, while the specificity changed from 88% to 95%. They also reported that a positive predictive value of PAD was about 80% with an accuracy only 84% by using ABI in persons with DPN.(45) Thus it was an assessment tools which appropriated for peripheral arterial disease.

However, vascular problem might appear when detected by Doppler Ultrasound. Some researcher had found that patient who had atherosclerosis in the superficial femoral artery (SFA) with a normal resting ankle brachial index. So, duplex assessment with Doppler ultrasound was an accurate screening tool which could rule out a vascular disease with short time of examination.(46)

Peripheral neuropathy in type-2 diabetes

Insulin resistance induced hyperglycemia was a risky factor of peripheral neuropathic symptoms.(6) The symptoms started in the distal and gradually affected proximal of the limbs, sensory loss was the first problem and followed by motor problems(14) Additionally, clinical signs of autonomic dysfunctions usually found in

peripheral neuropathy such as dry skin and loss of sweating which leaded to skin cracks, infections and ulcers in the foot.(13) Moreover, alteration of thermal perception thresholds(47), and neuropathic pain usually threatened daily life of the persons with type-2 diabetic peripheral neuropathy (type-2 DPN).(42)

In diabetes, the nerve fibers in epidermis of the skin were significantly affected. Thus, patients with type-2 diabetic peripheral neuropathy would feel like wearing a stocking and glove, loss of pain sensation or "Novocain-like" insensitivity tingling, pins and needles sensation, burning, electric shock, allodynia, and hyperalgesia.(15) These conditions disturbed during walking, increased the risk of falling and leaded to disability or infest individual's ability to perform daily activity and also risk to incur ulcer and amputation.(9, 14)

Approximately 34% of persons with type-2 DPN had neuropathic pain(48) and it had likely aggravated at night.(49) It disturbed patients when they were sleeping(10) So, the patients might have negative quality of life.(15) Moreover, diabetes costed a lot because it was a chronic disease.(15)

Pathophysiology of diabetic peripheral neuropathy

Oxidative stress was an important factors of vascular complications in diabetes patients because of free radical formation.(50) Chronic hyperglycemia leaded to micro and macro vascular alterations(7-10) which resulted in nerve damage or demyelination from nerve hypoxia(11, 12), especially c fiber.(13) As a result of hyperglycemia causing advanced glycation end products (AGE), oxidative stress induced vascular damages were increasing. Therefore, it would decrease blood flow that supplied to peripheral nerves and then the nerves and myelin sheath would be degenerated.(51)

In addition, level of interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF-α) were increased in chronic hyperglycemia(51). These cytokines express in macrophages(52) playing role in cell apoptosis(53) and induced peripheral diabetic neuropathy.(52) They were also the keys of inflammatory which would damage nerve cell together with disruption of sodium channels of sympathetic neurons that resulted in

neuropathic pain.(51) In 2011, Purwata, et al had found that level of TNF-α related with painful in diabetic peripheral neuropathy.(52) The peripheral neuropathy (peripheral nerve degeneration) was usually associated with micro vascular disturbance.(54)

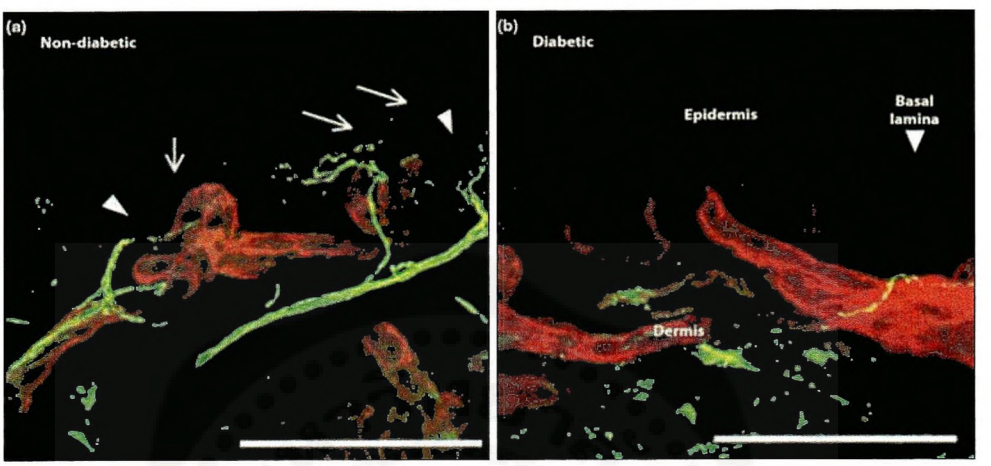


Figure 5 These 2 pictures showed quantity of nerve fiber (green color), Left side assessed in healthy subject while right side assessed in diabetes patient, figure from the study of Yagihashi et al, 2011.(42)

Moreover, Insulin was an activator which facilitated endothelial cells to produce nitric oxide via activation of phosphatidylinositol-3 kinase and Akt kinase (nitric oxide synthase). Nitric oxide released from endothelial cells which is the key to tell about health of blood vessels.(55, 56) As it was a major contributor to endothelium-dependent relaxation in arteries (vasodilator)(52, 57), it helped in maintaining tone of arterial at rest.(55) Nitric oxide was also a variable to protect arterial vessel(49) such as inhibit platelet activation and vascular smooth muscle cell migration(58) that's why type-2 diabetic patients who had insulin resistance consequently develop vascular diseases, especially atherosclerosis. The persons with type-2 Diabetes showed a reduction in nitric oxide concentrations and an increasing in the production of vasoconstrictors such as endothelin-1(49) which increased vascular tone and limited vascular smooth muscle cell growth.(58)

Abnormal metabolic was the factor of atherosclerosis, proatherogenic because it had higher level of c reactive protein (CRP) which was an inhibitor of endothelial cell nitric oxide synthase, so that patients would have a vascular problem and higher risk to turn to be peripheral arterial disease. Thus diabetic patients had a higher risk of cardiovascular disease than normal people.(58)

Generally, endothelial cells had a role to maintain vascular homeostasis for preventing thrombosis and leukocyte diapedesis and helped blood flowed smoothly.(48) It was also providing a physical barrier between vessel wall and lumen and secreted a number of mediators that regulated platelet aggregation, coagulation, fibrinolysis and vascular tone(57) resulting in irregular endothelial cells (endothelial dysfunction)(57) which leaded to increase synthesis of vasoconstrictor protanoids and endothelin, artherosclerosis and vascular smooth muscle cell apoptosis.(48)

Diabetic patients had less circulating Endothelial Progenitor Cells (EPCs) which were immature cells growth to be a mature endothelial cell. EPSs were direct contributors to the homeostasis and repaired of the endothelial layer. Thus, Endothelial Progenitor Cells (EPCs) dysfunction was associated with atherosclerosis.(57)

Endoplasmic reticulum stress was also a factor in vascular dysfunction in diabetes because it disrupted the mechanism of insulin signaling in liver, adipose tissue and pancreas, increase c-Jun N-terminal kinase (JNK) and catalytic I kappa B kinease subunits activity and induced inflammation associated with Insulin receptor substrate-1 (IRS-1) signaling impairment. So impaired vascular function by inflammation and oxidative stress were also from endoplasmic reticulum stress.(49)

The physiology and chemical had changed in the body draw type-2 diabetes patients into a circuit of vascular problems. In 2016, Fakhrzadeh et al showed that diabetes had high coronary artery calcium score that was an atherosclerosis marker. The higher score meant a higher risk of coronary heart disease. A homeostatic model assessment-insulin resistance predicted risk of coronary events as well. Beside that a decreasing response in flow mediated dilation showed a severity of vasodilation defect.(59)

In 2015, Lim et al had found that, after nerve injury, endothelial capillaries enlarged and thickened and also perineurial cell underwent aberrant fibrosis.(54) The vascular supply in peripheral nerves were sparse and then impaired blood supply in diabetic nerves(42). This caused decreases in gas, nutrient, and waste transport of the nerve(54) as endothelial cells disruption. Thereafter, it constituted the salient structural and changed in diabetes nerves.(42) Whereupon, Lim et al suggested to treat neuropathic pain, had to focus on hypoxia.(54)

Risk factors of peripheral neuropathy

The frequent complication in diabetes was diabetic peripheral neuropathy.(9) Risk factors of DPN were elderly, chronic diabetes mellitus(9, 14, 60), poor glycemic control, cardiovascular risk(14), severe hypertension(11, 15), family history(11), diabetes duration more than 5 years(61), type 2 diabetes, female, south Asians ethnicity(62), obesity(15, 60) or body mass index more than or equal 30 kg/m2 and waist circumference more than 40 inches(62), dyslipidemia, hyperglycemia, Tabaco use(15, 60), hypertension(61), micro-albuminuria, elevated blood fibrinogen level, physical inactivity(60) and hypercholesterolemia.(15) Furthermore, researcher had found that patients who received insulin with metformin and had diabetes duration more than 10 years demonstrated more chance to be a DPN.(9, 51, 63) Additionally, in 2010, Al-Mahroons et al examined the prevalence of diabetic peripheral neuropathy in primary care diabetes clinics in Bahrain. They had found that most of male who had diabetic neuropathy were in an age range between 60-69 years (43.6%) while those of female were in an age range more than 70 years (48.3%). If focused in both gender, 54 years old was mean age which always found diabetic. neuropathy(62) and it was close to a study of Janghorbani et al in 2006.(64) Same as the study of Sekhar et al, in 2015, had found that 40% of patients who were between 51-60 years old were the major factor to have painful diabetic peripheral neuropathy.(64)

Acute neuropathy could cause of Insulin neuritis since it was associated with magnitude and rate change of Hemoglobin A1c. It was possible that glycemic control

changed hemodynamic, so small fiber's endoneurial was hypoxia.(15) Somebody had no problem with nerve but also had a neuropathic symptoms because of other mechanism like hyperactivity of polyol pathways(65), oxidative and nitrosative stress, microvascular changes, channels sprouting, microglial activation, central sensitization, and brain plasticity.(66)

Assessment tools for peripheral neuropathy

The type-2 DPN complication affected to patient's life, so that assessment and treatment for peripheral neuropathy was very important. Standard method to assess diabetic peripheral neuropathy was nerve conduction velocity (NCV)(67) but it still had limitation to use especially in community because it had high cost and need specialist to do it. In 2015, Xiong et al had studied about diagnostic capabilities of the tools for diagnosing diabetic peripheral neuropathy which were neuropathy symptom and change score (NSC), neuropathy impairment score (NIS) and Michigan neuropathy screening instrument (MNSI). They had applied the tools to assess peripheral neuropathy in 131 type-2 diabetes patients and calculated the correlations of the assessment results with the standard methods, electromyography and nerve conduction velocity. They found that the NIS, NSC, and MNSI significantly correlated with standard methods by r=0.653, r=0.625 and r=0.440-0.618 in respective.(67)

Michigan neuropathy screening instrument (MNSI)

Michigan neuropathy screening instrument (MNSI) was an accuracy, useful for diabetic neuropathy.(68) In 2015, Damri et al translated Michigan neuropathy screening instrument into Thai language and found that it had high reliability and validity.(69) And it could separate normal people from diabetes peripheral neuropathy patients by subjective and physical examination scores. If the subjective examination score was more than 7, it could mean you have a diabetes peripheral neuropathy.(69) For the physical examination cut off score was 2 points which indicated peripheral neuropathic condition. MNSI had a sensitivity of 65% and specificity of 83%.(68) There was a significant positive relationship between number of neuropathies assessed by MNSI

and a mean of diabetes duration.(70) and a negative correlation with ankle brachial index.(71)

Anyway, MNSI couldn't absolutely confirm whether patients had diabetes neuropathy due to the research of Mete et al in 2013 had found that some patients who had dysfunction detected by neurothesiometer could not be detected by MNSI and EMG.(72) However, disadvantage of EMG and neurothesiometer weren't widely used because of high cost and the requirement of experienced assessor.

Due to MNSI assessment depended on only symptoms, it might be some mistaken diagnosis. On the other hand, the strength point of Michigan neuropathy screening instrument was telling what patients felt or what symptoms happened to them which were the main of the problem in patient that affected to everyday life. We could not deny that MNSI was easy to use, and cheap. Thus, it was appropriate to detect peripheral neuropathic symptoms.

Assessing diabetic peripheral neuropathy usually consisted of sensory and motor testing because most of peripheral nerves were mixed nerves which conducted both sensory and motor nerve impulses. If the nerve degenerated, it would show various types of sensory loss such as pain, pressure and vibration senses and also showed motor weakness or decreased in deep tendon reflex.(73) However, the sensory or the small nerve fibers usually degenerated before the motor or the large nerve fibers. Therefore, the early detection of peripheral neuropathic symptoms should concern on a sensory loss which could be assessed by monofilament testing with 10 g monofilament and, vibration perception testing with 128 Hz tuning fork.(73)

Monofilament sensory testing

Monofilament sensory testing by 10 g monofilament was generally used for detection of a sensory loss of light pressure(73) or protective sensation(74) of diabetic foot. Assessor used 10 g monofilament to test foot of patient about six sites on each foot.(73) Supine position was an appropriated position to test patients, at first, assessor had to demonstrate at patient's arm during closing their eyes and let them feel what they

could feel at the feet when an instrument placed against with their feet and randomly placed a filament not over three second per site.(73)

To perform the monofilament test, an assessor should avoid the callus(73), and cleaned an instrument with alcohol before use with other patients.(73) From the systematic review by Wand et al in 2017, they reported about the numbers of sites for monofilament test was between 3-10 points in each foot. The study of Jayaprakash in 2011, which was included in the systematic review by Wand et al, had studied in the biggest number of sample size (n=1044) used 4 sites in each foot. The 4 sites consisted of the plantar surface of great toe, base of first, third, and fifth metatarsals (Figure 6). The 4 sites test of the monofilament had sensitivity 60% and specificity 93% when used vibration perception test as a reference standard test. if used nerve conduction study as a reference standard test, the study of Lee et al in 2003 showed high sensitivity and specificity (93.1%, 100%) by using 10 sites test of the monofilament in each foot.(74) The 10 sites for monofilament test was showed in the Figure 7. The impaired pressure sensation was determined when the patients didn't feel a pressure from 10 g monofilament.

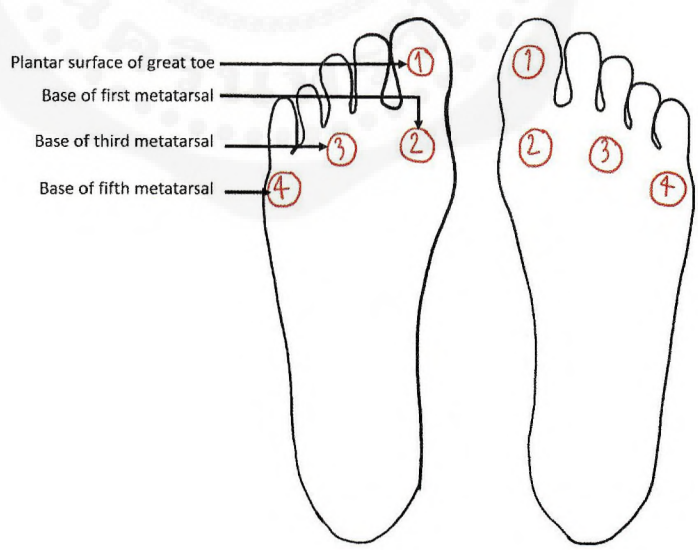


Figure 6 The 4 sites test of the monofilament from the study of Jayaprakash et al in 2011(74)

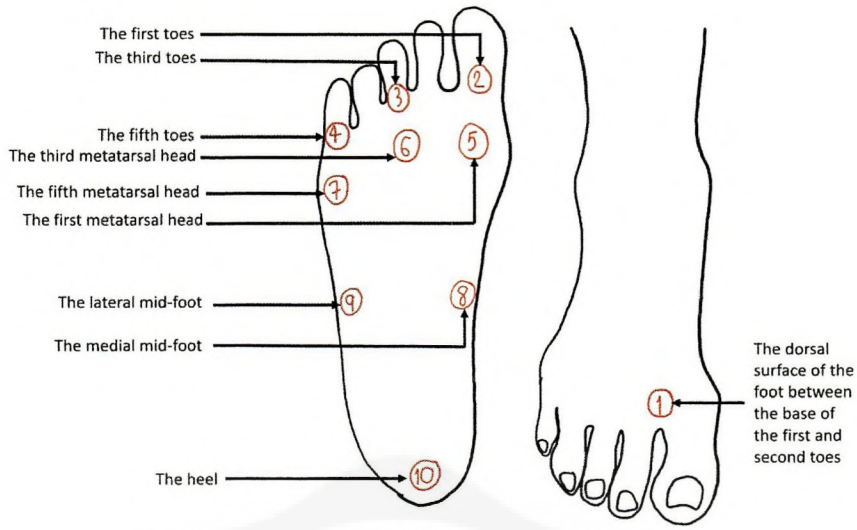


Figure 7 The 10 sites test of the monofilament from the study of Lee et al in 2011(75)

Vibration perception testing

Vibration perception testing, in 2005, Meijer et al recommended that 128 Hz tuning fork could be used for screening.(76) Most of patients who had diabetic ulcer often had problem to detect vibration sense.(77) Vibration perception testing oftenly tested at medial malleolus, fifth toe(78) and especially great toe.(77, 79) The test had sensitivity and specificity about 56% and 96%.(78) In 2007, Oyer et al evaluated accuracy and reliability of 128 Hz tuning fork test in diabetic patient who had peripheral neuropathy and found the mean duration of vibration sensation in diabetes patients was 10.2±1.3 seconds. They also reported about the degree of severity of neuropathy as follows. The mean vibration score which was more than or equal to 18 seconds meant that patient didn't have a neuropathy. The mean vibration score which was between 12-17 seconds meant that patient had mild severity of neuropathy. The mean vibration score between 5-11 seconds meant that patient had moderate severity of neuropathy and the score between 0-4 seconds meant that patient had high severity of neuropathy.(77)

To perform the vibration perception test, patient stayed in supine lying and an assessor held the bar of tuning fork with two fingers, avoided to place fingers or palm on the vibrating tines then hit the tuning fork with the palm of hand then clanging sound happened, if no sound, please try again with more force till sound occurs(77) after that,

assessor demonstrated what patient should feel when tuning fork placed on the sites by sample at wrist of patient at the first time.(79) When patient understood, start to place the tuning fork on the sites of foot such as great toe(78), don't forget to supports the under the toe that assessor tested(77) and count the time immediately and stop count the time when participants could not feel vibration from tuning fork, repeated test for 3 times per sites and calculated mean of the results, then assessor records the time.(79) If patient couldn't perceive the vibration sense while the assessor is still feeling it vibrated, this would demonstrate that patients had abnormal response of vibration sense.(80)

Peripheral blood circulation

Heart was a major organ pumping blood like a cycle to the body through blood vessels. So if heart had problem in function, blood flow would decrease. Additionally, blood flow depended on internal diameter of blood vessel that was increased (dilated) by relaxing of smooth muscle cells in the vessel's wall.(81)

Cardiovascular disease was another one factor which decreased blood flow for example coronary heart disease caused by forming of plaques in the vessel. The plaque formation resulted in structural change of the vessel into a narrow lumen that leaded to decrease blood flow. Risk factors of cardiovascular disease were smoking, obesity, hypertension and diabetes.(82)

Moreover, length of the vessel, viscosity of blood and hot environment and high blood pressure were also factors which related to blood flow.(81) In 1985, Levenson et al had found pre-hypertension patients had higher blood flow at brachial artery (136±11 ml/min) than healthy person (72±8).(83) So it was possible that high blood pressure was positive correlation with quantity of blood flow.

Assessment tools for peripheral blood flow

Doppler Ultrasound

Doppler Ultrasound had been found to insulate stenosis by evaluation of a diameter reduction greater than or less than 50% with a sensitivity of 77%-82% and a specificity of 92%-98%.(35) In 2007, Flanigan et al found evidence of early atherosclerotic

disease in the proximal superficial femoral artery about 75% of patients.(46) The abnormal superficial femoral artery was able to detected by duplex ultrasound although patients showed a normal ankle brachial index and without a history of clinically evidence atherosclerotic symptoms.(46)

Anyway, an abnormal ankle brachial index was also associated with an abnormal superficial femoral artery duplex ultrasound. So superficial femoral artery duplex ultrasound could be an indirect marker to identified early lower extremity atherosclerosis more accurate than using ankle brachial index(46) In 2014, Hatmi et al used ankle brachial index to detect coronary artery disease which was a vascular problem and found that ankle brachial index had low sensitivity to detect and predict this problem. Therefore, the assessor should consider other risk factors together with an evaluated ankle brachial index.(83)

Doppler ultrasound was non-invasive technique which didn't need to prepare patients before study and didn't have a radiation exposure(35) while ankle brachial index had some limitation such as it couldn't use with patients who had an excruciating pain in lower legs of feet or severe pain associated with lower extremity wound.(84) Patients who had neuropathic symptoms often had pain therefore the ABI assessment might be limited. Additionally, a deep vein thrombosis was also a contraindications for ankle brachial index assessment.(84)

Thus, the Doppler ultrasound was useful for screening and follow-up or diagnosis of peripheral arterial disease. The color mode of a Doppler ultrasound could detect stenosis or occluded segments, pulsed wave, and flow velocity in each artery.(35)

Quality of life in diabetes

Chronic disease was like diabetes affected in many ways. Some people with diabetes had to diet, avoid eating their favorite food, always taking a medicine and exercise strictly. All of these forces, people changed their lifestyle and some people felt unsafely as they didn't know when diabetes relapsed. Sometimes diabetes had also affected to socioeconomic because the patients had to pay for public services or to treat themselves from diabetes that made patients feel as a burden of family.

In 2016, Timar et al had found that Michigan neuropathy screening instrument had a correlation with patient's quality of life.(85) It meant people who had problem with peripheral neuropathy had tendency to have poor quality of life. In 2014, Dobrota et al reported that neuropathic pain was a major factor which extremely reduced quality of life in Diabetes contrasting with diabetes without neuropathic pain because neuropathic pain disturbed sleeping, and walking distance. Moreover, the patients with DPN had more medical treatment than patients without DPN.(86)

In 2011, Heebkaew et al used the WHOQOL-BREF-THAI-26 to assess a quality of life in type-2 diabetes and found that type-2 diabetes patients had moderate quality of life.(87) Relevant factors affect a quality of life of the patients including of income, duration of diabetes, stress and ability of independent self-care.(88) The diabetes patients also risked to have a depression although it had only 15.83% of risk.(89) Moreover, diabetes duration associated with depression(89) had more effect in female than in male.(89, 90) Some studies used SF-36 to measure a quality of life in diabetic patient such as Morales et al, in 2015 They had found that diabetes had problem in bodily pain(90) which affected to daily living, Contrastingly, In 2015, Duangjinda et al had found that type-2 diabetes patients had good quality of life.(87) This might be due to a different regions, socials, cultures, and tradition.

In 2015, Munparn et al applied a patient-reported outcome measure of pharmaceutical therapy quality of life (PROMPT-QOL) to assess a quality of life in chronic patients. It had been found that the patients had a moderate level of overall quality of life.(16)

From evidence-based review, not only clinical variables but also a quality of life in diabetes was affected by DPN. Thus assessing the quality of life of diabetic patients might also help to evaluate the improvement of the patient's well-being.(91)

Assessment tools for quality of life in diabetes

Asian Diabetes Quality of life (Asian DQOL)

Asian DQOL was valid and reliable to assessing quality of life in multi-ethnicity and multi-lingual Asian populations with type 2 diabetes.(92) However, this assessment tool had never been used in Thai People and translated in Thai.

Short-form 36 (SF-36)

This assessment tool was widely used to evaluate quality of life by self-evaluation. It consisted of 36 items that categorized into eight domains (physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional and mental health).(93, 94) SF-36 had good reliability and validity except vitality and role-emotional scales and it could discriminate people at least 88%.(95) In 2005, Leurmarnkul et al used a forward-backward translation for check internal consistency reliability of SF-36 (Thai-version) in 448 people and had found that it was acceptable internal consistency by getting 0.7 of Chronbach's alpha coefficients in all dimensions.(95) SF-36 was also used to assess a quality of life in diabetic patients(93) and Type-2 diabetes mellitus patients with poor glycemic control.(94) However, there was another instrument which was acceptable to use in diabetes patients and also assessed a quality of life with less questions than SF-36, that was WHOQOL-BREF-THAI (short form).

WHOQOL-BREF-THAI (short form)

WHOQOL-BREF-THAI (short form) was a questionnaire for quality of life assessment. It had 26 questions which developed from WHOQOL-BREF-THAI full version (100 questions). It had 24 dimensions by 1 question represents 1 dimension and other 2 questions were about general health. WHOQOL-BREF-THAI showed acceptable internal consistency (Cronbach's alpha coefficient is 0.8406) and concurrent validity was 0.6515 when compared with WHOQOL-BREF-THAI full version.(96) In 2014, Maudrene et al used WHOQOL-BREF (short form) among type-2 Diabetes Singaporean patients and had found that it also had acceptable internal consistency (Cronbach's alpha coefficient about 0.76-0.87) and the physical domain of WHOQOL-BREF (short form) was able to discriminate

people who had comorbidities from no comorbidities with the mean difference about 3.04.(96, 97)

Effects of massage in Diabetes

Systematic review of Ezzo et al in 2001 reported that one trial of Valtonen et al found syncardial massage whixh decreased diabetic neuropathic symptoms after 1 month.(22) In 2014, Lapanantasin et al found that massage improved neuropathic symptoms in type-2 diabetes especially massage with weight bearing exercise. Massage with weight bearing exerciser didn't only help patients to feel better but also increased strength of dorsiflexor and plantar flexor.(23) Moreover, deep massage and thumb pressure at foot helped diabetic patients to improve balance(98) In 2010, Çoban et al studied about effect of foot massage in pregnancy and they found that it could decrease edema at foot.(97)

However, massage also had adverse effects in diabetic patients such as the following. The patient who used insulin, massage could induce hypoglycemia. The patients who had vascular problem should avoid friction massage because it could induce vascular damage.(22)

Effects of exercise in Diabetes

Glycemic control was the major treatment of diabetes, but it was difficult to achieve for many patients.(14) Diabetes was a chronic disease which had physiological and chemical change that might result in a difficulty to recover. However, drug using purpose of getting better in physical, mental and social were effective, but sometimes drug also had side effect in negative ways.

Exercise training was non-pharmacological therapeutic option which was another way to improve quality of life in diabetic people who had micro-vascular disease because it did not only decreases risk of vascular disease and enhances glycemic control but also improved physical function,(17, 18) and Quality of life.(19, 20) In addition, exercise helped people to relieve psychological responses to stress.(21)

In 2016, Mitranun et al had found that all 3 groups of exercise training (crunch training, side crunch training and leg raise training) increased shear stress when measured by ultrasound Doppler at right brachial artery and also significantly increased blood flow in healthy subjects.(99)

Referring to blood pressure, In 2012, Dobrosielski et al had found that exercise (consisted of 2 sets of seven exercises at 10 to 15 repetitions per exercise at 50 % of 1-repetition maximum on a multistation machine) and aerobic exercise (exercise 45 minutes with treadmill or stationary cycle or stair stepper and also monitor heart rate by setting target range at 60% to 90% of maximum heart rate) 3 times per week for 6 months were able to increase aerobic capacity, strength fitness and lean body mass but had no reduction in blood pressure.(100)

In 2014, Mitranun et al reported that 3 months of interval aerobic exercise on treadmill (3 days per week) not only decreased systolic blood pressure but also improved muscle strength, maximal oxygen consumption, and blood flow.(101)

In addition, exercise training to prevent and delay peripheral arterial disease in type-2 diabetes was proved by Gibbs, et al in 2013. They gave supervision 45 minutes aerobic and resistance exercise training to person with type-2 diabetes for 6 months. After 6 months, they had found that ankle brachial index of subjects improved and The ABI correlated with decreased hemoglobin A1c and blood pressure.(102) Accordingly, Dijk et al had found that an endurance exercise was able to reduce hyperglycemia.(103) Exercise or physical activity about a minimum of 20-30 minutes per day improved insulin sensitivity, enhanced glucose uptake into exercising muscle, increased post-receptor insulin signaling and also decreased relative risk of type-2 diabetes, so it could be a guideline for designing a diabetes prevention exercise program.(41)

Several studies supported that weight bearing exercises were useful to type-2 diabetic patients in many ways. Weight bearing exercises not only improved cardiovascular fitness, physical activity or exercise capacity, glycemic control, muscle strength, balance, blood flow, quality of life or general well-being but also decreased

muscle fatigue, arterial stiffness, blood pressure, triglyceride, and body mass index.(21-25, 29-34)

In addition, exercise might induce shear stress which was a regulator of nitric oxide and supported vascular function.(104) In 2008, Padilla et al had found elevated shear stress after participants walking on treadmill immediately in healthy subjects and compared results which measured after walking 1 hours, 2 hours and 3 hours. They found acute effect of walking 45 minutes on treadmill got higher shear stress(104) so it was possible that habitual exercise would help endothelial repair.

Effects of meditation in Diabetes

In a Buddhist society, meditation was a widespread practice and also found in Christianity, Judaism and Islam.(105) Meditation was doing something and paid attention or concentrated on movement of the body(25, 33), to be conscious to internal and external sense(105) such as walking meditation so it was different from just a slow walking. Meditation was known for induction of an innate relaxation response which leaded to reduce psychological stress.(106) Heart rate variability was an indicator which showed balance status of autonomic nervous system that consisted of two branches, first was parasympathetic branch (Very Low Frequency: frequencies between 0.0033 to 0.04 Hz) and second was sympathetic branch (High Frequency: frequencies between 0.15 to 0.4 Hz).(107)

A high heart rate variability was a positive result in normal people, on the other hand decreased heart rate variability reflected over-activity of sympathetic nervous system.(106) Moreover, people who had mental problem might have reduction of heart rate variability by provoke cardiac rhythm.(108)

Numerous studies reported that meditation was not only benefits on psychological stress but also on physiological. In 2003, Matzner studied about heart rate variability before and during meditation in four different subjects who were advanced practitioners of yoga meditation and found that meditation induced a balance between sympathetic and parasympathetic nervous system by increasing power in the Low

Frequency band or intervening band(107) which was related to a balance of autonomic nervous system(109) because it was an important variable which reflected an activity of parasympathetic and sympathetic.(110) In 2017, Kiran et al included participants who were meditators and non-meditators and found that mean values of heart rate in meditators had lower heart rate more than non-meditators significantly. They had described about the difference that meditation was an activity which induced parasympathetic to predominance and reduced sympathetic activity.(111) In addition, they also advised that meditation at least 15-30 minutes was appropriate to decrease sympathetic activity which could reduce cardiovascular risks and stress.(111) Accordingly, a study of Ankad et al. in 2011 had found that resting pulse rate, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure were reduced after practiced pranayama and meditation for 15 days.(112) So, it might conclude that meditation had benefit on cardiovascular functions. Moreover, in 2006, Labrador et al investigated participants who had stable chronic heart disease and separated them into two groups, a transcendental meditation group and a health education group. After 16 weeks of intervention, they had found that transcendental meditation improved systolic blood pressure, insulin resistance and also heart rate variability.(113)

In 2014, Prakinkit et al had discovered that aerobic walking exercise with Buddhist walking meditation in depressed elderly was salutary. It significantly decreased depression score of the elderly.(33) This research(33) suggested that the effects of walking exercise with meditation on functional fitness and vascular function should be further investigated.

In 2008, Fang had found that 4 months of Brocade (movement of limb combined with breathing and minds concentration) practice in type-2 diabetic patients was able to improve Hemoglobin-A1c.(24) Similarly, Gainey et al, in 2016, had found that Buddhist walking meditation helped to control blood sugar such as hemoglobinA1c, decreased blood pressure as well as improved vascular function in type2 diabetes.(25)

In 2012, Hartmann et al had found that body and meditation practices decreased level of stress, and diastolic blood pressure, as well as improved health status in type-2

diabetes.(26) In 2014, Qiu et al had found that walking especially walking with motivation reduced Hemoglobin A1c and also lowered body mass index and diastolic blood pressure which were the risks of cardiovascular diseases.(27) In the same year, Goyal et al had reviewed that mindfulness meditation programs improved anxiety, depression, stress, pain, attention, and quality of life.(114)

In conclusion, from evidence-based review, walking was a simple weight bearing exercise for diabetes which was easily to follow and its effects were not only enhancing cardiopulmonary fitness and functional ability but also being useful on glycemic control. Accordingly, walking meditation had benefit to control blood sugar such as a hemoglobin A1c, and decreased blood pressure and also improved vascular function in type2 diabetes.(27) Moreover, the walking meditation also combined with mindfulness practice which was helpful to reduce cardiovascular risks and stress, promoted relaxation and increased happiness.(105)

However, the effects of walking meditation on peripheral blood circulation and neuropathic symptoms in persons with type-2 diabetic peripheral neuropathy hadn't been proved. Furthermore, massage had positive effects on blood circulation and diabetic peripheral neuropathy though it was still lack of comparative evidence between walking meditation and massage on peripheral blood circulation and neuropathic symptoms in persons with type-2 diabetic peripheral neuropathy.

Therefore, the effects of walking meditation on peripheral blood circulation, neuropathic symptoms, and quality of life among persons with type-2 diabetic peripheral neuropathy were interesting to investigate and compare with the effects of massage.

CHAPTER 3
METHODOLOGY

Research design

This study was a randomized controlled trial. The study was approved by The Ethics Committee of Strategic Wisdom and Research Institute, Srinakharinwirot University (Ethical code: SWUEC-160/61E), and was registered the Thai Clinical Trials Registry (TCTR), Thailand with the number TCTR20190125001 since January 24, 2019.

Research Setting

The research was conducted at the That Phanom Community Health Center, Nakhon Phanom, Thailand.

Participants

Inclusion criteria

The inclusion criteria included of the following;

1. Type-2 diabetes patients diagnosed by a physician
2. Had neuropathic symptoms: defined by MNSI score in subjective examination more than 7 points or objective examination more than or equal to 2 points.
3. Age 40-70 years old.
4. Duration of diabetes more than 5 years.
5. Patient didn't have injury condition recently(99) such as acute severe pain, ankle sprain or muscle strain.

Exclusion criteria

The exclusion criteria included of the following;

1. Abnormal peripheral blood flow indicated by abnormal ankle brachial index (ABI) which was under 0.91 or over 1.3
2. Smoking or just quit smoking less than 1 month.(115)

3. Patient who had severe cardiovascular diseases(99, 101, 115) such as myocardial infarction and unstable angina pectoralis.
4. Patient who had neurological diseases that affected balance and walking ability(99, 101) such as stroke and parkinsonism.
5. Patient who had malignancy.
6. Patient who had liver failure or renal failure/dialysis
7. Any conditions that would be contraindication to participated in walking such as ulcer at foot, fracture, foot and leg amputation, uncontrolled hypertension and severe osteoporosis or any orthopedic condition which physician not allowed to do weight bearing exercise etc.
8. Any conditions that would be contraindication to participated in massage such as thrombophlebitis, deep vein thrombosis, varicose veins, cancer, fractured or broken bones at massage area (lower limb) and infectious diseases of the skin etc.
9. People who participated in any research or exercise within 6 months ago.(100, 102)

Discontinuation criteria

Participant who attended the research interventions less than 11 times from the total of 12 times within 4 weeks will be excluded from the study.

Sample size calculation

The sample size for the research was calculated based on the means and standard deviations of peak shear rate from the previous study of Prakhinkit et al that investigated effects of Buddhism walking meditation on depression, functional fitness, and endothelium- dependent vasodilation in depressed elderly.(33) This study used the data of peak shear rate and standard deviation from the previous study of Prakhinkit et al to calculate the sample size of the study.(33)

Calculation of Variance explained by effect from SD2post 1 – SD2post2

SD2post 1 – SD2post2 = 29.922-25.22

= 895.2064-635.04

= 260.1664

Calculation of Variance within group from SD2pre – SD2post

SD2pre – SD2post = 18.72-29.922

= 350.4384-895.2064

= 544.768

Use Varaince within group and Varaince explaned by effect for calculating an effect size = 0.6910665

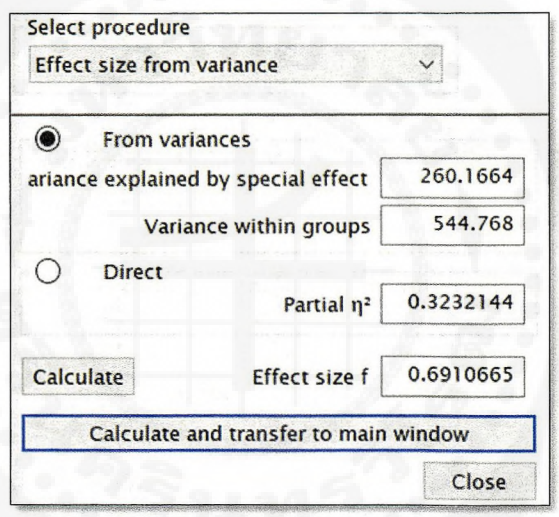


Figure 8 Effect size calculated by G*Power 3.1.9.2 program

Use G*Power 3.1.9.2 to calculated sample size by choosing F test: fixed effects, omnibus, one-way as shown in figure 9.

identify an effect size f : 0.6910665

identify α error probability : 0.05

identify power (1-β error probability) : 0.80

sample size : 24

drop out 25% : 30

each group (3groups) : 10

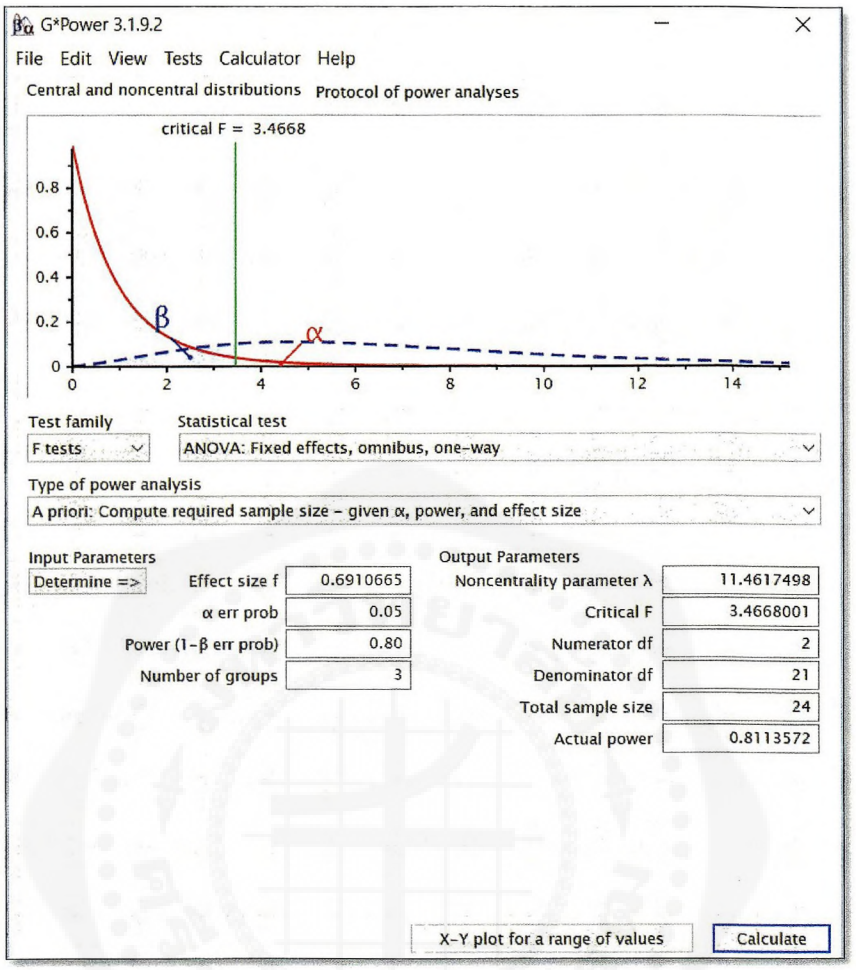


Figure 9 Effect size calculated by G*Power 3.1.9.2 program

Therapists

Two licensed physical therapists who had clinical experiences at least 1 year conducted the research. One therapist gave the interventions to the participants, and another was an assessor. The assessor was blinded to a group randomization of the participants.

Materials and equipments

Materials and equipment used in this research including of the following:

1. Vascular Doppler

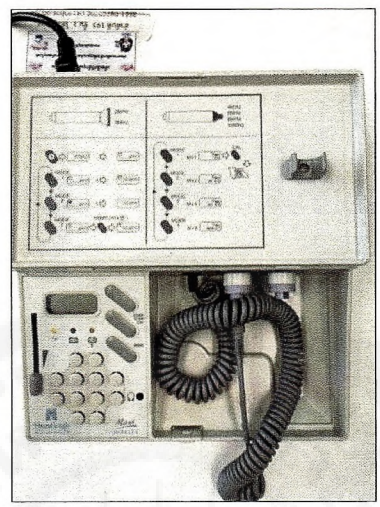


Figure 10 Vascular Doppler

2. Reflex hammer



Figure 11 Reflex hammer

3. Tuning fork

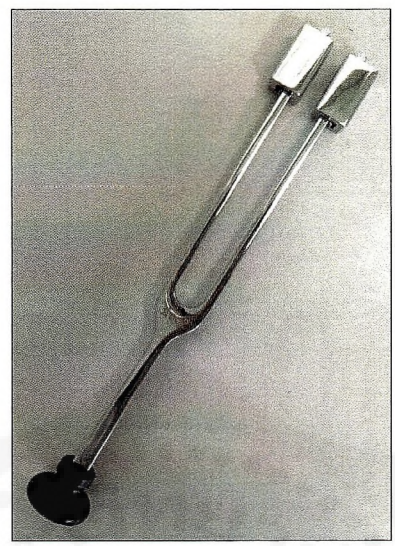


Figure 12 Tuning fork

4. 10 g. monofilament

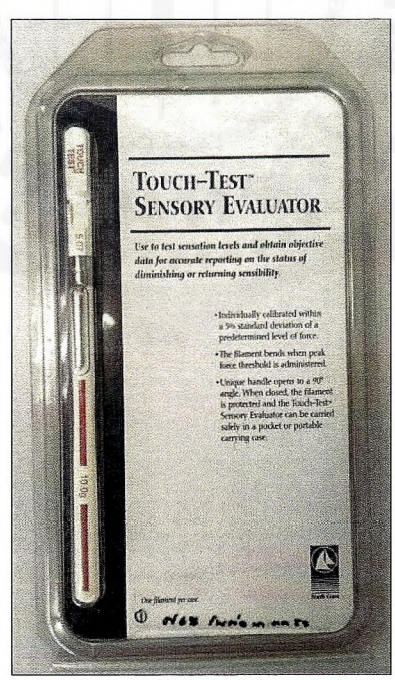


Figure 13 10 g Monofilament

5. Doppler Ultrasound scanning



Figure 14 Ultrasound Doppler



Figure 15 Ultrasound Doppler probe

Procedures

The research procedure was conducted as the following steps;

1. All the volunteers who met the inclusion criteria were informed about the study procedures and signed an informed consent before participation.
2. The recruited participants were measured baseline peripheral neuropathic symptoms, peripheral blood flow, and a quality of life as mentioned above by the principle investigator. Before measurement, the participants had to avoid drinking caffeine for 12 hours.(104)

3. The participants were randomized into 3 groups; 1) walking meditation, 2) massage, and 3) control
4. All participants were educated how to do a foot-care and proper nutrition for diabetes.
5. The participants in walking meditation group enrolled walking meditation protocol on the supervision of the physical therapist for 4 weeks (30 minutes/day, 3 days/week) at the That Phanom Community Health Center, Nakhon Phanom, Thailand, where was the research setting.
6. The participants in massage group did self-massage of their foot and lower leg on the supervision of the physical therapist for 4 weeks (30 minutes/day, 3 days/week) at the That Phanom Community Health Center, Nakhon Phanom, Thailand, where was the research setting.
7. The participants in control group did only a self- stretching of lower limb muscles same as warm-up and cool-down of the walking meditation and massage protocols for 4 weeks (10 minutes/day, 3 days/week) at their homes.
8. After 4 week, peripheral neuropathic symptoms, peripheral blood flow, and a quality of life of the participants were reassessed after 48-72 hours to prevent resulting from an acute effect.(101)
9. All outcome data were statistically analyzed.

Ankle brachial index (ABI) measurement for Peripheral arterial disease screening

Before participation, all volunteers were assessed for the exclusion criterion, peripheral arterial disease, by Ankle brachial index (ABI). ABI were measured by using a hand-held continuous-wave Doppler ultrasound probe (5-10 MHz) and a sphygmomanometer (blood pressure cuff).(44) For measurement of the systolic blood pressure of ankle at dorsalispedis and posterior tibial arteries, the volunteers were in lying position and an ankle cuff placed above the malleolus. The Doppler ultrasound probe placed at the superficial part of the arteries as presented in Figure 17-18.(116) The systolic blood pressure of the brachial, dorsalis pedis and posterior tibialis arteries measured

bilaterally, at resting.(116) Choose the highest systolic pressure of the dorsalispedis or posteriortibial artery to calculate an ABI for each leg.(84) The volunteers who had ABI under 0.91 or over 1.3 had excluded.

$$\text{Ankle brachial index} = \frac{\text{The highest systolic pressures of the dorsalispedis or posterior tibial artery}}{\text{The higher systolic pressures of brachial artery}}$$

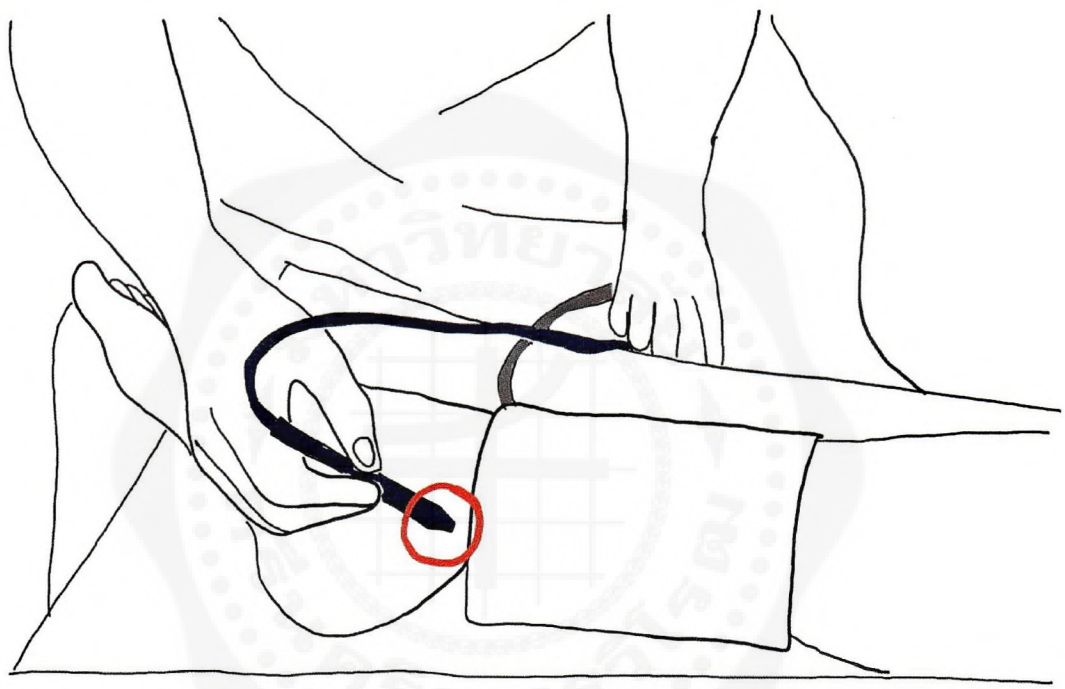


Figure 16 position of ABI measurement at tibialis posterior artery(117)

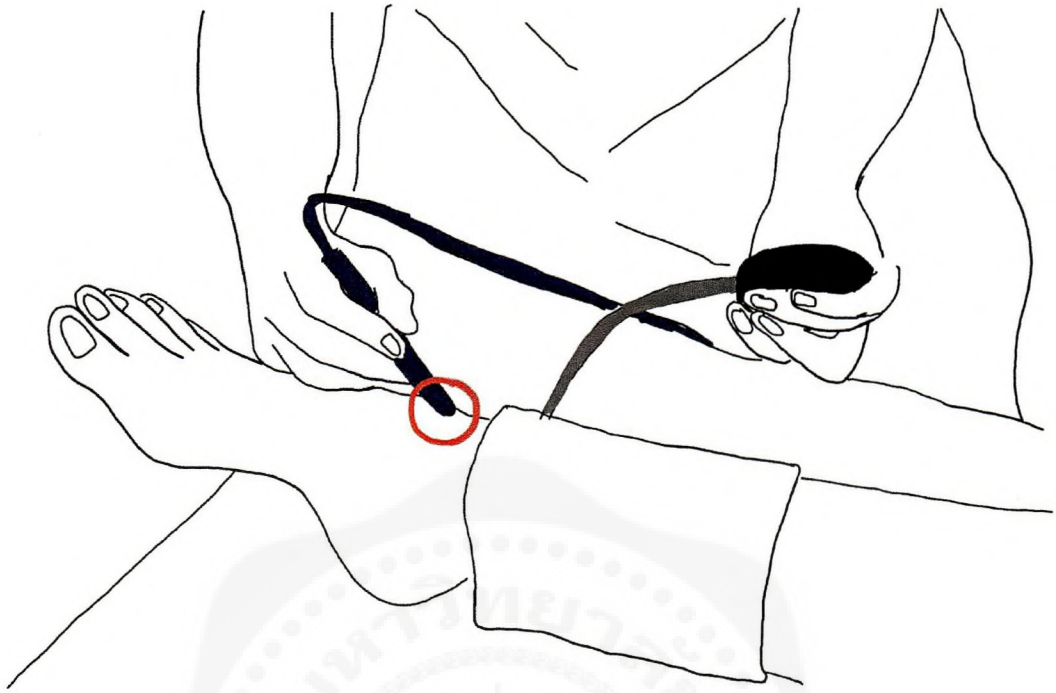


Figure 17 position of ABI measurement at dorsalispedis artery(117)

Screening for peripheral neuropathy by Michigan neuropathy screening instrument (MNSI)

Before participation, all volunteers were assessed for the inclusion criterion, peripheral neuropathy, by the MNSI. MNSI consists of 2 parts. The first part was a historic questionnaire like subjective examination includes of 15 questions. The volunteers would answer only "yes or no". The second part was a physical examination by the assessor. It included of an inspection of the feet and evaluations of ankle reflexes, vibration sensation and fine touch.(71, 117) If the subjective examination showed a total score more than 7 and/or the objective examination showed a total score more than or equal to 2 point, these meant the volunteer had a diabetes peripheral neuropathy and were included to a research participant.(71)

Peripheral blood flow measurement by Ultrasound Doppler

All the participants had been measured peripheral blood flow of both feet by Ultrasound Doppler.(33-35) The peripheral blood flow of foot had been measured via both posterior tibial and dorsalispedis arteries in supine lying position with hip abduction

and external rotation, and the knee would be flexed like frog legs (Figure 19). Then placed an ultrasound Doppler probe on the most superficial part of the measured artery and used a color mode for scanning to find a vessel (Figure 20). After finding the exact vessel, turned to 2D mode, froze a picture and set a line of perpendicular to the vessel wall. After that unfroze and monitored for 1 minute to evaluate a mean vascular diameter in centimeters by computer-based analysis program (Figure 21). Then used pulsed wave (PW) Doppler mode to monitor for 1 minute for assessing of blood flow velocity in centimeter per second (Figure 22).(101) The peripheral blood flow were calculated by a mean vascular diameter x a blood flow velocity. In addition, a shear stress was calculated by blood velocity divided by vascular diameter.

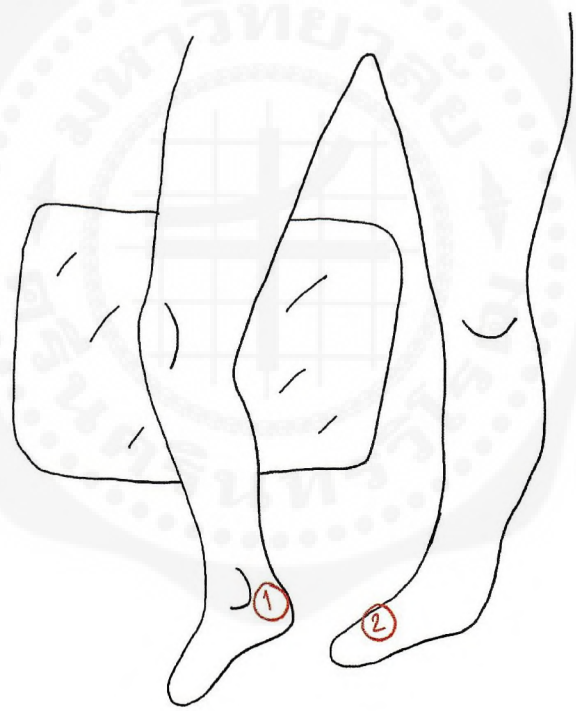


Figure 18 The participant was in supine position when assessment of blood flow by ultrasound Doppler; number1 is a position of posterior tibial artery and number 2 is a position of dorsalis pedis artery.(35)



Figure 19 Color mode by Ultrasound Doppler



Figure 20 2D mode by Ultrasound Doppler

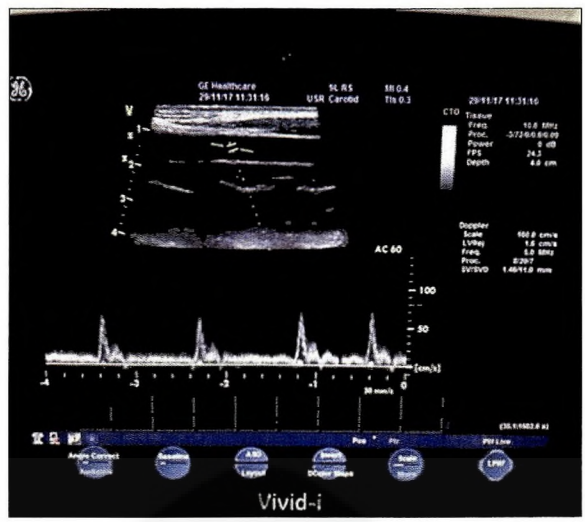


Figure 21 PW Doppler mode by Ultrasound Doppler

Methods for assessing of peripheral neuropathic symptoms

This research applied a monofilament sensory testing and a vibration perception testing to assess peripheral neuropathic symptoms at both feet of the participants.

Monofilament sensory testing

Assessor used 10 g monofilament to test pressure sensation on ten sites of each foot of a participant as shown in Figure 7.(73) The assessor demonstrated the feeling of pressure from the monofilament on the hand of the participant for understanding before testing. Supine position was an appropriated position to test patients, used 10 sites in each foot for tested sensory of patients.(74) The impaired pressure sensation had determined when the patient didn't feel a pressure from 10 g monofilament.

Vibration perception testing

Assessor used 128 Hz tuning fork to test a vibration perception.(76) at a great toe.(77, 79) The assessor demonstrated the feeling of vibration from the tuning fork on a wrist bone of the participant for understanding before testing. To performed the test, the participant were in supine lying.(77) Assessor placed the tuning fork on the great toe(79), started to record the time in seconds when tuning fork placed on site, stoped to record the time when patients didn't sense the vibration from tuning fork and repeated the test

for 3 times. Then assessor calculated a mean time from the 3 tests to represent as vibration sensory perception of the participant.(79)

Quality of life assessment by WHOQOL-BREF-THAI (short form).(96)

This research used WHOQOL-BREF-THAI (short form) questionnaire to evaluate the quality of life of the participants. This questionnaire consisted of 2 types of questions which were perceived objective and self-report subjective. The questions had categorized as 4 domains which were about physical, psychological, social and environment.(96) There were 23 positive questions and 3 negative questions (i.e. Question number 2, 9, 11) and the rating of the questionnaire separated to 2 parts. For the part one, the positive questions, 5 points meant disagree and 1 point meant agree. The part two, the negative questions, 5 points meant agree and 1 point meant disagree. The total score of all 26 questions was 130 points. This questionnaire classified the quality of life into 3 levels by the evaluated score as follows;

26-60 points were defined as a bad quality of life

61-95 points were defined as a moderate quality of life

96-130 points were defined as a good quality of life

The 26 questions of WHOQOL-BREF-THAI (short form) were grouping into 4 domains that were also considered as 3 levels of the quality of life in each domain as following;

Physical	:	question number 2, 3, 4, 10, 11, 12, 24
Psychological	:	question number 5, 6, 7, 8, 9, 23
Social	:	question number 13, 14, 25
Environment	:	question number 15, 16, 17, 18, 19, 20, 21, 22

Table 2 Domain and Level of quality of life in WHOQOL-BREF-THAI(96)

Domains	Bad quality of life (point)	Moderate quality of life (point)	Good quality of life (point)
Physical	7-16	17-26	27-35
Psychological	6-14	15-22	23-30
Social	3-7	8-11	12-15
Environment	8-18	19-29	30-40
Overall	26-60	61-95	96-130

Question number 26 was different from other questions because it showed overall quality of life and health.

Protocol for a control group

The participants in control group did only stretching exercise at home which were warmed up and cooled down for 10 minutes by stretching gluteus maximus, quadriceps, hamstrings and gastrocnemius of both sides. The assisted researcher called them by phone to alert the participants to do stretching exercise every 3 days a week.

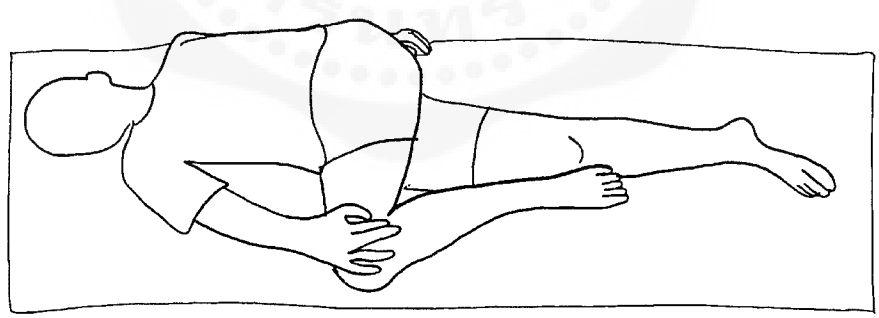


Figure 22 Stretching of gluteus maximus muscle

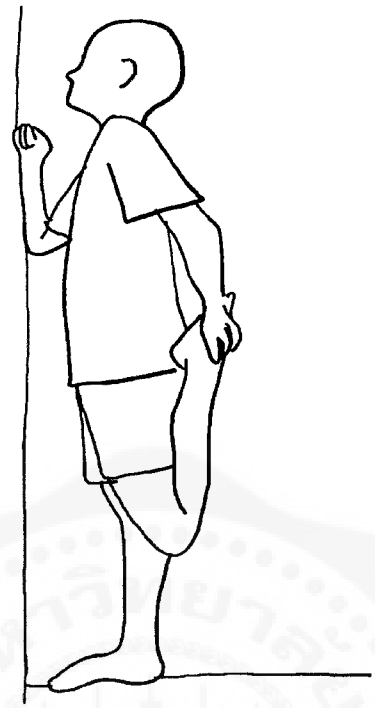


Figure 23 Stretching of quadriceps muscle

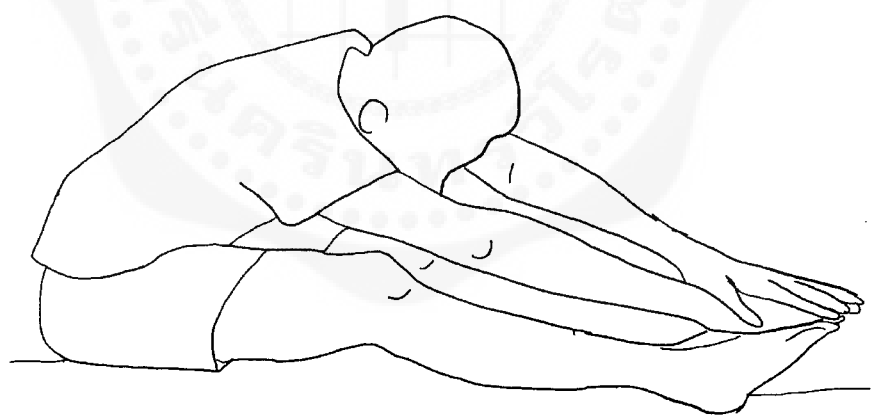


Figure 24 Stretching of hamstrings muscle

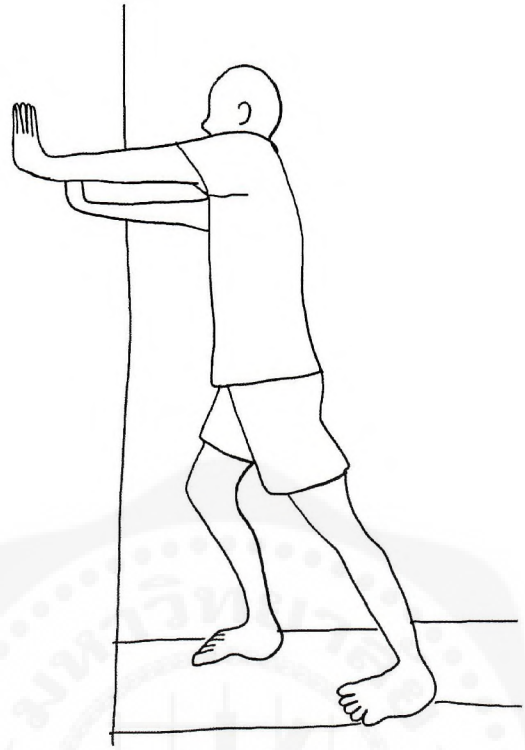


Figure 25 Stretching of gastrocnemius muscle

Protocol of walking meditation

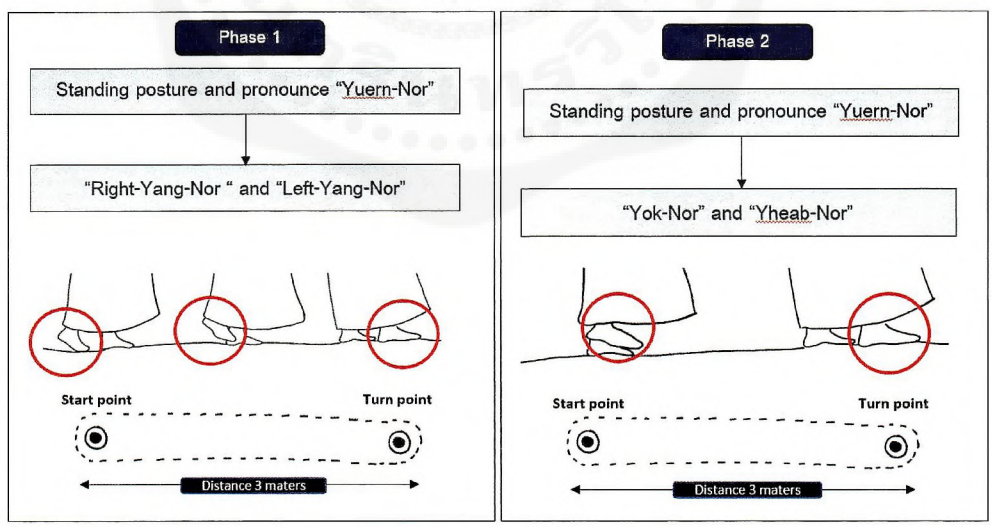


Figure 26 Flow chart presenting an overview of walking meditation in phase 1 and phase 2

An overall protocol of walking meditation about frequency, duration, intensity, and sequence of activities had shown in the following table. The activities in walking meditation protocol were described in details as follows.

Table 3 Walking meditation protocol(117)

	Walking meditation protocol
Frequency	: 3 times per week, 4 weeks
Intensity	: Comfortable
sequence of activities	: Warm-up 5 minutes
	: Walking meditation 20 minutes by concentrate mindfulness during walking.
	: Cool-down 5 minutes
Total duration/ Time	: 30 minutes

For walking meditaion group, they had participated an activity at the That Phanom Community Health Center, Nakhorn Phanom, Thailand. From six phases of walking meditation as demonstrating by Wat Boromsathol which were Thai traditional walking meditation, this research had chosen only 2 phases which were phase-1 and phase-2 to practice mindfulness during walking (Figure 26). Before and after doing walking meditation, the participants warmed up and cooled down for 5 minutes each in order by stretching gluteus maximus, quadriceps, hamstrings and gastrocnemius of both sides same as control group.

Firstly, the participants had learnt how to do walking meditation from the video clip of Wat Boromsathol, then the participants practiced walking meditation along with the video clip and to make sure they had practiced their mind, the researcher also let them utter followed the meditator in the video clip during practice.

Phase 1

The participants perceived their standing posture and pronounce "Yuern-Nor (ยืนหนอ)" while they were standing for 3 times as shown in figure 27.

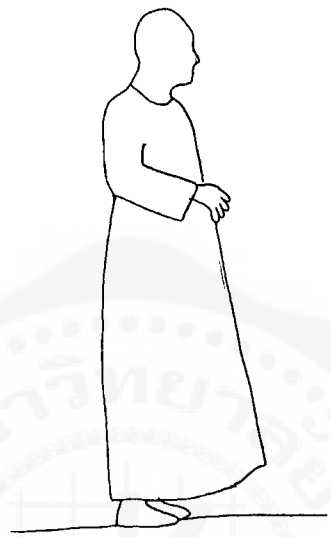


Figure 27 standing posture during walking meditation in phase-1. (117)

Then the participants started walking by focusing on foot moving alternately while voicing "Right-Yang-Nor (ขวา-ย่าง-หนอ)" and "Left-Yang-Nor (ซ้าย-ย่าง-หนอ)" about 3 meters as shown in figure 28. After that the participants turned around and did phase-1 of walking meditation repeatedly for 10 minutes.

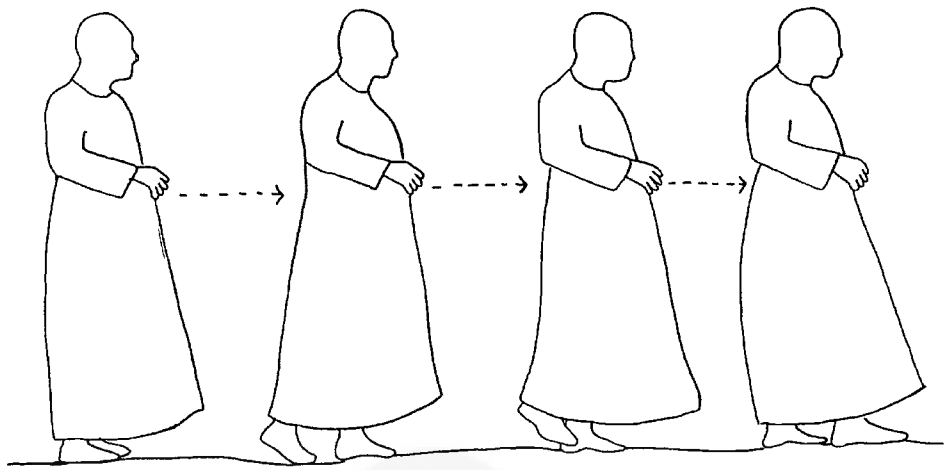


Figure 28 walking meditation in phase-1.(118)

Phase 2

Participants perceived their standing posture and pronounce "Yuern-Nor (ยืน-หนอ)" while they were standing for 3 times same as phase-1 as shown in figure 27.

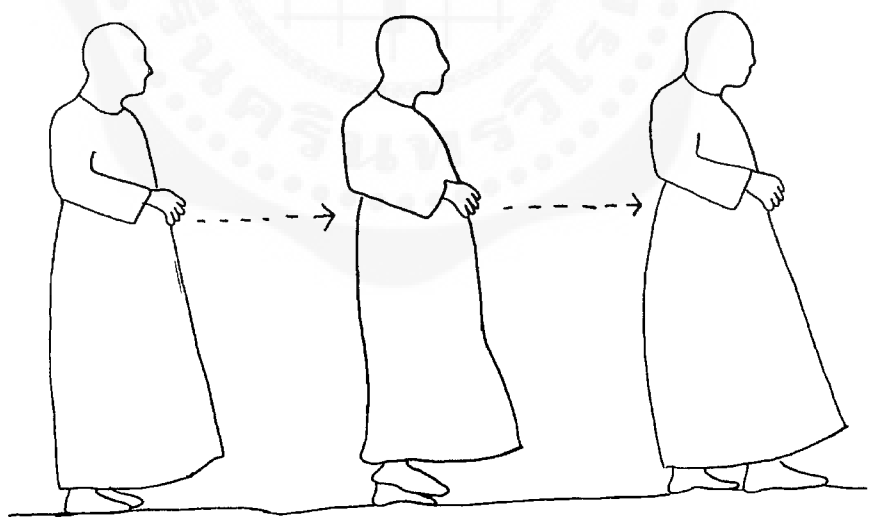


Figure 29 walking meditation in phase-2.(121)

Then the participants started walking by lifting their foot while voicing "Yok-Nor (ยก-หนอ)" to step forward and then voiced "Yheab-Nor (เหยียบ-หนอ)" simultaneously with

placed their stepping foot on the floor as shown in figure 29, and did it same way in every steps as walking about 3 meters. After that the participants turned around and did phase-2 of walking meditation repeatedly for 10 minutes.

Protocol of massage

An overall protocol of massage about frequency, duration, and sequence of activities were shown in the following table (Table 4). The activities in the massage protocol had described in details as follows.

Table 4 Massage protocol

Massage protocol	
Frequency	: 3 times per week, 4 weeks
Sequence of activities	: Warm up 5 minutes : Massage 20 minutes: by massage at foot and lower leg with superficial stroking, deep stroking and kneading technique either dorsal or plantar of foot to popliteal fossa of both sides, 10 minutes in each side : Cool down 5 minutes
Total duration/ Time	: 30 minutes

For massage group, they participated an activity at the That Phanom Community Health Center, Nakhon Phanom, Thailand, same as walking meditation group. At the first time, all participants in this group were trained how to do self-massage by a physical therapist same as the protocol in the video. The sequences of massage were as the following. The participants did superficial stroking and deep stroking cover from dorsal and plantar of their foot along to popliteal fossa about 5 minutes each side (figure 30-34), and then did thumb kneading on either dorsal or plantar of foot and digital kneading on leg to popliteal fossa for 5 minutes each side (figure 35-39). Before and after doing foot

massage, the participants warmed-up and cooled-down for 5 minutes each in order same as mentioned above in the walking meditation protocol.

Superficial stroking, deep stroking technique either dorsal or plantar of foot to popliteal fossa about 5 minute each side

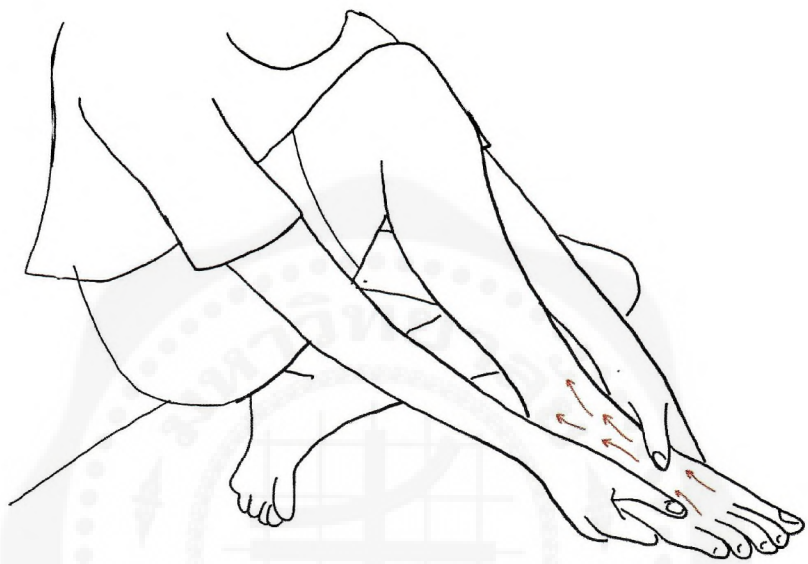


Figure 30 superficial and deep stroking technique on dorsal foot.



Figure 31 superficial and deep stroking technique on lower leg



Figure 32 superficial and deep stroking technique on popliteal fossa.

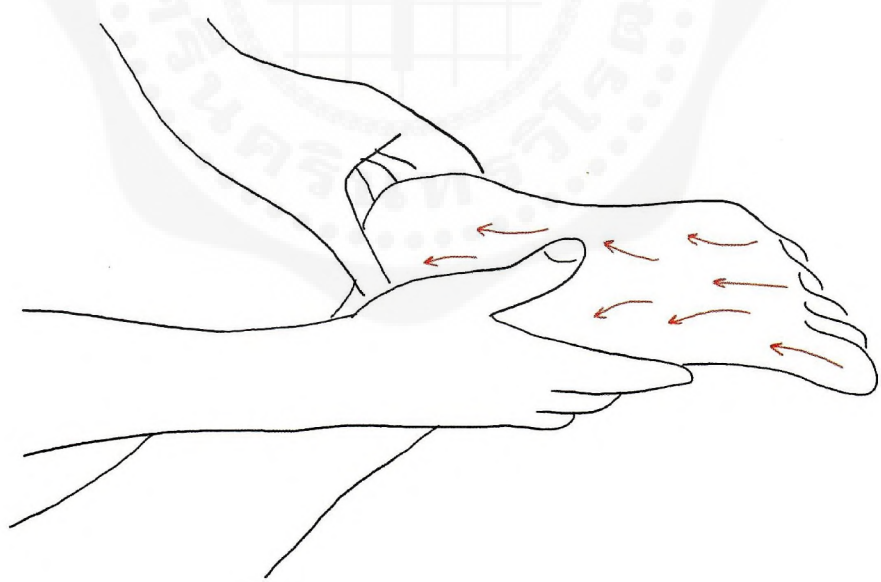


Figure 33 superficial and deep stroking technique on plantar foot.



Figure 34 superficial and deep stroking technique on calf.

Kneading technique either dorsal or plantar of foot to popliteal fossa about 5 minute each side



Figure 35 Thumb kneading on dorsal foot.

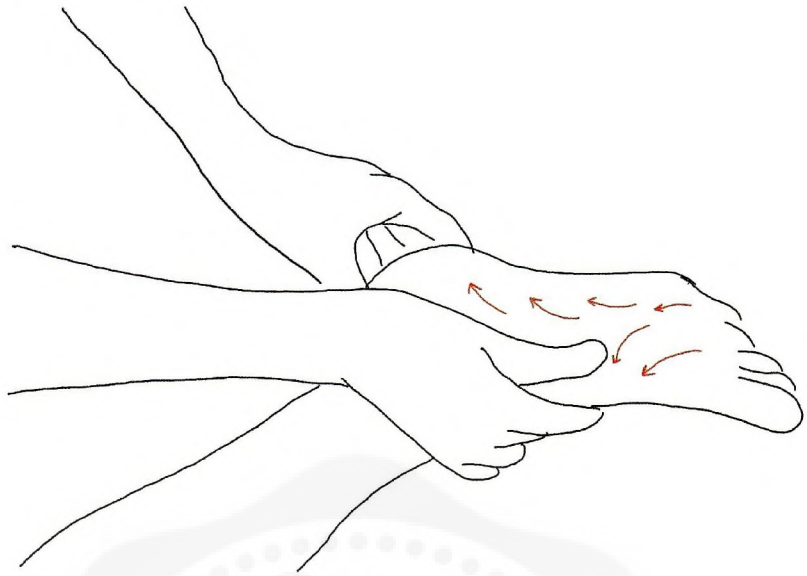


Figure 36 Thumb kneading on plantar foot.



Figure 37 Digital kneading on pretibial.

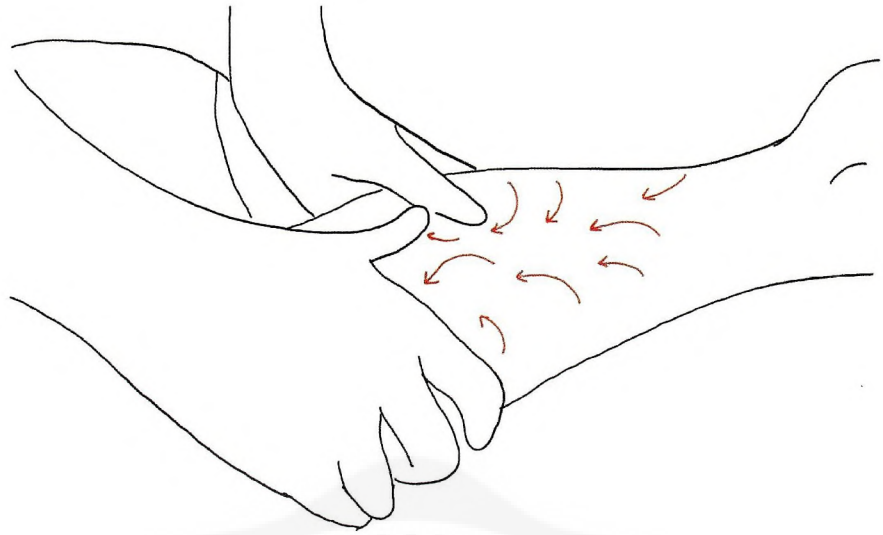


Figure 38 Digital kneading on calf.

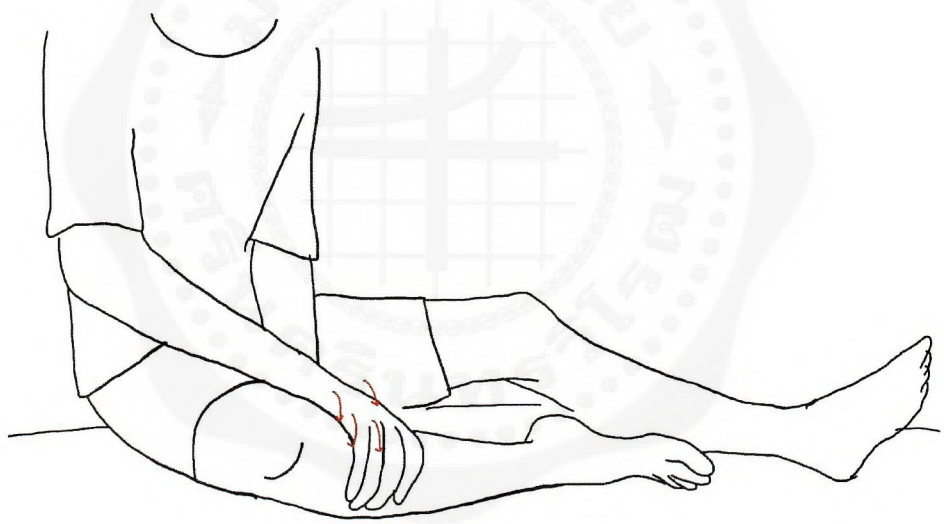


Figure 39 Digital kneading on popliteal fossa.

Flow chart of the study process

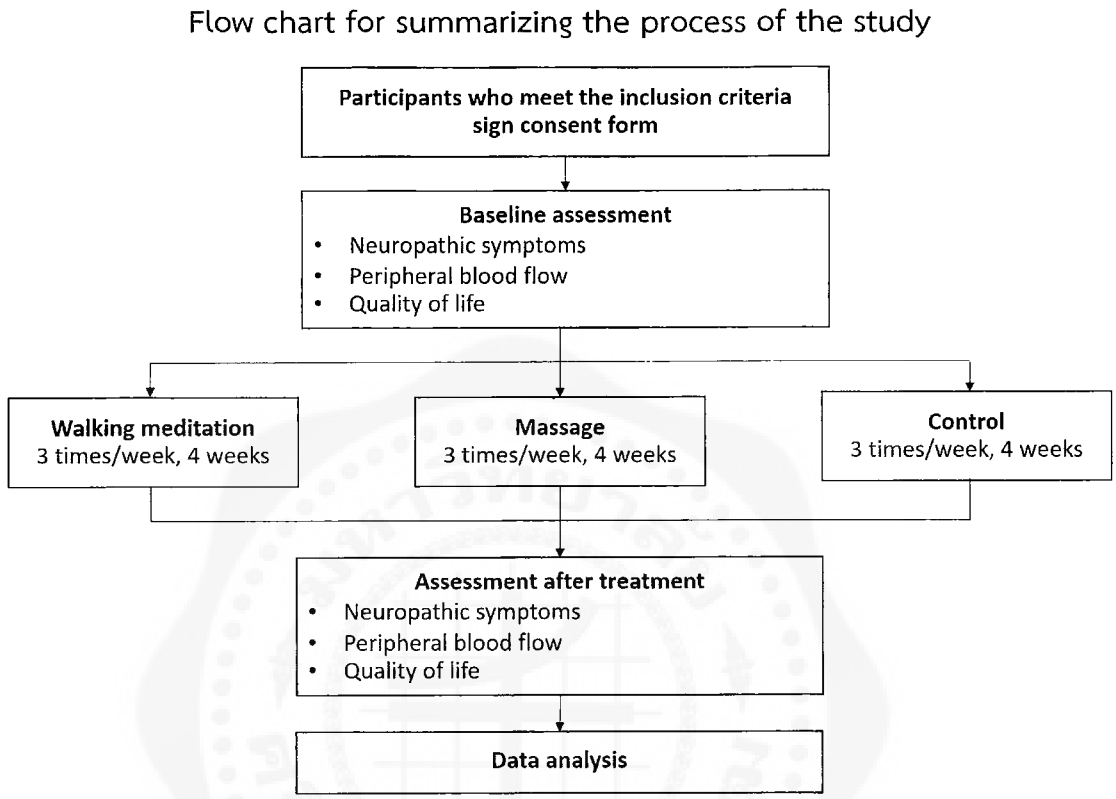


Figure 40 Flow chart of the study process

Data analysis

The general and clinical characteristics of participants were described by descriptive statistical analysis. The outcome data were tested for normal distribution by Kolmogorovsmirnov test. Comparison of the research outcomes among walking meditation, massage and control groups were analyzed by Kruskal Wallis test, and then comparison between each other group was analyzed by Mann-Whitney U test. Wilcoxon's matched pairs test had been used for comparison between post-intervention and baseline within each group. The level of significance was set at $p<0.05$.

CHAPTER 4
RESULTS

The purpose of this study was for investigation in the comparative effects of walking meditation (WM) and massage (M) on peripheral blood circulation, neuropathic symptoms of diabetic foot and also the quality of life (QoL) in persons with type-2 diabetic peripheral neuropathy (type-2 DPN). The research findings were as follows.

Participants and baseline characteristics

There were 54 persons with diabetes who passed the inclusion and exclusion screening, but only 30 persons volunteered to attend the research protocol. The others who refused attending the research because of inconvenience were mostly due to working.

The thirty volunteers with type-2 diabetes (type-2 DM) aged between 42-69 years were randomized into WM (n = 10), M (n = 10), and control (n = 10) groups. Four participants withdrew from the study; two participants in WM group, one participant in M group, and one participant in control group. Three of them temporary moved their residence to other province, and the other one was inconvenient to continue throughout the research intervention. Therefore, throughout the research, there were seventeen participants in the experimental groups (WM: n = 8, M: n = 9), and 9 participants in the control group.

The baseline characteristics about gender, age, body mass index, waist circumference, and ankle brachial index (ABI) of each group were presented in Table 5. The baseline characteristics related to neuropathic symptoms represented by pressure sense, as the percentage of the intact spots out of 12 tested spots from 10-gram monofilament testing, and by vibration sense, as the perception time of a vibration from 128-Hz tuning fork (the length of time since feeling the vibration until not feeling) were also shown in Table 5. In addition, the peripheral blood flow at dorsalis pedis and posterior tibial arteries measured by ultrasound Doppler, and the score of QoL assessed by World Health Organization Quality of life BREF Thai (WHOQOL-BREF-THAI) before training were presented in Table 5. At

baseline, there was no significant difference among three groups in all characteristics mentioned above as shown in Table 5.

Table 5 Baseline characteristics of the participants in walking meditation (WM), massage (M) and control (C) groups.

Characteristics of participants	Mean ± SD			p-value$
	WM group (n=8)	M group (n=9)	C group (n=9)	
Gender: Male/Female	3/5	2/7	2/7	
Age (years)	53.50 ± 6.07	56.88 ± 10.06	55.88 ± 5.75	.634
Body Mass Index (kg/m^2)	25.67 ± 3.92	25.27 ± 3.23	25.18 ± 3.25	1.00
Waist circumference (cm)	84.87 ± 7.05	85.66 ± 6.76	84.44 ± 4.92	.954
Ankle Brachial Index (ABI)				
- Left side	1.09 ± .08	1.01 ± .09	1.06 ± .07	.233
- Right side	1.02 ± .03	1.01 ± .10	1.08 ± .08	.094
Pressure sense testing (%)	63.75 ± 12.46	68.33 ± 10.60	69.44 ± 20.68	.481
Vibration testing (sec)				
- Left side	10.50 ± 3.32	11.02 ± 3.62	10.05 ± 6.11	.921
- Right side	7.12 ± 3.42	8.34 ± 3.43	8.27 ± 4.77	.821
Peripheral Blood Flow (TTcm^3/s)				
- Left Dorsalis Pedis artery	.24 ± .07	.13 ± .03	.19 ± .10	.295
- Right Dorsalis Pedis artery	.26 ± .07	.16 ± .04	.24 ± .09	.716
- Left Posterior Tibial artery	.21 ± .04	.20 ± .04	.17 ± .05	.565
- Right Posterior Tibial artery	.21 ± .06	.26 ± .05	.21 ± .05	.750
Quality of life (points)	98 ± 14.65	94.55 ± 8.81	106.44 ± 10.60	.074

p-value$ = p-value from comparison among the three groups by Kruskal-Wallis test.

Comparison of the studied outcomes among walking meditation, massage, and control groups, and between pre- and post- training within each group.

The primary outcomes of the study included of neuropathic symptoms and peripheral blood flow of both feet. The secondary outcome of the study was QoL. The studied outcomes of the WM, M, and control groups were shown as mean ± SD in Table 6. After training, the WM and M groups demonstrated higher percentages of the intact pressure sense than baseline significantly (p=.012), while the control group did not. Similarly, both WM and M groups showed significant longer perception time of vibration from tuning fork testing than baseline (p=.012), especially the WM group had longer vibration perception time at both left and right sides while the M group only presented at the right side (Table 6). Moreover, at post-training, the WM and the M groups revealed significantly higher percentages of the intact pressure sense when compared to the control group at p=.001 and p=.014 respectively as shown in Table 7. However, there was no significant difference in the percentage of intact pressure sense between WM and M groups (Table 7).

Considering of the studied outcomes related to peripheral blood flow, both WM and M groups had significantly higher blood flow at post-training than their baseline, particularly the M group, whereas the control group did not show in Table 6. At post-training, the M group got significantly higher peripheral blood flow to the foot in three arteries, i.e. left posterior tibial, left and right dorsalis pedis arteries, when compared to the baseline ($p<0.01$) as presented in Table 6. Meanwhile, the WM presented significantly higher peripheral blood flow to the foot in the right posterior tibial artery compared to the baseline (p=.017) as showed in Table 6. In addition, at post-training, either WM or M group significantly demonstrated higher blood flow to both feet than the control group ($p<0.05$), but no significant difference in the blood flow between the WM and M groups was found as showed in Table 7. The M group showed significantly higher blood flow in the left and right dorsalis pedis and the left posterior tibial arteries when compared to a control group at p=.034, p=.015, and p=.019 in order (Table 7). Also, the WM group significantly presented a higher blood flow compared to the control group in the left and right dorsalis pedis arteries at p=.007 and p=.021 respectively as showed in Table 7.

Furthermore, at post-training, this study had been found that the diameters of the interested arteries, dorsalis pedis and posterior tibial arteries of both feet, in both WM and M groups were significantly larger than their baseline ($p<0.05$) and also larger than the control group ($p<0.05$) as showed in Table 8 and Table 9 in respective. In contrast, the dorsalis pedis and posterior tibial arteries' diameters of the control group did not change when compared between pre- and post-training. For the meantime, it had been found that the flow velocity (Table 8) and the shear stress (Table 10) measured at dorsalis pedis and posterior tibial arteries of both feet were not significantly different either between pre- and post-training or between groups, except the flow velocity of the right dorsalis pedis in the M group at post-training was faster than at pre-training significantly as showed in Table 8.

Considering of the QoL assessed by WHOQOL-BREF-THAI, there was no significant difference between pre- and post-training within each group, and among the three groups (WM, M, and control groups) as well (Table 6). Moreover, there was no report about the adverse effect during and after participated in every subject who attended this study.

Table 6 Comparison of the studied outcomes among the three groups (walking meditation, massage and control groups), and between pre- and post-training within each group

Studied outcomes	Walking meditation group (Mean ± SD)			Massage group (Mean ± SD)			Control group (Mean ± SD)			p^2
	Pre	Post	p^1	Pre	Post	p^1	Pre	Post	p^1	
Pressure sense testing (%)	63.75 ± 12.46	92.50 ± 5.34	.012*	68.33 ± 10.60	87.77 ± 8.70	.012*	69.44 ± 20.68	72.22 ± 12.27	.139	.002**
Vibration testing (sec)										
Left side	10.50 ± 3.32	16.33 ± 6.28	.012*	11.02 ± 3.62	12.51 ±2.89	.155	10.05 ± 6.11	11.55 ± 5.39	.139	.273
Right side	7.12 ± 3.42	14.62 ± 4.80	.012*	8.34 ± 3.43	13.92 ± 5.66	.012*	8.27 ± 4.77	10.77 ± 5.15	.139	.468
Peripheral Blood Flow (TTcm^3/s)										
Left Dorsalis Pedis artery	.24 ± .07	.35 ± .07	.208	.13 ± .03	.33 ± .07	.011*	.19 ± .10	.12 ± .03	.889	.018*
Right Dorsalis Pedis artery	.26 ± .07	.44 ± .10	.123	.16 ± .04	.63 ± .20	.008**	.24 ± .09	.18 ± .04	.441	.021*
Left Posterior Tibial artery	.21 ± .04	.35 ± .08	.051	.20 ± .04	.71 ± .18	.011*	.17 ± .05	.16 ± .05	.944	.036*
Right Posterior Tibial artery	.21 ± .06	.38 ± .08	.017*	.26 ± .05	.45 ± .11	.068	.21 ± .05	.29 ± .09	.327	.357
Quality of life (points)	98 ± 14.65	98.75 ± 11.20	.726	94.55 ± 8.81	95.55 ± 10.82	.906	106.44 ± 10.60	97.11 ± 14.85	.139	.843

p1, p-value from comparison between pre- and post-training within each group by Wilcoxon test. p2, p-value from comparison of the post-score among three groups by Kruskal Wallis test. *, Significant difference at $p<0.05$.

Table 7 Comparison of pressure sense testing and peripheral blood flow at post-training between each group, walking meditation versus control groups, massage versus control groups, and walking meditation versus massage groups

Studied outcomes	Mean ± SD					
	WM : Control	p-value	M : Control	p-value	WM : M	p-value
Pressure sense testing (%)	92.50 ± 5.34 : 72.22 ± 12.27	.001**	87.77 ± 8.70 : 72.22 ± 12.27	.014*	92.50 ± 5.34 : 87.77 ± 8.70	.167
Peripheral Blood Flow ($\pi cm^3/s$)						
Left Dorsalis Pedis artery	.35 ± .07 : .12 ± .03	.007**	.33 ± .07 : .12 ± .03	.034*	.35 ± .07 : .33 ± .07	.847
Right Dorsalis Pedis artery	.44 ± .10 : .18 ± .04	.021*	.63 ± .20 : .18 ± .04	.015*	.44 ± .10 : .63 ± .20	.736
Left Posterior Tibial artery	.35 ± .08 : .16 ± .05	.135	.71 ± .18 : .16 ± .05	.019*	.35 ± .08 : .71 ± .18	.149
Right Posterior Tibial artery	.38 ± .08 : .29 ± .09	.268	.45 ± .11: .29 ± .09	.200	.38 ± .08 : .45 ± .11	.700

* Significant difference between groups at p<0.05 by Mann Whitney-U test. **, Significant difference between groups at p<0.01 by Mann Whitney-U test, WM : Control = walking meditation versus control groups, M : Control = massage versus control groups, WM : M = walking meditation versus massage groups

Table 8 Comparison of vessel diameter and blood flow velocity among the three groups (walking meditation, massage and control groups), and between pre- and post-training within each group

Studied Parameters	Meditation group (Mean ± SD)			Massage group (Mean ± SD)			Control group (Mean ± SD)			Comparison among groups	
	Pre	Post	p^1	Pre	Post	p^1	Pre	Post	p^1	p^2 (Pre)	p^2 (Post)
Diameter of Vessel (mm.)											
Left Dorsalis Pedis	1.53 ± .28	2.12 ± .66	.075	1.40 ± .29	1.86 ± .45	.012*	1.31 ± .44	1.27 ± .15	.719	.169	.001*
Right Dorsalis Pedis	1.58 ± .31	2.13 ± .62	.035*	1.34 ± .34	2.00 ± .49	.007*	1.52 ± .43	1.28 ± .23	.206	.465	.001*
Left Posterior Tibialis	1.70 ± .39	2.10 ± .51	.035*	1.50 ± .22	2.22 ± .33	.012*	1.44 ± .64	1.23 ± .52	.106	.765	.001*
Right Posterior Tibialis	1.62 ± .44	2.00 ± .44	.011*	1.73 ± .33	1.97 ± .32	.074	1.44 ± .59	1.41 ± .61	.546	.442	.028*
Velocity of Blood Flow (cm/s)											
Left Dorsalis Pedis artery	11.8 ± 2.17	12.71 ± 3.83	.674	9.0 ± 2.17	16.0 ± 4.19	.110	11.44 ± 3.23	9.8 ± 2.19	.678	.546	.724
Right Dorsalis Pedis artery	13.8 ± 3.65	12.88 ± 3.12	.674	11.6 ± 2.75	19.8 ± 4.64	.021*	11.27 ± 1.75	16.34 ± 4.14	.314	.904	.756
Left Posterior Tibial artery	8.8 ± 1.46	10.62 ± 2.11	.327	11.4 ± 2.19	15.42 ± 3.27	.374	8.06 ± 2.03	10.93 ± 3.27	.263	.432	.440
Right Posterior Tibial artery	10.0 ± 2.79	13.17 ± 3.13	.050	10.8 ± 2.11	14.94 ± 3.23	.139	9.94 ± 2.22	13.30 ± 3.57	.263	.967	.943

p^1= p-value from comparison between pre- and post-training within each group by Wilcoxon test. p^2= p-value from comparison among the three groups by Kruskal Wallis test, * Significant difference at $p<0.05$.

Table 9 Comparison of vessel diameters at post-training between each group, walking meditation versus control groups, massage versus control groups, and walking meditation versus massage groups

Studied Parameters	Mean ± SD					
	WM : Control	p-value	M : Control	p-value	WM : M	p-value
Diameter of Vessel (mm.)						
Left Dorsalis Pedis artery	2.12 ± .66 : 1.27 ± .15	.005**	1.86 ± .45 : 1.27 ± .15	.001**	2.12 ± .66 : 1.86 ± .45	.497
Right Dorsalis Pedis artery	2.13 ± .62 : 1.28 ± .23	.001**	2.00 ± .49 : 1.28 ± .23	.002**	2.13 ± .62 : 2.00 ± .49	.808
Left Posterior Tibial artery	2.10 ± .51 : 1.23 ± .52	.004**	2.22 ± .33 : 1.23 ± .52	.001**	2.10 ± .51 : 2.22 ± .33	.308
Right Posterior Tibial artery	2.00 ± .44 : 1.41 ± .61	.038*	1.97 ± .32 : 1.41 ± .61	.013*	2.00 ± .44 : 1.97 ± .32	.884

*Significant difference between groups at p<0.05 by Mann Whitney-U test, ** Significant difference between groups at p<0.01 by Mann Whitney-U test, WM : Control = walking meditation versus control groups, M : Control = massage versus control groups, WM : M = walking meditation versus massage groups

Table 10 Comparison of shear stress among the three groups (walking meditation, massage and control groups) and between pre- and post-training within and between each group

Studied Parameters	Meditation group (Mean ± SD)			Massage group (Mean ± SD)			Control group (Mean ± SD)			Comparison among groups	
	Pre	Post	p^1	Pre	Post	p^1	Pre	Post	p^1	p^2 (Pre)	p^2 (Post)
Shear stress (s^{-1})											
Left Dorsalis Pedis artery	75.0 ± 10.93	77.69 ± 32.02	.327	70.15 ± 18.81	84.80 ± 25.95	.678	91.61 ± 26.63	76.11 ± 15.80	.953	.982	.791
Right Dorsalis Pedis artery	91.8 ± 26.52	65.83 ± 17.31	.093	67.22 ± 17.69	106.0 ± 25.01	.314	80.11 ± 10.21	137.58 ± 36.08	.173	.545	.286
Left Posterior Tibial artery	52.4 ± 8.71	54.63 ± 12.01	.889	57.98 ± 11.39	77.33 ± 16.19	.374	58.79 ± 12.34	78.43 ± 24.66	.441	.991	.661
Right Posterior Tibial artery	64.3 ± 19.53	71.71 ± 18.98	.401	58.9 ± 15.35	77.90 ± 16.96	.314	75.75 ± 10.87	82.17 ± 20.59	.594	.213	.935

p^1= p-value from comparison between pre- and post-training within each group by Wilcoxon test. p^2= p-value from comparison among the three groups by Kruskal Wallis test, * Significant difference at $p<0.05$.

CHAPTER 5
DISCUSSION AND CONCLUSION

The current study gave an education and motivated type-2 diabetes patients to look back and take care themselves by doing the activities as walking with meditation or self-massaging their legs about three times per week for four weeks. Post intervention, either the walking meditation (WM) group or the massage (M) group showed significant improvement in pressure sense testing when compared to baseline and also to the control group (WM: p=.012, M: p=.001). Additionally, the WM and M groups significantly presented better vibration perception after the intervention compared to baseline (p=.012). The results of this study also showed that either WM or M clinically improved neuropathic symptoms in type-2 diabetes from moderate to minimal severity which related to the classification of neuropathic symptoms severity assessed with 128 Hz tuning fork by Oyer et al in 2007.(77) They divided the severity of diabetic peripheral neuropathic (DPN) symptoms into three levels by using a 128 Hz tuning fork as follows. The severity of DPN symptoms at minimal, moderate, and maximal levels referred to patients who were able to detect vibration from the tuning fork for 12-17 seconds, 5-11 seconds, and $\leq$ 4 seconds respectively.(77) So, the findings related to the improvements of the pressure and vibration senses in WM and M groups of this study suggested that either WM or M was able to improve the protective sensation of the diabetic foot. Since the impaired protective sensation of the diabetic peripheral neuropathy was one important factor resulting in increased foot ulcer.(118-120) Therefore, either WM or M might be an intervention for prevention or reducing the risk of foot ulcer in persons with diabetic peripheral neuropathy.

Besides the improvement of the pressure and vibration senses, the WM and M groups also significantly presented increasing in peripheral blood flow at both feet after intervention (WM group; Left Dorsalis Pedis: p=.007, Right Dorsalis Pedis: p=.021 and M group; L Left Dorsalis Pedis: p=.034, Right Dorsalis Pedis: p=.015, Left Posterior Tibialis: p=.019). These were confirmed by the study findings of higher peripheral blood flow in

dorsalis pedis and posterior tibial arteries at post intervention of the WM and M groups compared to baseline and to the control group, particularly the M group. In addition, the improvement of peripheral blood flow in dorsalis pedis and posterior tibial arteries by WM or M for 4 weeks (30 minutes/time, 3 times/week) of this study resulted from an increase in "diameter of vessel" rather than an increase in "blood flow velocity" supported by the increase in the diameter at post-intervention compared to baseline and the control group. One of the causes of diabetic peripheral neuropathy was a poor blood circulation to the peripheral nerve of the diabetic foot.(42, 66, 121) In case of the person with DM who had foot ulcer, the poor blood circulation at the foot would lead to increase an amputation risk due to gangrene.(122, 123) Thus, the improvement of peripheral blood flow by WM and M protocol in this study would be benefit for foot care to the persons with type 2 DM and persons with type-2 diabetic peripheral neuropathy as well.

Although massage had benefit for persons with type 2 DM and persons with type-2 diabetic peripheral neuropathy as found in this study. However, some people with diabetes often found edema at foot.(124) It might be caused by vascular alteration, imbalance of fluid in capillary and interstitial spaces, problem of venous return, or retention of some fluid as water and salt etc. Then interstitial fluid volume had increased.(125) Therefore, for individuals with diabetes who had foot edema, they should concern about the direction of massage because it might affect to lymphatic system and its pathway and should be ruled out all the contraindications of massage before applying a foot massage.(126)

The improvements of the pressure and vibration senses as well as the increase in peripheral blood flow of the feet for the WM and M groups might arise from the physical and mental effects. Considering the increased peripheral blood flow by the physical effect, WM was like a weight bearing exercise which could induce shear stress to the lower limbs' blood vessels that would activate the endothelium of the vessels to release Nitric Oxide (NO). The released NO acts as the vasodilation factor resulting in dilation of the blood vessel. Due to vasodilation, the volume of blood flow was increased.(127) In addition, active lower limbs' muscle contraction during walking activity of the WM practice

could be an active muscle pumping that also helped blood circulation improved.(128-130) Similarly, foot and leg massage could induce shear stress to the blood vessels and could be a passive muscle pumping in the massaged area by massaging pressure. So, the WM and massage might also increase peripheral blood flow of the feet by the same physical mechanisms, but in alternative way as WM was an active activity of foot and leg while M was a passive activity on foot and leg. However, this study did not find statistically significant change of the shear stress in all groups because it was assessed in resting position, but not during the activity.

Moreover, this study also supported that massage could increase blood flow according to the previous studies.(131, 132) Although no prior study related to WM effects on peripheral blood flow of diabetic foot, Kwon et al in 2011 had found that walking exercise improved endothelium independent vasodilation (EID) and flow mediated dilation (FMD) representing an elasticity of vessels, vascular health and function in patients with diabetes by Ultrasound Doppler.(133) Therefore, alike walking exercise, this could also supported that the blood flow improvement in WM might due to the physical effect of walking activity.

Furthermore, the improved peripheral blood flow to the feet in WM and M groups would provide more blood supply to peripheral nerve and sensory mechanoreceptors sufficiently. Therefore, these might consequently promote better pressure and vibration senses that significantly found in WM and M groups. In addition, from the study of Gholami et al. in 2018, they studied about effect of walking exercise on nerve conduction in type 2 diabetic peripheral neuropathy, the participants walked on treadmill with moderate intensity of heart rate reserve (HRR) for 3 months. Post-intervention, They found an improvement of nerve conduction velocity in an experimental group when compared with a control group.(134) Moreover, a systematic review by Feter et al. in 2017, they had studied about effect of intensity exercise on myelin regeneration in rat and they found that the low and moderate intensity exercise, such as endurance and treadmill training enhanced a regeneration of myelin sheath in the myelinated nerve fibers.(135) Thus, this might support the significant improvement of pressure and vibration sense in WM group

because the walking activity of 30-minute WM practice might approximately be the low and moderate physical exercise that might improve myelin regeneration. However, the effect of intensity exercise on myelin regeneration was found in rodents trial, it still need more researches to confirm the effect in human.

Although we didn't measure the mental effect directly but the assisted researcher reported that all of participants of walking meditation group had practiced their mind along walking because they voiced follow the position that they did during practice. As the mental effects, the prior studies had found that meditation practice improved parasympathetic function and balance of autonomic nervous system which could decrease heart rate and relax blood vessel.(107, 136) In 2013, Krygier et al had found that after subjects participated meditation for 10 times, they had improvement of relative high frequency power in normal unit (normalized HF) representing an improvement of parasympathetic function.(136) Matzner et al, in 2003, had detected the heart rate variability (HRV) and intervening low frequency band (LF) of subjects during Kundalini Yoga meditation for 15 minutes and found that during Kundalini Yoga meditation showed adaptation of heart rate and less intervening low frequency band (LF) which represented the balance of autonomic nervous system.(107) According to the previous studies, meditation practice during walking as in the WM group of this study might affect autonomic nervous system by improving parasympathetic and reducing sympathetic tone which resulted in vasodilation and increase peripheral blood flow as finding.

As mention above, walking mediation not only had physical effect but also had meditation or mental effect. This could be confirmed by the following studies. Gaineya et al., in 2016, had studied about effect of walking meditation on vascular function and blood sugar in patients with diabetes and they found that the patients who performed walking with meditation had a reduction of blood sugar, and also decreased in blood pressure and stress.(25) Prakhinkit et al., in 2014, had compared the effects of a novel Buddhism-based walking meditation (BWM) with a traditional walking exercise (TWE) in elderly female with mild-to-moderate depression. They reported that BWM improved vascular

function superior to TWE, and only the BWM presented a decrease in mentally depression.(33)

From the literature review, the slow and gentle massage also had effect on autonomic nervous system, especially activated parasympathetic function.(111, 137) The slow and gentle massage could stimulate parasympathetic nervous system by activating Baroreceptors and mechanoreceptors under the skin which sent the signal to activate autonomic nervous system, especially parasympathetic nervous system(138, 139) to help muscle relaxation and vasodilation. Therefore, another reason of peripheral blood flow improvement by massage for this study might due to vasodilation from increased parasympathetic tone as well.

The results of vibration testing, M group showed significant change between pre-test and post-test only the right foot ($p = .012$). Since the study of Lapanatasin et al., in 2014, had found that massage for 40 minutes a day improved peripheral neuropathic symptoms significantly.(140) Therefore, foot and leg massage for 20 minutes (10 minutes each side) in this study which less than the prior study might not enough to get markedly improvement of neuropathic symptoms. However, the mechanisms of massage gave positive benefit to the participants, particularly peripheral blood flow increment. Additionally, stretching during warm up and cool down didn't affect to all studied outcomes because there was no significant difference of the outcomes between pre and post-test of the control group which received only stretching as warmup and cool down. Therefore, the significant findings of the improvements for peripheral blood flow and protective sensation in WM and M groups should be clearly caused by the interventions of WM practice and massage.

Also, in this study, both WM and M groups had shown that increase in diameter of blood vessel was a primary factor of peripheral blood flow improvement rather than blood flow velocity. Since these two activities could activate nitric oxide released from the endothelium cell, and enhance parasympathetic autonomic nervous system that resulting in vasodilation and then volume of blood flow will be increased.(141, 142)

For the QoL, even though Timar et al. in 2016 found a correlation between QoL and a high score of MNSI in patients with type-2 diabetes.(85), there was no significant differences in QoL between pre- and post-intervention within each group and among groups for this study. It might because the most of participants in this study (92.30%) still had positive neuropathic symptoms just only by the objective physical examination part of MNSI, but not that of the subjective examination part which involved in the bothersome neuropathic symptoms. Thus, their neuropathic symptoms might be not too much to disturbed their QoL. In addition, at the baseline, majority of the participants in all groups had QoL in a good level which was better than QoL level of Thai elderly people reported by Whangmahaporn et al. in 2018.(143) Moreover, besides neuropathic symptoms, the study was unable to control other factors influencing on QoL of the participants, for example family and economic factors., therefore, just the improvement of neuropathic symptoms in WM and M groups of this study might not adequate to change the participants' QoL

Limitation of the study

The results of this study couldn't extrapolate to people with type-2 DM who had abnormal ankle brachial index or other conditions which indicated in the exclusion criteria of the study. Moreover, there was multifactor influencing on participants' QoL that was unable to control for this study. Furthermore, the change of autonomic function was unable to represent directly because the study did not detect the HRV variables.

Lastly, the results of the study related to vascular function could be clearer confirmed if the endothelium dependent and independent vasodilation were measured.

Further study

The effect of a longer practice duration of WM and also the comparative effect between the different speeds of walking during WM practice on the peripheral blood flow and neuropathic symptoms in persons with type-2 DM are interested to be investigated further. Additionally, in order to see the more obvious effects of walking meditation, the future study in a larger population with long term follow-up after WM practice are recommended.

Also, the other outcome measures related to vascular function, such as the endothelium dependent and independent vasodilation should be studied further.

Conclusion

Walking meditation and massage at least 4 weeks (30 minutes a day, 3 days a week) reduced the neuropathic symptoms of a diabetic foot as impaired pressure and vibration sensation, and also improved peripheral blood flow in persons with type-2 diabetic peripheral neuropathy. Therefore, either walking meditation or foot-leg massage could be an alternative intervention that should be recommend to persons with type-2 diabetes for taking care themselves in order to decrease or prevent foot ulcer and amputation risk.

REFERENCES

1. World Health Organization. Global report on diabetes. World Health Organization. 2016.

2. Papier K, Jordan S, D'Este C, Bain C, Peungson J, Banwell C, et al. Incidence and risk factors for type 2 diabetes mellitus in transitional Thailand: results from the Thai cohort study. British medical journal. 2016;6:1-8.

3. Griffith ML, Younk LM, Davis SN. Visceral adiposity, insulin resistance, and type 2 diabetes. American journal of lifestyle medicine. 2010;6:1-8.

4. Olokoba AB, Obateru OA, Olokoba LB. Type 2 diabetes mellitus: a review of current trends. Oman medical journal. 2012;27(4):269-73.

5. ราชวิทยาลัยอายุรแพทย์แห่งประเทศไทย ในพระบรมราชูปถัมภ์, สมาคมโรคเบาหวานแห่งประเทศไทย ในพระราชูปถัมภ์สมเด็จพระเทพรัตนราชสุดาฯ สยามบรมราชกุมาร, สมาคมต่อมไร้ท่อแห่งประเทศไทย, สถาบันวิจัยและประเมินเทคโนโลยีทางการแพทย์ กรมการแพทย์ กระทรวงสาธารณสุข,สำนักงานหลักประกันสุขภาพแห่งชาติ. แนวทางเวชปฏิบัติสำหรับโรคเบาหวาน. 2560.

6. Davies M, Brophy S, Williams R, Taylor A. The prevalence, severity, and impact of painful diabetic peripheral neuropathy in type 2 diabetes. Diabetes care. 2006;29(7): 1518-22.

7. Tesfaye S. Recent advances in the management of diabetic distal symmetrical polyneuropathy. Journal of diabetes investigation. 2011;2(1):33-42.

8. Pratley RE. The Early Treatment of Type 2 Diabetes. The American journal of medicine. 2013;126(9):S2-9.

9. Lazo MdlA, Bernabé-Ortiz A, Pinto ME, Ticse R, Malaga G, Sacksteder K, et al. Diabetic peripheral neuropathy in ambulatory patients with type 2 diabetes in a general hospital in a middle income country : a cross sectional study. The national center for biotechnology information. 2014;9(5):e95403.

10. Tabit CE, Chung WB, Hamburg NM, Vita JA. Endothelial dysfunction in diabetes mellitus: molecular mechanisms and clinical implications. National institutes of health. 2010;11(1):61-74.

11. Kasim K, MorsyAmar, Sadek AAE, AbdelGawad S. Peripheral neuropathy in type-II diabetic patients attending diabetic clinics in Al-Azhar university hospitals, Egypt. International journal of diabetes mellitus. 2010;20(1):20-3.

12. Kolluru GK, Bir SC, Kevil CG. Endothelial dysfunction and diabetes: effects on angiogenesis, vascular remodeling, and wound healing. International journal of vascular medicine. 2012.

13. Vinik AI, Maser RE, Mitchell BD, Freeman R. Diabetic autonomic neuropathy. Diabetes care. 2003;26(5):1553-79.

14. Tesfaye S, Hallamshire R. Advances in the epidemiology, pathogenesis and management of diabetic peripheral neuropathy. Diabetes/metabolism research and reviews. 2011;28(Suppl 1):8-14.

15. Juster-Switlyka K, Smith AG. Updates in diabetic peripheral neuropathy. 2016.

16. Munpan W, Sakthong P. Quality of life in medication use in patients with chronic diseases at Phramongkutklao hospital. Royal Thai army medical journal 2015;68(2).

17. Mueller MJ, Tuttle LJ, LeMaster JW, Strube MJ, McGill JB, Hastings MK, et al. Weight-bearing versus nonweight-bearing exercise for persons with diabetes and peripheral neuropathy: a randomized controlled trial. National institutes of health. 2013;94(5):829-38.

18. Kruse RL, LeMaster JW, Madsen RW. Fall and balance outcomes after an intervention to promote leg strength, balance, and walking in people with diabetic peripheral neuropathy: "feet first" randomized controlled trial. Physical therapy. 2010;90(11):1568-79.

19. Maharaj SS, Nuhu JM. The effect of rebound exercise and treadmill walking on the quality of life for patients with non-insulin-dependent type 2 diabetes. International journal of diabetes in developing countries. 2015;35:223-9.

20. Aylin K, Arzu D, Sabri S, Handan TE, Ridvan A. The effect of combined resistance and home-based walking exercise in type 2 diabetes patients. International journal of diabetes in developing countries. 2009;29(4):159-65.

21. Jung HY, Lee H, Park J. Comparison of the effects of Korean mindfulness-based stress reduction, walking, and patient education in diabetes mellitus. Nursing and health sciences. 2015;17(4):516-25.

22. Ezzo J, Donner T, Nickols D, Cox M. Is massage useful in the management of diabetes? a systematic review. Diabetes spectrum. 2001;14(4):218-24.

23. Lapanantasin S, Jedtanaprakrit S, Assarach R, Inklum W, Jamnongphon S. Effect of massage with peripheral vascular circulation exercise on neuropathic symptoms of lower legs in type 2 diabetic patients: a pilot study. Thai journal of physical therapy. 2014;36(3):97-105.

24. Wang T-J, Lee S-C, Liang S-Y, Tung H-H, Wu S-FV, Lin Y-P. Comparing the efficacy of aquatic exercises and land-based exercises for patients with knee osteoarthritis. Clinical nursing. 2011;20((17-18)):2609-22.

25. Gainey A, Himathongkam T, Tanaka H, Suksom D. Effects of buddhist walking meditation on glycemic control and vascular function in patients with type 2 diabetes. Complementary therapies in medicine. 2016;26:92-7.

26. Hartmann M, Kopf S, Kircher C, Faude-Lang V, Djuric Z, Augstein F, et al. Sustained Effects of a mindfulness-based stress-reduction intervention in type 2 diabetic patients. Diabetes care. 2012;35(5):945-7.

27. Qiu S, Cai X, Schumann U, Velders M, Sun Z, Steinacker JM. Impact of walking on glycemic control and other cardiovascular risk factors in type 2 diabetes: a meta-analysis. Diabetes care. 2014;9(10).

28. Taylor JD, Fletcher JP, Tiarks J. Impact of physical therapist-directed exercise counseling combined with fitness center-based exercise training on muscular strength and exercise capacity in people with type 2 diabetes: a randomized clinical trial. Physical therapy. 2009;89(9):884-92.

29. El-Kader A, OH A-J, FM A-S. Aerobic exercises alleviate symptoms of fatigue related to inflammatory cytokines in obese patients with type 2 diabetes. African health sciences. 2015;15(4):1142-8.

30. Sung K, Bae S. Effects of a regular walking exercise program on behavioral and biochemical aspects in elderly people with type II diabetes. Nursing and health sciences. 2012;14:438-45.

31. Shenoy S, Guglani R, Sandhu JS. Effectiveness of an aerobic walking program using heart rate monitor and pedometer on the parameters of diabetes control in Asian Indians with type 2 diabetes. Primary care diabetes. 2010;4:41-5.

32. Behboudi L, Azarbayjani M-A, Aghaalinejad H, Salavati M. Effects of aerobic exercise and whole body vibration on glycaemia control in type 2 diabetic males. Asian journal of sports medicine. 2011;2(2):83-90.

33. Prakhinkit S, Suppapitiporn S, Tanaka H, Suksom D. Effects of Buddhism walking meditation on depression, functional fitness, and endothelium-dependent vasodilation in depressed elderly. The journal of alternative and complementary medicine. 2014;20(5):411-6.

34. Leoniuk J, Łukasiewicz A, Szorc M, Sackiewicz I, Janica J, Łebkowska U. Doppler ultrasound detection of preclinical changes in foot arteries in early stage of type 2 diabetes. Polish journal of radiology. 2014;79:283-9.

35. Hwang JY. Doppler ultrasonography of the lower extremity arteries: anatomy and scanning guidelines. Ultrasonography. 2017;36(2):111-9.

36. Deerochanawong C, Ferrario A. Diabetes management in Thailand: A literature review of the burden, costs, and outcomes. Globalization and Health. 2013;9(1):1-18.

37. Sobhani S, Asayesh H, Sharifi F, Djalalinia S, Baradaran HR, Arzaghi SM, et al. Prevalence of diabetic peripheral neuropathy in Iran: a systematic review and meta analysis. Journal of diabetes & metabolic disorders. 2014;13:1-7.

38. Jambart S, Ammache FH Z, Younes AH A, Abdalla K, Selwan CA, Sunna N, et al. Prevalence of painful diabetic peripheral neuropathy among patients with diabetes mellitus in the middle east region. The journal of international medical research. 2011;39(2):366-77.

39. Katulanda P, Ranasinghe P, Jayawardena R, Constantine GR, Sheriff R, Matthews DR. The prevalence, patterns and predictors of diabetic peripheral neuropathy in a developing country. Diabetology & metabolic syndrome. 2012;4:1-8.

40. Cavan D, Fernandes J, Makarof L, Ogurtsova K, Webber S. IDF Diabetes atlas. Brussels, Belgium: International diabetes federation. 2015.

41. Wilcox G. Insulin and insulin resistance. The Clinical Biochemist Reviews. 2005;26(2):19–39.

42. Yagihashi S, Mizukami H, Sugimoto K. Mechanism of diabetic neuropathy: where are we now and where to go. Journal of diabetes investigation. 2011;2(1):18-32.

43. Wongkongkam K, Thosingha O, Utriyaprasit K, Riegel B, Ruangsetakit C, Viwatwongkasem C. Relationship between diabetic duration and the severity of peripheral arterial disease among thai patients with type-2 diabetes. Journal of nursing science. 2011;29(3):124-32.

44. Potier L, Khalil CA, Mohammedi K, Roussel R. Use and utility of ankle brachial index in patients with diabetes. The National Center for Biotechnology Information. 2011;41(1):110-6.

45. Williams DT, Harding KG, Price P. An evaluation of the efficacy of methods used in screening for lower-limb arterial disease in diabetes. Diabetes care. 2005;28(9):2206-10.

46. Flanigan DP, Ballard JL, DoreenRobinson, Galliano M, Blecker G, R.S.Harward T. Duplex ultrasound of the superficial femoral artery is a better screening tool than ankle-brachial index to identify at risk patients with lower extremity atherosclerosis. The society for vascular surgery. 2008;47(4):789-92.

47. Marchettini P, Lacerenza M, Mauri E, Marangoni C. Painful peripheral neuropathies. Current Neuropharmacology. Current Neuropharmacology. 2006;4(3):175-81.

48. Paneni F, Beckman JA, Creager MA, Cosentino F. Diabetes and vascular disease pathophysiology, clinical consequences, and medical therapy: part I. European heart journal. 2013;34(31):2436-46.

49. Kassan M, Galán M, Choi S-K, Matrougui K. Endoplasmic reticulum stress and microvascular endothelial dysfunction in diabetes. Journal of diabetes & metabolism. 2011;2(9):1-5.

50. Ullah A, Khan A, Khan I. Diabetes mellitus and oxidative stress-a concise review. Saudi pharmaceutical journal. 2016;24(5):547-53.

51. Yoo M, Sharma N, Pasnoor M, Kluding PM. Painful diabetic peripheral neuropathy: presentations, mechanisms, and exercise therapy. Journal of diabetes & metabolism. 2013;10:1-10.

52. Purwata TE. High TNF-alpha plasma levels and macrophages iNOS and TNF-alpha expression as risk factors for painful diabetic neuropathy. Journal of pain research. 2011;4:169-75.

53. Sharma R, Anker SD. From tissue wasting to cachexia: changes in peripheral blood flow and skeletal musculature. European heart journal. 2002;4:D12-7.

54. Lim TKY, Shi XQ, Johnson JM, Rone MB. Peripheral nerve injury induces persistent vascular dysfunction and endoneurial hypoxia, contributing to the genesis of neuropathic pain. The journal of neuroscience 2015;35(8):3346-59. 2015;35(8):3346-59.

55. Raitakari OT, Celermajer DS. Flow-mediated dilatation. British journal of clinical pharmacology. British journal of clinical pharmacology. 2000;50(5):397-404.

56. Tessari P, Cecchet D, Cosma A, Vettore M, Coracina A, Millioni R, et al. Nitric oxide synthesis is reduced in subjects with type 2 diabetes and nephropathy. American diabetes association. 2010;59(9):2152-9.

57. Avogaro A, Albiero M, Menegazzo L, Kreutzenberg Sd, Fadini GP. Endothelial dysfunction in diabetes the role of reparatory mechanisms. Diabetes care. 2011;34(2):S285-90.

58. Marso SP, Hiatt WR. Peripheral arterial disease in patients with diabetes. Journal of the American college of cardiology. 2006;47(5):921-9.

59. Fakhrzadeh H, Sharifi F, Alizadeh M, Arzaghi S, Tajallizade-Khoob Y, Tootee A, et al. Relationship between insulin resistance and subclinical atherosclerosis in individuals with and without type 2 diabetes mellitus. Journal of diabetes & metabolic disorders 2016;15(41):1-7. 2016;15(41):1-7.

60. Cade WT. Diabetes-related microvascular and macrovascular diseases in the physical therapy setting. Physical therapy. 2008;88(11):1322-35.

61. Al-Mahroos F, Al-Roomi K. Diabetic neuropathy, foot ulceration, peripheral vascular disease and potential risk factors among patients with diabetes in Bahrain: a nationwide primary care diabetes clinic-based study. Annals of Saudi medicine. 2007;27(1):25-31.

62. Abbott CA, Malik RA, Ross EREv, Kulkarni J, Boulton AJM. Prevalence and characteristics of painful diabetic neuropathy in a large community-based diabetic population in the U.K. Diabetes care. 2011;34(10):2220-4.

63. Ko S-H, Cha BY. Diabetic peripheral neuropathy in type 2 diabetes mellitus in Korea. Diabetes and metabolism journal. 2012;36(1):6-12.

64. Janghorbani M, H. HR, A. AK, Ghorbani A. Peripheral neuropathy in type 2 diabetes mellitus in Isfahan, Iran: prevalence and risk factors. International journal of diabetes and metabolism. 2006;114(6):384-91.

65. Fowler MJ. Microvascular and macrovascular complications of diabetes. American diabetes association. 2008;26(2):77-82.

66. Schreiber AK, Nones CF, Reis RC, Chichorro JG, Cunha JM. Diabetic neuropathic pain: physiopathology and treatment. World journal of diabetes. 2015;6(3):432-44.

67. Xiong Q, Lu B, Ye H, Wu X. The diagnostic value of neuropathy symptom and change score, neuropathy impairment score and Michigan neuropathy screening instrument for diabetic peripheral neuropathy. European neurology. 2015;74(5):233-327.

68. Moghtaderi AR, Bakhshipour A, Rashidi H. Validation of Michigan neuropathy screening instrument for diabetic peripheral neuropathy. Clinical neurology and neurosurgery. 2006;108(5):477-81.

69. Damri T, Chatchawan U. Validity and reliability of the Michigan neuropathy screening instrument (MNSI) on the diabetic type II patients (Thai version). Journal of medical technology and physical therapy. 2015;27:307-19.

70. Fateh HR, Madani SP, Heshmat R, Larijani B. Correlation of Michigan neuropathy screening instrument, United Kingdom screening test and electrodiagnosis for early detection of diabetic peripheral neuropathy. Journal of diabetes & metabolic disorders. 2016;15(8):1-5.

71. Chang C-H, Peng Y-S, Chang C-C, Chen M-Y. Useful screening tools for preventing foot problems of diabetics in rural areas: a cross-sectional study. BMC Public health. 2013;13(1):612-9.

72. Mete T, Aydin Y, Saka M, Yavuz HC, Bilen S, Yalcin Y, et al. Comparison of efficiencies of Michigan neuropathy screening instrument, neurothesiometer, and electromyography for diagnosis of diabetic neuropathy. International journal of endocrinology. 2013;11:821745.

73. Gow D, Moore P. Assessing diabetic peripheral neuropathy in primary care. Biomedical and pharmacology journal. 2014;61:37-47.

74. Wang F, Zhang J, Yu J, Liu S, Zhang R, Ma X, et al. Diagnostic accuracy of monofilament tests for detecting diabetic peripheral neuropathy: a systematic review and meta-analysis. Journal of diabetes research. 2017;41:1-12.

75. Lee S, Kim H, Choi S, Park Y, Kim Y, Cho B. Clinical usefulness of the two-site semmes-weinstein monofilament test for detecting diabetic peripheral neuropathy. Journal of Korean medical science. 2003;18(1):103-7.

76. Meijer J-WG, Smit AJ, Lefrandt JD, Hoeven JHvd, Hoogenberg K, Links TP. Back to basics in diagnosing diabetic polyneuropathy with the tuning fork! Diabetes care. 2005;28(9):2201-5.

77. Oyer D, Saxon D, Shah A. Quantitative assessment of diabetic peripheral neuropathy with use of the clanging tuning fork test. Endocrine practice. 2007;13(1):5-10.

78. Morshed G, Mashahit M, Shaheen H. Simple screening tests for peripheral neuropathy as a prediction of diabetic foot ulceration. The foot and ankle online Journal. 2011;11(2):1-4.

79. Takahara M, Fujiwara Y, Sakamoto F, Katakami N, Matsuoka Ta, Kaneto H, et al. Assessment of vibratory sensation with a tuning fork at different sites in Japanese patients with diabetes mellitus. Journal of diabetes investigation. 2014;5(1):90-3.

80. Yang Z, Zhang Y, Chen R, Huang Y, Ji L, Sun F, et al. Simple tests to screen for diabetic peripheral neuropathy (Protocol). Cochrane library. 2014;2:1-30.

81. Siddiqui A. Effects of vasodilation and arterial resistance on cardiac output. Journal of clinical and experimental cardiology. 2011;2(11):1-6.

82. Levenson J, Simon AC, Safar ME, Bouthier JD, London GM. Elevation of brachial arterial blood velocity and volumic flow mediated by peripheral beta-adrenoreceptors in patients with borderline hypertension. Pathophysiology and natural history. 1985;71(4):663-8.

83. Hatmi ZN, Dabiran S, Kashani AS, Heidarzadeh Z, Darvishi Z, Raznahan M. Ankle-brachial index as a prognostic factor and screening tool in coronary artery disease: does it work? The journal of Tehran university heart center. 2014;9(4):174-8.

84. Subcommittee WCPW. Ankle brachial index: quick reference guide for clinicians. Journal of wound, ostomy and continence nursing. 2012;39(25):S21-S9.

85. Timar R, Velea I, Timar B, Lungeanu D, Oancea C, Roman D, et al. Factors influencing the quality of life perception in patients with type 2 diabetes mellitus. Patient preference and adherence. 2016;10:2471-7.

86. Dobrota VD, Hrabac P, Skegro D, Smiljanic R, Dobrota S, Prkacin I, et al. The impact of neuropathic pain and other comorbidities on the quality of life in patients with diabetes. Health and quality of life outcomes. 2014;12(171):1-8.

87. Duangjinda E. Quality of life of patients with diabetes mellitus type II, Nongyasai district, Suphanburi province. Journal of health science. 2015;24(6):1118-26.

88. Heepkaew S, Laohasiriwong W. Quality of life of patients with type II diabetes mellitus in Kuchinarai district, Kalasin province. Research and development health system journal. 2011;4(1):22-36.

89. Rungreangkulkij S, Thavornpitak Y, Kittiwatanapaisan W, Kotnara I, Kaewjanta N. Prevalence and factors of depression among type 2 diabetic patients. The psychiatric association of Thailand. 2014;59(3):287-98.

90. Morales MC, Navas AF, Filomena M, Jimenez R. Health-related quality of life in patients with type 2 diabetes mellitus in a rural area. Diabetes & metabolism. 2015;6(7):1-5.

91. Shaheen F, Basit A, Riaz M, Fawwad A. Assessing health related quality of life in diabetic subjects by SF 36 questionnaire in a tertiary care diabetes unit of Karachi, Pakistan. International journal of advanced research. 2014;2(6):13-7.

92. Goh S, Rusli B, Khalid B. Development and validation of the Asian diabetes quality of life (AsianDQOL) questionnaire. Diabetes research and clinical practice. 2015;108(3):489-98.

93. Saraç ZF, Tütüncüoglu P, Parildar S, Saygili F, Yilmaz Ce, Tüzün M. Quality of life in Turkish diabetic patients. Turkish journal of endocrinology and metabolism. 2007;11:48-53.

94. Musa KI, Ismail A, Naing L, Mohamad WAe. Type 2 diabetes mellitus patients with poor glycaemic control have lower quality of life scores as measured by the short form-36. Singapore medical journal. 2015;51(2):157-62.

95. Leurmarnkul W, Meetam P. Properties testing of the retranslated SF-36 (Thai version). Thai Journal of Pharmaceutical Sciences. 2005;29(1-2):69-88.

96. Mahatnirunkul S. World health organization quality of life brief Thai In: health Dom, Editor. 2002. 2002.

97. Maudrene TS, Tan BDC, Hao KY, Konstadina G, Michelle N, Mohammad A, et al. WHOQOL-BREF among Singaporean patients with type II diabetes mellitus: what does it measure? Journal of medicine & medical research. 2014;4(17):3293-316.

98. Chatchawan U, Eungpinichpong W, Plandee P, Yamauchi J. Effects of Thai foot massage on balance performance in diabetic patients with peripheral neuropathy: A randomized Parallel-controlled trial. Medical science. 2015;21:68-75.

99. Mitranun W, Phongsri K. The acute effects on endothelial function in the different abdominal training postures. Songklanakarin journal of science and technology. 2015;37:545-51.

100. Dobrosielski DA, Gibbs BB, Ouyang P, Bonekamp S, Clark JM, Wang N-Y, et al. Effect of exercise on blood pressure in type 2 diabetes: a randomized controlled trial. Journal of general internal medicine. 2012;27(11):1453-6.

101. Mitranun W, Deerochanawong C, Tanaka H, Suksom D. Continuous vs interval training on glycemic control and macro and microvascular reactivity in type 2 diabetic patients. Scandinavian Journal of Medicine & Science in Sports. 2014;24:e69-e76.

102. Gibbs BB, Dobrosielski DA, Althouse AD, Stewart KJ. The effect of exercise training on ankle-brachial index in type 2 diabetes. National institutes of health. 2013;230(1):125-30.

103. Dijk J-Wv, Tummers K, Stehouwer CDA, Hartgens F, Loon LJCv. Exercise therapy in type 2 diabetes is daily exercise required to optimize glycemic control? Diabetes Care. 2012;35(5):948-54.

104. Padilla J, Harris RA, Rink LD, Wallace JP. Characterization of the brachial artery shear stress following walking exercise. Vascular medicine. 2008;13(2):105-11.

105. Levine GN, Lange RA, Bairey-Merz CN, Davidson RJ, Jamerson K, Mehta PK, et al. Meditation and cardiovascular risk reduction a scientific statement from the American heart association. The American heart association. 2017;6(10):1-57.

106. Terathongkum S. Relationships among stress, blood pressure, and heart rate variability in meditators. Virginia: Virginia commonwealth university. 2006.

107. Matzner SA. Heart rate variability during meditation. Journal of anthropological research. 2003:1-4.

108. Wood R, Maraj B, Lee M, Reyes R. Short-term heart rate variability during a cognitive challenge in young and older adults. Age and ageing. 2002;31(2):131-5.

109. Bigger J. Heart rate variability standards of measurement, physiological interpretation, and clinical use. European heart journal. 1996;17:354-81.

110. Boulton AJM. Management of Diabetic Peripheral Neuropathy. American diabetes association. 2005;23(1):9-15.

111. Kiran, Arora AK, Kaur D, Ghay R. Impact of meditation on autonomic nervous system - A research study. International journal of basic and applied medical sciences. 2011;1(1):144-8.

112. Ankad RB, Herur A, Patil S, Shashikala, Chinagudi S. Effect of short-term pranayama and meditation on cardiovascular functions in healthy individuals. Heart Views. 2011;12(2):58-62.

113. Paul-Labrador M, Polk D, Dwyer JH, Velasquez I, Nidich S, Rainforth M, et al. Effects of a randomized controlled trial of transcendental meditation on components of the metabolic syndrome in subjects with coronary heart disease. Archives of internal medicine. 2006;166(11):1218-24.

114. Goyal M, Singh S, Sibinga EMS, Gould NF, Rowland-Seymour A, Sharma R, et al. Meditation programs for psychological stress and well-being a systematic review and meta-analysis. American medical association. 2014;174(3):357-68.

115. Nagaraj HM, Pednekar A, Corros C, Gupta H, Lloyd SG. Determining exercise-induced blood flow reserve in lower extremities using phase contrast MRI. Journal of magnetic resonance imaging. 2008;27:1096-102.

116. Aboyans V, Criqui MH, Abraham P, Allison MA, Creager MA, Diehm C, et al. Measurement and interpretation of the ankle-brachial index a scientific statement from the American heart association. American heart association. 2012;126(24):2890-909.

117. วัดบรมสถล. การเดินจงกรม 6 ระยะ 2559 [cited Retrieved December 25, 2019] Available from: https://wwwyoutubecom/watch?v=skmUAdElJLg.

118. Boulton AJM, Armstrong DG, Albert SF, Frykberg RG, Hellman R, Kirkman MS, et al. Comprehensive foot examination and risk management. Diabetes care 2008;31(8):1679-85.

119. Smieja M, Hunt DL, Edelman D, Etchells E, Cornuz J, Simel DL, et al. Clinical examination for the detection of protective sensation in the feet of diabetic patients. Journal of general internal medicine. 1999;14(7):418-24.

120. Gin H, Rigalleau V, Baillet L, Rabemanantsoa C. Comparison between monofilament, tuning fork and vibration perception tests for screening patients at risk of foot complication. Diabetes & metabolism. 2002;28(6 Pt 1):457-61.

121. An Y, Kang Y, Lee J, Ahn C, Kwon K, Choi C. Blood flow characteristics of diabetic patients with complications detected by optical measurement. Biomedical engineering. 2018;17(25):1-13.

122. Swaminathan A, Vemulapalli S, Patel MR, Jones WS. Lower extremity amputation in peripheral artery disease: improving patient outcomes. Vascular health and risk management. 2014;10:417-24.

123. Uccioli L, Meloni M, Izzo V, Giurato L, Merolla S, Gandini R. Critical limb ischemia: current challenges and future prospects. Vascular health and risk management. 2018;14:63-74.

124. Wu SC, Crews RT, Skratsky M, Overstreet J, Yalla SV, Winder M, et al. Control of lower extremity edema in patients with diabetes: double blind randomized controlled trial assessing the efficacy of mild compression diabetic socks. Diabetes research and clinical practice. 2017;127:35-43.

125. Pomero F, Re R, Meschi M, Montemurro D, Spadafora L, Borretta V, et al. Approach to leg edema. Italian journal of medicine. 2017;11:267-77.

126. McIntosh C, Green T. An overview of lower limb lymphoedema and diabetes. Journal of lymphoedema. 2009;4(1):49-58.

127. Tinken TM, Thijssen DHJ, Hopkins N, Dawson EA, Cable NT, Green DJ. Shear stress mediates endothelial adaptations to exercise training in humans. American heart association. 2010;55(2):312-8.

128. Tschakovsky ME, Shoemaker JK, Hughson R. Vasodilation and muscle pump contribute to immediate exercise hyperemia. The American journal of physiology. 1996;271(4):H1697-701.

129. Tschakovsky ME, Sheriff DD. Immediate exercise hyperemia: contributions of the muscle pump vs. rapid vasodilation. Journal of applied physiology. 2004;97:739-47.

130. Joyner MJ, Casey DP. Regulation of increased blood flow (hyperemia) to muscle during exercise: a hierarchy of competing physiological needs. Physiological reviews. 2015;95:549-601.

131. Gasibat Q, Suwehli W. Determining the benefits of massage mechanisms: a review of literature. Rehabilitation science. 2017;2(3):58-67.

132. Weerapong P, Hume PA, Kolt GS. The mechanisms of massage and effects on performance, muscle recovery and injury prevention. Sports medicine. 2005;35(3):235-56.

133. Kwon HR, Min KW, Ahn HJ, Seok HG, Lee JH, Park GS, et al. Effects of aerobic exercise vs. resistance training on endothelial function in women with type 2 diabetes mellitus. Diabetes and metabolism journal. 2011;35(4):364-73.

134. Gholami F, Nikookheslat S, Salekzamani Y, Boule N, Jafari A. Effect of aerobic training on nerve conduction in men with type 2 diabetes and peripheral neuropathy: A randomized controlled trial. Clinical neurophysiology. 2018;48(4):195-202.

135. Feter N, Freitas M, Gonzales N, Umpierre D, Cardoso R, Rombaldi A. Effects of physical exercise on myelin sheath regeneration: A systematic review and mete-analysis. Science & sports. 2017;33(1):8-21.

136. R.Krygier J, A.J.Heathers J, SaraShahrestania, MareeAbbott, J.Gross J, H.Kemp A. Mindfulness meditation, well-being, and heart rate variability: a preliminary investigation into the impact of intensive Vipassana meditation. International journal of psychophysiology. 2013;89(3):305-13.

137. Guan L, Collet J-P, Yuskiv N, Skippen P, Brant R, Kissoon N. The effect of massage therapy on autonomic activity in critically Ill children. Evidence-based complementary and alternative medicine. 2014;2014(656750):1-8.

138. Lee Y-H, Park BNR, Kimcorresponding SH. The effects of heat and massage application on autonomic nervous system. Yonsei medical journal. 2011;52(6):982-9.

139. Field T, Diego M, Hernandez-Reif M. Moderate pressure is essential for massage therapy effects. International journal of neuroscience. 2010;120:381-5.

140. Gnanadesigan E, Anand P, Balumahendran K, Gnanagurudasan E. Autonomic nervous system and type 2 diabetes mellitus. Asian journal of biomedical and pharmaceutical sciences. 2013;3(18):4-9.

141. Jin RC, Loscalzo J. Vascular nitric oxide: formation and function. Journal of blood medicine. 2010;1:147-62.

142. Calabrese V, Mancuso C, Calvani M, Rizzarelli E, Butterfield DA, Stella AMG. Nitric oxide in the central nervous system: neuroprotection versus neurotoxicity. Neuroscience. 2007;8:766-75.

143. Whangmahapom P, Simmonds P, Whangmahapom B. Factors affecting quality of life of the elderly in Thailand. Asian political science review. 2018;2(2):79-87.

Appendix

APPENDIX 1

RAW DATA

Table 11 Raw Data of Michigan Neuropathy Screening Instrumental (MNSI) score of walking meditation, massage and control groups

Group	No.	Subjective examination	Objective examination	interpretation of peripheral neuropathy
		Point	Point	
Walking meditation	1	4	2.5	yes
	2	6	3	yes
	3	3	3	yes
	4	1	2	yes
	5	1	2	yes
	6	4	2.5	yes
	7	2	2	yes
	8	3	3	yes
Massage	1	5	2.5	yes
	2	3	3	yes
	3	8	3.5	yes
	4	1	3.5	yes
	5	4	2.5	yes
	6	2	3.5	yes
	7	6	4	yes
	8	3	3.5	yes
	9	4	4	yes
Control	1	1	3	yes
	2	3	2	yes
	3	3	3	yes
	4	4	3	yes
	5	5	2	yes
	6	8	4	yes
	7	2	4	yes
	8	2	2	yes
	9	7	2.5	yes

Cut-off score for peripheral neuropathy by subjective examination is > 7 point, cut-off score for peripheral neuropathy by subjective examination is ≥ 2 point

Table 12 Raw data of Subject's Characteristics of walking meditation, massage and control groups

Groups	No.	Characteristics of subjects					
		Gender (Male/Female)	Age	BMI	Waist	ABI	
						Left	Right
Walking Meditation	1	3/5	56	29.41	88	1.07	1.07
	2		51	28.08	97	1.27	1
	3		62	29.74	90	1	1
	4		55	20.22	74	1.07	1
	5		45	20.83	80	1	1
	6		58	29.22	85	1.15	1
	7		56	23.69	85	1.07	1.07
	8		45	24.24	80	1.15	1.07
Massage	1	2/7	55	25.31	89	1.10	1.20
	2		51	23.74	82	.92	.92
	3		69	31.13	100	1	1.07
	4		61	23.88	77	1.08	1
	5		42	23.83	84	.92	.92
	6		42	30.22	90	1	.92
	7		63	22.06	86	.92	1.15
	8		62	24.81	83	1	.92
	9		67	22.48	80	1.18	1
Control	1	2/7	54	27.77	84	1.13	1.13
	2		49	21.23	84	1.07	1.23
	3		58	26.25	94	1.07	1
	4		57	23.81	89	1.09	1.09
	5		61	24.27	82	1	1.07
	6		51	32.00	85	1.15	1.15
	7		50	24.90	80	.93	.93
	8		67	21.71	77	1	1.07
	9		56	24.76	85	1.16	1.08

Table 13 Raw data of Diameter of vessel (mm.) of walking meditation, massage and control groups

Groups	No.	Left Dorsalis Pedis		Right Dorsalis Pedis		Left Posterior Tibialis		Right Posterior Tibialis	
		Pre	Post	Pre	Post	Pre	Post	Pre	Post
Walking	1	1.80	1.30	2.10	1.90	1.80	1.50	1.70	1.80
Meditation	2	1.30	3.40	1.20	3.60	2.40	3.00	2.60	2.90
	3	1.30	1.40	1.30	1.50	1.40	1.50	1.30	1.40
	4	1.80	2.30	1.80	1.90	1.30	1.80	1.50	1.80
	5	1.20	2.50	1.50	2.00	1.20	2.60	1.10	2.10
	6	1.70	1.90	1.90	2.10	1.80	2.20	1.50	1.80
	7	1.30	2.30	1.50	2.10	1.70	2.10	1.70	2.30
	8	1.90	1.90	1.40	2.00	2.00	2.10	1.60	1.90
Massage	1	1.40	1.50	1.70	2.00	1.40	2.20	2.10	1.70
	2	1.50	1.50	1.50	2.10	1.90	1.90	2.10	2.20
	3	1.70	1.90	.70	1.60	1.50	2.20	1.90	2.40
	4	2.00	2.80	1.80	2.70	1.80	2.40	1.50	2.20
	5	1.10	1.90	1.30	2.10	1.30	1.60	1.50	1.70
	6	1.20	1.60	1.00	1.90	1.80	2.30	1.90	2.40
	7	1.20	1.70	1.20	1.40	1.60	2.40	1.90	1.70
	8	1.20	2.40	1.50	2.80	1.30	2.20	1.60	1.90
	9	1.30	1.50	1.40	1.50	1.40	2.80	1.10	1.60
Control	1	2.40	1.50	2.60	1.40	1.90	1.30	2.00	2.10
	2	1.30	1.10	1.50	1.50	1.60	1.50	1.80	1.90
	3	.80	1.10	1.30	1.20	1.20	1.00	1.20	1.00
	4	1.20	1.40	1.60	.90	2.20	1.80	1.80	1.70
	5	1.20	1.40	1.20	1.10	1.80	1.30	1.70	1.60
	6	1.30	1.10	1.60	1.20	.00	.00	.00	.00
	7	1.40	1.30	1.10	1.40	1.40	1.10	1.70	1.40
	8	1.10	1.20	1.40	1.70	1.10	1.60	1.30	1.50
	9	1.10	1.40	1.40	1.20	1.80	1.50	1.50	1.50

Table 14 Raw data of Velocity of flow (cm/sec) of walking meditation, massage and control groups

Groups	No.	Left Dorsalis Pedis		Right Dorsalis Pedis		Left Posterior Tibialis		Right Posterior Tibialis	
		Pre	Post	Pre	Post	Pre	Post	Pre	Post
Walking Meditation	1	13.99	36.90	11.06	16.13	11.26	14.12	8.64	12.89
	2	8.09	8.82	7.24	7.77	6.42	9.13	8.39	6.58
	3	12.52	16.76	23.85	16.72	11.88	11.22	18.97	19.86
	4	7.52	3.23	4.20	5.72	3.19	3.52	4.30	5.94
	5	3.31	2.73	3.72	3.77	3.36	3.30	1.24	3.21
	6	15.02	13.37	21.95	13.35	9.39	12.45	10.28	11.53
	7	10.55	8.68	7.77	8.35	14.43	9.42	4.19	14.66
	8	23.76	11.21	31.18	31.30	11.24	21.85	24.44	30.69
Massage	1	6.78	28.70	7.03	25.44	8.05	29.59	8.79	11.56
	2	10.72	34.55	11.46	45.65	15.27	29.00	7.89	33.63
	3	9.39	18.29	4.57	12.84	6.98	6.61	6.85	10.82
	4	3.81	2.41	5.11	2.63	2.51	3.43	.62	2.93
	5	10.51	8.11	8.77	5.39	10.16	5.35	9.58	3.66
	6	1.45	3.80	1.84	6.89	10.23	20.33	8.28	11.22
	7	1.37	3.95	20.88	25.39	23.56	19.76	19.73	19.35
	8	17.73	13.85	23.69	27.41	7.23	11.32	19.61	19.02
	9	19.52	30.50	21.45	26.75	18.66	13.39	15.87	22.35
Control	1	22.75	14.18	19.00	27.16	20.71	24.07	18.97	26.26
	2	3.68	8.30	9.69	4.48	7.17	11.49	7.55	9.13
	3	7.29	5.74	14.03	9.10	7.18	2.96	7.24	6.66
	4	5.79	7.71	7.77	18.13	5.07	10.73	13.36	12.72
	5	4.26	5.89	9.93	25.69	9.02	25.57	9.61	31.07
	6	11.35	13.51	12.13	12.21	.00	.00	.00	.00
	7	5.28	3.72	3.71	5.68	3.72	1.06	2.93	5.20
	8	32.12	4.76	18.83	4.53	14.13	4.08	19.97	6.31
	9	10.47	24.45	6.38	40.16	5.59	18.47	9.86	22.35

Table 15 Raw data of Peripheral Blood Flow (TTcm^3/s) of walking meditation, massage and control groups

Groups	No.	Left Dorsalis Pedis		Right Dorsalis Pedis		Left Posterior Tibialis		Right Posterior Tibialis	
		Pre	Post	Pre	Post	Pre	Post	Pre	Post
Walking	1	.35	.48	.38	.45	.28	.24	.19	.32
Meditation	2	.10	.80	.08	.79	.29	.64	.44	.43
	3	.16	.25	.31	.29	.18	.19	.25	.30
	4	.19	.13	.10	.16	.04	.08	.07	.15
	5	.03	.13	.06	.11	.03	.17	.01	.11
	6	.34	.37	.62	.46	.23	.47	.18	.29
	7	.13	.36	.13	.28	.32	.32	.09	.60
	8	.67	.31	.47	.98	.35	.75	.49	.86
Massage	1	.10	.50	.15	.79	.12	1.12	.30	.26
	2	.26	.61	.13	1.58	.30	.82	.39	1.27
	3	.21	.51	.01	.25	.12	.25	.19	.48
	4	.11	.14	.12	.15	.06	.15	.01	.11
	5	.09	.22	.11	.18	.13	.10	.16	.08
	6	.01	.07	.01	.19	.26	.84	.23	.50
	7	.01	.08	.23	.39	.47	.89	.55	.43
	8	.20	.62	.41	1.68	.09	.43	.39	.53
	9	.25	.23	.33	.47	.28	1.80	.15	.44
Control	1	1.02	.25	1.00	.41	.58	.31	.59	.90
	2	.04	.07	.17	.07	.14	.20	.19	.23
	3	.03	.05	.18	.10	.08	.02	.08	.05
	4	.06	.11	.15	.11	.19	.27	.33	.28
	5	.04	.09	.11	.24	.22	.33	.21	.62
	6	.12	.12	.24	.13	.00	.00	.00	.00
	7	.08	.04	.03	.08	.05	.01	.06	.08
	8	.30	.05	.28	.10	.13	.01	.26	.11
	9	.09	.37	.07	.45	.14	.32	.17	.39

Table 16 Raw data of Shear Stress of Vessel (s^{-1}) of walking meditation, massage and control groups

Groups	No.	Left Dorsalis Pedis		Right Dorsalis Pedis		Left Posterior Tibialis		Right Posterior Tibialis	
		Pre	Post	Pre	Post	Pre	Post	Pre	Post
Walking Meditation	1	77.72	283.84	52.66	84.89	62.55	94.13	50.82	71.61
	2	62.23	25.94	60.33	21.58	26.75	30.43	32.26	22.68
	3	96.30	119.71	183.46	111.46	84.85	74.80	145.92	141.85
	4	41.77	14.04	23.33	30.10	24.53	19.55	28.66	33.00
	5	27.58	10.92	24.80	18.85	28.00	12.69	11.27	15.28
	6	88.35	70.36	115.52	63.57	52.16	56.59	68.53	64.05
	7	81.15	37.73	51.80	39.76	84.88	44.85	24.64	63.73
	8	125.05	59.00	222.71	156.50	56.20	104.04	152.75	161.52
Massage	1	48.42	191.33	41.35	127.20	57.50	134.50	41.85	68.00
	2	101.80	230.33	52.60	217.38	56.42	152.63	54.57	152.86
	3	55.23	96.26	65.28	80.43	46.53	30.04	36.05	45.08
	4	19.05	8.60	28.38	9.74	13.94	14.29	4.13	13.31
	5	95.54	42.68	67.00	25.66	78.15	33.43	63.86	21.52
	6	12.08	23.75	18.40	36.26	56.83	88.39	43.57	46.75
	7	1.37	23.29	20.88	181.35	23.56	82.33	19.73	113.82
	8	147.75	57.70	157.93	97.89	55.61	51.45	122.56	100.10
	9	150.15	89.26	153.21	178.33	133.28	108.92	144.27	139.68
Control	1	94.79	94.53	73.07	194.00	109.00	185.15	94.85	125.04
	2	28.30	75.45	64.60	29.86	44.81	76.60	41.94	50.72
	3	91.12	52.18	107.92	75.83	59.83	29.60	60.33	66.60
	4	48.25	55.07	48.56	201.44	23.04	59.61	74.22	74.82
	5	91.12	42.07	107.92	233.54	59.83	196.69	60.33	194.18
	6	48.25	122.81	48.56	101.75	23.04	-	74.22	-
	7	35.50	28.61	82.75	40.57	50.11	9.63	56.52	37.14
	8	292.00	39.66	134.50	26.64	128.45	25.50	153.61	42.06
	9	95.18	174.64	53.16	334.66	31.05	123.13	65.73	149.00

Table 17 Raw data of Monofilament testing from 20 points at plantar surface of both feet of walking meditation, massage and control groups

Groups	No.	Numbers of the intact points		Percentage of the intact points	
		Pre	Post	Pre	Post
Walking Meditation	1	13.00	18.00	65.00	90.00
	2	15.00	12.00	75.00	60.00
	3	5.00	16.00	25.00	80.00
	4	17.00	14.00	85.00	70.00
	5	10.00	17.00	50.00	85.00
	6	14.00	11.00	70.00	55.00
	7	18.00	16.00	90.00	80.00
	8	16.00	14.00	80.00	70.00
Massage	1	14.00	17.00	70.00	85.00
	2	13.00	17.00	65.00	85.00
	3	14.00	17.00	70.00	85.00
	4	16.00	19.00	80.00	95.00
	5	13.00	17.00	65.00	85.00
	6	16.00	20.00	80.00	100.00
	7	13.00	16.00	65.00	80.00
	8	15.00	20.00	75.00	100.00
	9	9.00	15.00	45.00	75.00
Control	1	13.00	18.00	65.00	90.00
	2	15.00	12.00	75.00	60.00
	3	5.00	16.00	25.00	80.00
	4	17.00	14.00	85.00	70.00
	5	10.00	17.00	50.00	85.00
	6	14.00	11.00	70.00	55.00
	7	18.00	16.00	90.00	80.00
	8	16.00	14.00	80.00	70.00
	9	17.00	12.00	85.00	60.00

Table 18 Raw data of Vibration test (seconds) of walking meditation, massage and control groups

Groups	No.	Left side		Right side	
		Pre	Post	Pre	Post
Walking Meditation	1	5.60	17.00	6.00	20.66
	2	12.66	16.66	5.33	18.33
	3	9.60	10.00	6.00	11.66
	4	9.00	14.33	5.33	11.00
	5	9.60	10.33	5.30	10.00
	6	8.60	14.00	9.00	13.00
	7	12.33	30.00	5.00	10.66
	8	16.66	18.33	15.00	21.66
Massage	1	10.33	11.00	4.60	14.33
	2	11.33	10.66	4.66	9.33
	3	8.60	11.66	7.00	7.33
	4	10.33	10.66	10.33	10.33
	5	16.33	18.00	14.33	17.66
	6	8.00	11.33	7.30	12.33
	7	17.00	13.00	9.60	14.00
	8	11.33	16.66	12.00	26.66
	9	6.00	9.66	5.30	13.33
Control	1	3.00	6.33	3.00	8.66
	2	6.66	12.33	6.33	13.33
	3	4.00	6.00	4.00	6.00
	4	11.00	16.66	8.60	15.00
	5	16.66	16.33	11.33	13.00
	6	3.60	4.00	2.60	2.00
	7	17.66	18.33	12.66	18.66
	8	17.60	8.66	16.66	7.33
	9	10.33	15.33	9.30	13.00

Table 19 Raw data of Quality of life (points) of walking meditation, massage and control groups

Groups	No.	Point	
		Pre	Post
Walking Meditation	1	85.00	92.00
	2	117.00	111.00
	3	99.00	88.00
	4	92.00	103.00
	5	81.00	94.00
	6	114.00	94.00
	7	112.00	119.00
	8	84.00	89.00
Massage	1	87.00	91.00
	2	93.00	98.00
	3	87.00	93.00
	4	98.00	109.00
	5	85.00	78.00
	6	98.00	90.00
	7	92.00	87.00
	8	97.00	112.00
	9	114.00	102.00
Control	1	98.00	116.00
	2	104.00	97.00
	3	93.00	99.00
	4	117.00	87.00
	5	102.00	77.00
	6	114.00	101.00
	7	94.00	89.00
	8	122.00	123.00
	9	114.00	85.00

APPENDIX 2

DATA COLLECTION FORM

รหัสผู้เข้าร่วมวิจัย_____

คุณคือเพศ ___ หญิง ___ ชาย

ส่วนสูง_____เซนติเมตร น้ำหนัก_____กิโลกรัม

เกิดวันที่_____เดือน_____พศ._____ มีอายุ_____ปี

คุณเป็นเบาหวานมานานเท่าไหร่_____

คุณสูบบุหรี่หรือไม่

___ สูบ ___ เคยสูบ (เลิกแล้ว ประมาณ___เดือน) ___ ไม่สูบ

คุณมีโรคประจำตัวอย่างอื่น/ภาวะอื่น ๆ ร่วมหรือไม่

___ โรคหัวใจ ___ โรคเกี่ยวกับระบบประสาท

___ โรคมะเร็ง ___ โรคตับวาย

___ โรคไตวาย ___ แผลที่เท้า

___ กระดูกหัก ___ มีการตัดเท้าหรือตัดขา

___ ความดันโลหิตสูงชนิดควบคุมไม่ได้ ___ ภาวะกระดูกพรุนรุนแรง

___ โรคอื่น ๆ ที่แพทย์ห้ามเดินลงน้ำหนัก ___ ภาวะหลอดเลือดดำอักเสบ

___ ภาวะหลอดเลือดดำอุดตัน ___ ภาวะหลอดเลือดขอด

___ อาการติดเชื้อที่ผิวหนัง

คุณออกกำลังกายบ่อยแค่ไหนใน 6 เดือนที่ผ่านมา

___ ไม่เคยออกกำลังกาย___ ออกกำลังกาย (___นาที/ครั้ง, ___ครั้ง/สัปดาห์)

คุณเคยเข้าร่วมโครงการวิจัยอื่น ๆ ใน 6 เดือนที่ผ่านมาหรือไม่

___ ไม่เคย ___ เคย คือ _____

คุณมีภาวะแทรกซ้อนจากโรคเบาหวานหรือไม่

___ ไม่มี ___ มี คือ _____

คุณมีข้อจำกัดในการออกกำลังกายหรือไม่

___ ไม่มี ___ มี คือ _____

APPENDIX 3

MICHIGAN NEUROPATHY SCREENING INSTRUMENTAL

History (To be completed by the person with diabetes)

กรุณาสละเวลาประมาณ 2-3 นาที เพื่อให้ข้อมูลเกี่ยวกับความรู้สึกที่ชาและเท้าของคุณ โดยเลือกคำตอบ "ใช่" หรือ "ไม่ใช่" ตามอาการและความรู้สึกของคุณ ขอขอบคุณมา ณ ที่นี้

	คำถาม	ใช่	ไม่ใช่
1.	คุณรู้สึกชาที่ขา และ/หรือเท้าหรือไม่ ?		
2.	คุณเคยหรือสึกปวดและแสบปวดร้อนที่ขา และ/หรือเท้าหรือไม่ ?		
3.	เวลาถูกสัมผัสบริเวณเท้าคุณรู้สึกไวเป็นพิเศษหรือไม่ ?		
4.	คุณเป็นตะคริวบริเวณขา และ/หรือเท้าหรือไม่ ?		
5.	คุณเคนรู้สึกเหมือนเข็มทิ่มแทงที่บริเวณขา และ/หรือเท้าหรือไม่ ?		
6.	คุณรู้สึกเจ็บที่ผิวหนังเวลาโดนกับผ้าปูที่นอนหรือไม่ ?		
7.	เวลาคุณอาบน้ำ คุณบอกได้หรือไม่ว่าเป็นน้ำร้อน หรือน้ำเย็น ?		
8.	คุณเคยมีแผลเปิดที่เท้าหรือไม่ ?		
9.	แพทย์เคยบอกว่าคุณมีอาการปลายประสาทเสื่อจากเบาหวาน ?		
10.	คุณรู้สึกอ่อนแรงเกือบตลอดเวลาหรือไม่ ?		
11.	อาการไม่ปกติของคุณจะหนักขึ้นช่วงกลางคือหรือไม่ ?		
12.	คุณเจ็บเท้าเวลาเดินหรือไม่ ?		
13.	คุณรับรู้ความรู้สึกที่เท้าเวลาเดินหรือไม่ ?		
14.	ผิวหนังที่เท้าของคุณแตกหรือไม่ ?		
15.	คุณเคยถูกตัดเท้าหรือนิ้วเท้าหรือไม่ ?		

Physical Assessment (To be completed by health professional)

1. Appearance of Feet

	Right	Left
a. Normal	☐ 0 Yes ☐ 1 No	Normal ☐ 0 Yes ☐ 1 No
b. If no, check all that apply:		If no, check all that apply:
Deformities	☐	Deformities ☐
Dry skin, callus	☐	Dry skin, callus ☐
Infection	☐	Infection ☐
Fissure	☐	Fissure ☐
Other	☐	Other ☐
specify: _____		specify: _____

	Right			Left		
2. Ulceration	Absent ☐ 0	Present ☐ 1		Absent ☐ 0	Present ☐ 1	
3. Ankle Reflexes	Present ☐ 0	Present/ Reinforcement ☐ 0.5	Absent ☐ 1	Present ☐ 0	Present/ Reinforcement ☐ 0.5	Absent ☐ 1
4. Vibration perception at great toe	Present ☐ 0	Decreased ☐ 0.5	Absent ☐ 1	Present ☐ 0	Decreased ☐ 0.5	Absent ☐ 1
5. Monofilament	Normal ☐ 0	Reduced ☐ 0.5	Absent ☐ 1	Normal ☐ 0	Reduced ☐ 0.5	Absent ☐ 1

Signature_____ Total score_____/10 point

APPENDIX 4

ANKLE BRACHIAL INDEX

Data		Results		
ABI				
SBP	Results		SBP LW = _____ =_____	
Lt. Brachial			SBP UP	
Rt. Brachial		✓	Level of ABI	Results
Lt. Dorsalispedis			More than 1.30	Poorly compressible vessel
Rt. Dorsalispedis			0.91-1.30	Normal
Lt. Posterior tibialis			0.7-0.9	Mild occlusion
Rt. Posterior tibialis			0.4-0.69	Moderate occlusion
			Less than 0.40	Severe occlusion

APPENDIX 5

DOPPLER ULTRASOUND SCANNING

TAMAX

	Left Posterior tibialis	Left Dorsalis pedis	Right Posterior tibialis	Right Dorsalis pedis
1				
2				
3				
4				
5				
6				
7				
8				
9				
10				
Mean				

Diameter

	Left Posterior tibialis	Left Dorsalis pedis	Right Posterior tibialis	Right Dorsalis pedis
1				
2				
3				
Mean				

PERIPHERAL BLOOD CIRCULATION

Variable from Doppler Ultrasound	Left		Right	
	Dorsalis Pedis	Posterior Tibilis	Dorsalis Pedis	Posterior Tibilis
● Peripheral Blood Flow				
● Diameter of vessel flow				
● Blood velocity				
● Shear stress (blood velocity/vascular diameter)				

APPENDIX 6

WORLD HEALTH ORGANIZATION QUALITY OF LIFE – BREF THAI

คำชี้แจง: ข้อคำถามต่อไปนี้จะถามถึงประสบการณ์อย่างใดอย่างหนึ่งของท่านในช่วง 2 สัปดาห์ที่ผ่านมาให้ท่านสำรวจตัวท่านเองและประเมินเหตุการณ์หรือความรู้สึกของท่านแล้วทำเครื่องหมายถูกลงในช่องคำตอบที่เหมาะสมและเป็นจริงกับตัวท่านมากที่สุดโดยคำตอบมี 5 ตัวเลือกคือ

ไม่เลย หมายถึง ท่านไม่มีความรู้สึกเช่นนั้นเลยรู้สึกไม่พอใจมากหรือรู้สึกแย่มาก

เล็กน้อย หมายถึง ท่านมีความรู้สึกเช่นนั้นนาน ๆ ครั้งรู้สึกเช่นนั้นเล็กน้อยรู้สึกไม่พอใจหรือรู้สึกแย่

ปานกลาง หมายถึง ท่านมีความรู้สึกเช่นนั้นปานกลางรู้สึกพอใจระดับกลาง ๆ หรือรู้สึกแย่ระดับกลางๆ

มาก หมายถึง ท่านมีความรู้สึกเช่นนั้นบ่อย ๆ รู้สึกพอใจหรือรู้สึกดี

มากที่สุด หมายถึง ท่านมีความรู้สึกเช่นนั้นเสมอรู้สึกเช่นนั้นมากที่สุดหรือรู้สึกว่าสมบูรณ์รู้สึกพอใจมากรู้สึกดีมาก

ข้อที่	ในช่วง 2 สัปดาห์ที่ผ่านมา	ไม่เลย	เล็กน้อย	ปานกลาง	มาก	มากที่สุด
1	ท่านพอใจกับสุขภาพของท่านในตอนนี้เพียงใด					
2	การเจ็บปวดตามร่างกาย เช่น ปวดหัว ปวดท้อง ปวดตามตัว ทำให้ท่านไม่สามารถทำในสิ่งที่ต้องการมากน้อยเพียงใด					
3	ท่านมีกำลังเพียงพอที่จะทำสิ่งต่าง ๆ ในแต่ละวันไหม (ทั้งเรื่องงาน หรือการดำเนินชีวิตประจำวัน)					
4	ท่านพอใจกับการนอนหลับของท่านมากน้อยเพียงใด					
5	ท่านรู้สึกพึงพอใจในชีวิต (เช่น มีความสุข ความสงบมีความหวัง) มากน้อยเพียงใด					
6	ท่านมีสมาธิในการทำงานต่าง ๆ ดีเพียงใด					
7	ท่านรู้สึกพอใจในตนเองมากน้อยแค่ไหน					
8	ท่านยอมรับรูปร่างหน้าตาของตัวเองได้ไหม					
9	ท่านมีความรู้สึกไม่ดี เช่น รู้สึกเหงา เศร้า หดหู่ สิ้นหวัง วิตกกังวล บ่อยแค่ไหน					
10	ท่านรู้สึกพอใจมากน้อยแค่ไหนที่สามารถทำอะไร ๆ ผ่านไปได้ในแต่ละวัน					

ข้อที่	ในช่วง 2 สัปดาห์ที่ผ่านมา	ไม่เลย	เล็กน้อย	ปานกลาง	มาก	มากที่สุด
11	ท่านจำเป็นต้องไปรับการรักษาพยาบาลมากน้อยเพียงใดเพื่อที่จะทำงานหรือมีชีวิตอยู่ไปได้ในแต่ละวัน					
12	ท่านพอใจกับความสามารถในการทำงานได้อย่างที่เคยทำมามากน้อยเพียงใด					
13	ท่านพอใจต่อการผูกมิตรหรือเข้ากับคนอื่น อย่างที่ผ่านมาแค่ไหน					
14	ท่านพอใจกับการช่วยเหลือที่เคยได้รับจากเพื่อน ๆ แค่ไหน					
15	ท่านรู้สึกว่าชีวิตมีความมั่นคงปลอดภัยดีไหมในแต่ละวัน					
16	ท่านพอใจกับสภาพบ้านเรือนที่อยู่ตอนนี้มากน้อยเพียงใด					
17	ท่านมีเงินพอใช้จ่ายตามความจำเป็นมากน้อยเพียงใด					
18	ท่านพอใจที่จะสามารถไปใช้บริการสาธารณสุขได้ตามความจำเป็นเพียงใด					
19	ท่านได้รู้เรื่องราวข่าวสารที่จำเป็นในชีวิตแต่ละวันมากน้อยเพียงใด					
20	ท่านมีโอกาสได้พักผ่อนคลายเครียดมากน้อยเพียงใด					
21	สภาพแวดล้อมดีต่อสุขภาพของท่านมากน้อยเพียงใด					
22	ท่านพอใจกับการเดินทางไปไหนมาไหนของท่าน (หมายถึงการคมนาคม) มากน้อยเพียงใด					
23	ท่านรู้สึกว่าชีวิตท่านมีความหมายมากน้อยแค่ไหน					
24	ท่านสามารถไปไหนมาไหนด้วยตนเองได้ดีเพียงใด					
25	ท่านพอใจในชีวิตทางเพศของท่านแค่ไหน?(ชีวิตทางเพศหมายถึง เมื่อเกิดความรู้สึกทางเพศขึ้นแล้วท่าน มีวิธีจัดการทำให้ผ่อนคลายลงได้ รวมถึง การช่วยตัวเองหรือการมีเพศสัมพันธ์)					
26	ท่านคิดว่าท่านมีคุณภาพชีวิต (ชีวิตความเป็นอยู่) อยู่ในระดับใด					

APPENDIX 7

RESEARCH ETHICAL APPROVEMENT

MF4Version1:15/7/2556

ใบรับรองจริยธรรมการวิจัยของข้อเสนอการวิจัย

เอกสารข้อมูลคำอธิบายสำหรับผู้เข้าร่วมการวิจัยและใบยินยอม

หมายเลขข้อเสนอการวิจัย SWUEC- 160/61E

ข้อเสนอการวิจัยนี้และเอกสารประกอบของข้อเสนอการวิจัยตามรายการแสดงด้านล่าง ได้รับการพิจารณาจากคณะกรรมการสำหรับพิจารณาโครงการวิจัยที่ทำในมนุษย์ของมหาวิทยาลัยศรีนครินทรวิโรฒแล้ว คณะกรรมการฯ มีความเห็นว่าข้อเสนอการวิจัยที่ระดำเนินการมีความสอดคล้องกับหลักจริยธรรมสากล ตลอดจนกฎหมาย ข้อบังคับและข้อกำหนดภายในประเทศ จึงเห็นสมควรให้ดำเนินการวิจัยตามข้อเสนอการวิจัยนี้ได้

ชื่อโครงการวิจัยเรื่อง: ผลเปรียบเทียบระหว่างการเล็งจงกรมและการนวดต่อการไหลเวียนเลือดส่วนปลายและอาการเส้นประสาทส่วนปลายเสื่อมในผู้ที่มีภาวะเส้นประสาทส่วนปลายเสื่อมจากเบาหวานชนิดที่ 2

ชื่อผู้วิจัยหลัก: นางสาวพิชญา สุขไพบูลย์

สังกัด: คณะกายภาพบำบัด มหาวิทยาลัยศรีนครินทรวิโรฒ

เอกสารที่รับรอง:
1. แบบเสนอโครงการวิจัย
2. โครงร่างการวิจัย
3. เอกสารชี้แจงผู้เข้าร่วมการวิจัย
4. หนังสือให้ความยินยอมเข้าร่วมโครงการวิจัย

เอกสารที่พิจารณาทบทวน

1.	แบบเสนอโครงการวิจัย	ฉบับที่ 2 วันเดือนปี 20 ก.ย. 2561
2.	โครงร่างการวิจัย	ฉบับที่ 2 วันเดือนปี 20 ก.ย. 2561
3.	เอกสารชี้แจงผู้เข้าร่วมการวิจัย	ฉบับที่ 2 วันเดือนปี 20 ก.ย. 2561
4.	หนังสือให้ความยินยอมเข้าร่วมโครงการวิจัย	ฉบับที่ 2 วันเดือนปี 20 ก.ย. 2561

(ลงชื่อ).....

(นายปิยชาติ บุญเพิ่ม)

กรรมการและผู้ช่วยเลขานุการคณะกรรมการจริยธรรมสำหรับพิจารณาโครงการวิจัยที่ทำในมนุษย์

(ลงชื่อ).....

(แพทย์หญิงสุรีพร ภัทรสุวรรณ)

ประธานคณะกรรมการจริยธรรมสำหรับพิจารณาโครงการวิจัยที่ทำในมนุษย์

หมายเลขรับรอง : SWUEC/E-160/2561

วันที่ให้การรับรอง : 26/09/2561

วันหมดอายุใบรับรอง : 26/09/2562

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