Scientific Foundation SPIROSKI, Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences. 2020 Feb 05; 8(E):1-6.
https://doi.org/10.3889/oamjms.2020.4261
eISSN: 1857-9655
Category: *E - Public Health*
Section: *Public Health Disease Control*

Effects of Lower Extremity Exercises on Ankle-Brachial Index Values among Type 2 Diabetes Mellitus Patients

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Edited by: Sasho Stoleski
Citation: Suza DE, Hijriana I, Ariani Y, Hariati H. Effects of Lower Extremity Exercises on Ankle-Brachial Index Values among Type 2 Diabetes Mellitus Patients. Open Access Maced J Med Sci. 2020 Feb 05; 8(E):1-6. https://doi.org/10.3889/oamjms.2020.4261
Keywords: Ankle-brachial index; Lower extremity exercises; Type 2 diabetes mellitus patients
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Received: 05-Jan-2020
Revised: 15-Jan-2020
Accepted: 24-Jan-2020

Funding: This research did not receive any financial support
Competing Interests: The authors have declared that no competing interests exist

Abstract

BACKGROUND: Diabetes mellitus (DM) is caused by more complications. One complication that often occurs is peripheral vascular disease. An early diagnostic to assess peripheral vascular disease is very important; measurement of the ankle-brachial index (ABI) is one of the non-invasive measures to assess the peripheral vascular disease risk in primary care and to identify the effect of lower extremity joint movement exercises on ABI values in Type 2 DM (T2DM) patients.

AIM: The aimed to determine the effect of lower extremity on Ankle-Brachial Index Value among Type 2 Diabetes Mellitus Patients.

METHODS: The method used was a quasi-experimental pre- and post-test group design without a control group. The sample was 35 T2DM patients using a consecutive sampling technique. The interventions given were lower extremity joint movement exercises which were performed actively once a day, with each movement ten repetitions and for 4 weeks of observation.

RESULTS: There was a significant difference between pre and post the lower extremity joint movement intervention toward the value of the left limb ABI with mean pre 0.93 and post 1.02 (p = 0.00) and the value of the ABI in the right limb ABI with mean pre 0.92 and post 1.01 (p = 0.00) in patients suffering from DM under 10 years. There was a significant difference between pre and post the lower extremity joint movement intervention toward the value of the left limb ABI with mean pre 0.89 and post 1.98 (p = 0.00) and the value of the ABI in the right limb ABI with mean pre 0.88 and post 0.96 (p = 0.00) in patients suffering from DM over 10 years.

CONCLUSION: Joint exercise can improve blood flow throughout the body, so it is important for T2DM patients to do regular joint exercise so that it is beneficial in improving health and preventing disability.

Introduction

Diabetes mellitus (DM) is a risk factor for cardiovascular disease and has been linked to mortality 2–4 times higher [1]. The International Diabetes Federation reported that (1) an estimated 463 million adults aged with diabetes and by 2045 will increase to 700 million, (2) the proportion of people with type 2 diabetes has increased in most countries, (3) 79% of people aged adults with diabetes live in low- and middle-income countries, (4) the largest number of people with diabetes are in the range of 40–59 years, (5) one in two people with undiagnosed diabetes, (6) diabetes causes 4.2 million deaths, and (7) 374 million people are at risk of developing type 2 diabetes [2].

The World Health Organization predicts a significant increase estimated of diabetic people in the coming years; in Indonesia, the number of people with DM was estimated to increase from 8.4 to 21.3 million in 2030 [3]. A report of Basic Health Research showed that the number of DM in Indonesia urban areas for ages over 15 years was 2%, while the prevalence in Sumatra Utara was 2% which had previously increased by 0.2% from 2013. Complications from diabetes are a significant cause of morbidity and mortality [4].

Diabetes complications usually develop gradually and occur when diabetes is not managed properly. Some complications in DM often occur in patients in Asian, namely, cardiovascular disease and kidney damage [5]. Type 2 DM (T2DM) sufferers are prone to amputation due to complications from ulcers that do not heal. Uncontrolled blood glucose levels in a long time can cause nerve damage, one of which is in the legs. The peripheral arterial disease was the most risk factor for amputation caused by high blood glucose levels which cause nerve damage to the legs and blood vessels [6].

An early diagnostic is very important to assess the peripheral arterial disease. Ankle-brachial index (ABI) measurement is one of the non-invasive measures to assess the cardiovascular disease risk in health care [7]. ABI functions as a measurement of systemic atherosclerosis and is thus related to atherosclerosis risk factors and the prevalence of cardiovascular disease and other vascular diseases. Several studies have evaluated the association of ABI with cardiovascular disease risk factors and are directly

related to DM. ABI was an atherosclerosis severity measure on the legs and a risk independent indicator of atherothrombotic in other blood vessels [8].

Based on the previous studies have shown that joint exercise can help prevent and speed up the onset of T2DM and control blood sugar levels. Research conducted by Hammad *et al*. revealed that the intervention group with the post-ABI exercises provides clinical and prognostic information for diabetes sufferers who experience normal and abnormal resting ABI [9]. Gibbs, Dobrosielski, Althouse, and Stewart identified the effect of joint exercise on ABI. This study found that a significant increase in ABI value at intervention group, an increase in diastole so that exercise has a very important role in preventing the occurrence of peripheral arterial disease especially T2DM patients [10]. Shanmugan and Thenmozhi revealed that there was a significant increase in ABI scores in preventing peripheral arterial disease in DM people at the intervention group after performing Allen Buerger exercise $p < 0.05$ and there was a significant relationship between duration of DM and ABI pre-test scores [11]. Francia *et al*. conducted that a sports therapy program in patients with DM who were monitored for 12 weeks significantly improves joint movement, muscle ability, and speed walking in patients [12]. Then, reducing diabetic foot pathogenic factors and potentially preventing disability. Kumari *et al*. found that the average post-intervention ABI score at the intervention group was significantly higher than the control group. Post-intervention capillary refill time was lower in the intervention group than the control group [13]. Buerger Allen exercise is effective increasing foot perfusion in terms of ABI scores, reducing capillary filling time. Patients who significantly show ABI positive or symptomatic findings are advised to do joint or exercise latency [14]. Claudication pain is an obstacle for patients with DM afraid to do joint exercise. A qualitative study shows that the obstacles of diabetic patients performing joint exercise are due to the low level of patient education, leg pain, and lack of knowledge about joint exercise benefits, and information [15].

Joint exercise has been considered as an effort to increase insulin sensitivity, facilitate glucose absorption and help in controlling blood glucose in the treatment of DM, but in fact, DM sufferers still rarely do joint exercise, so the development of further complications continues to increase. Hawkins *et al*. suggested that low joint activity is related to changes in ABI values so that the consequences will increase the risk of cardiovascular events and death [16]. These few studies are investigating the effects of lower extremities joint movement among T2DM patients. Based on the above problem, the problem formulation in this study is how does the effect of lower extremity joint movement exercise on changing ABI values among T2DM patients?

Materials and Methods

Research design

The quantitative research design used to determine the quasi-experimental pre- and post-test design without a control group. The design aimed to determine the effect of actions on desired outcomes in the intervention group.

Sample and sample size

The sample was T2DM patients. The sample size was determined from the sample to mean in the previous studies; it was found that the level of significance (α): 0.5; effect size: 0.70; and power: 0.80. The sample in this study amounted to 33 to prevent drop out then added 10% so that the sample became 35 respondents for intervention without a control group. The sampling technique was carried out convenience sampling. Inclusion criteria were: (1) T2DM patients >3 years, (2) willing to be a respondent, (3) cooperative, and (4) never received the same intervention from other researchers and health professionals. The exclusion criteria were: (1) Severe pain in the joints, (2) patients in the presence of diseases or disorders that can increase energy requirements and harm such as cardiovascular and respiratory diseases, and (3) had macrovascular complications.

Instruments

The instruments used were: (1) A format for assessing patient characteristics, consisting of age, sex, education, occupation, length of DM, and history of the family with DM, (2) ABI instrument consisting of ABI assessment using ABN brand sphygmomanometer, and doppler vascular Hi-dop BT-200V. Probes with a frequency range of 8 MHz for normal foot circumference, 5 MHz for obese or edema foot circumference, Probe 4 MHz for deep vein thrombosis measurement, and (3) range of motion (ROM) procedure. The preparation of the ROM module is based on Potter and Perry [17], Berman *et al*. [18], and Ohio Rehabilitation Services Department [19]. The instrument used to measure ABI was the EBN tensile aneroid and 8 MHz Doppler Probe. The tension meter used in this study was still original and has never been used before, while the 8 MHz Doppler Probe has been calibrated.

Intervention

The interventions carried out were joint exercises. The lower extremity joint movement exercises consist of several joint movements, namely, the knee joint, ankle, foot, and toes, with the position of movements which include the knee joint (flexion and

extension), ankle (dorsal flexion and plantar flexion), foot (inversion and eversion), and toes (flexion, extension, abduction, and adduction). The exercise was performed actively once every day with each movement of ten repetitions for 4 weeks.

Data collection

The preparation phase for data collection was performed through administration procedures by submitting an application for a research permit to the Nursing Faculty of Universitas Sumatra Utara and submitting a request for a research location permit to the director of a government hospital. After obtaining permission, the researcher introduced herself to prospective respondents and explained the aimed and procedures intervention. After the explanation was complete, the researcher asked the respondent's willingness to sign an informed consent as proof of willingness to participate during the research process. The research was assisted by three research assistants with the latest educational background of the nursing profession who were declared competent in assisting research by medical surgical nursing specialists.

The process of this study consists of several stages:

- Pre-test
  Before conducting the intervention, the researcher first filled in patient characteristics assessment format and recorded the patient's full address, and the research assistant makes a time contract with the respondent for a home visit whose purpose was to measure the ABI value and provides exercise intervention for lower extremity joint movements. In the 1st week, researchers and research assistants measured brachial systolic pressure and dorsalis pedis/ posterior tibial is systolic pressure using an aneroid type EBN brand Sphygmomanometer and BT-200V Doppler Hi-dop to determine ABI and then document it in the tabulation datasheet.
- Intervention
  After the respondent was given a pretest, the next step was to provide joint exercise training interventions. The lower extremity joint movement exercises consisted of several joint movements, namely, the knee joint, ankle, foot, and toes, with the position of movements which include the knee joint (flexion and extension), ankle (dorsal flexion and plantar flexion), foot (inversion and eversion), and toes (flexion, extension, abduction, and adduction). The exercise is done actively once every day, with each movement of ten repetitions, for 4 weeks. Respondents were given a module as the next guide for respondents at home. Furthermore, researchers and research assistants meet respondents again by home visit every day. This home visit was carried out for 4 weeks to observe respondents in the intervening ROM based on modules that have been previously divided.
- Post-test
  The evaluation was given in 5 weeks after the intervention was carried out. Re-measure brachial systolic pressure and dorsal pedis/ posterior tibialis systolic pressure to determine ABI values.

Data analysis

In the study using the Wilcoxon Signed-Ranks test, $p < 0.00$, which was less than $\alpha = 0.05$ so that it could be concluded that there were differences in ABI values before and after lower extremity joint movement exercises.

Ethical consideration

Ethical considerations related to this research were carried out after obtaining permission from the Ethics Committee of Nursing Faculty, Universitas Sumatra Utara.

Results

Characteristic of respondents

In Table 1, the proportion of females was higher than males 68.60%. The majority of patients were >65 years old 34.30%. The majority of the family had a history with DM 77.10%.

Table 1: Characteristic of respondents (n=35)

Characteristic	Frequency	Percentage
Gender		
Male	11	31.40
Female	24	68.60
Age (years)		
36–45	1	2.90
46–55	6	17.10
56–65	7	20.00
>65	12	34.30
Family's history with DM		
Yes	27	77.10
No	8	22.90

DM: Diabetes mellitus.

The pre-test value of the ABI

In Table 2, the pre-test value of the ABI according to the long history of DM <10 years among the left and right extremity had a similar.

Table 2: The pre-test value of ABI according to the long history of DM <10 years

Variable	Mean	Median	SD	Min-Max
Left extremity	0.93	0.89	0.06	0.85–1.12
Right extremity	0.92	0.89	0.07	0.85–1.12

ABI: Ankle-brachial index, DM: Diabetes mellitus.

In Table 3, the pre-test value of the ABI according to the long history of DM >10 years was similar.

Table 3: The pre-test value of ABI according to the long history of DM >10 years

Variable	Mean	Median	SD	Min-Max
Left extremity	0.89	0.87	0.07	0.83–0.93
Right extremity	0.88	0.86	0.02	0.83–0.93

ABI: Ankle-brachial index, DM: Diabetes mellitus.

The post-test value of the ABI

In Table 4, the post-test value of ABI according to the long history of DM <10 years was similar.

Table 4: The post-test value of ABI according to the long history of DM <10 years

Variable	Mean	Median	SD	Min-Max
Left extremity	1.02	1.00	0.05	0.96–1.12
Right extremity	1.01	1.00	0.05	0.92–1.12

ABI: Ankle-brachial index, DM: Diabetes mellitus.

In Table 5, the post-test value of ABI according to the long history of DM >10 years was similar.

Table 5: The post-test value of ABI according to the long history of DM >10 years

Variable	Mean	Median	SD	Min-Max
Left extremity	0.98	0.98	0.04	0.89–1.04
Right extremity	0.96	0.96	0.04	0.89–1.04

ABI: Ankle-brachial index, DM: Diabetes mellitus.

The difference in ABI values before and after extremity joint movements

In Table 6, the results of statistical tests used the Wilcoxon Signed-Ranks test, which shows that there was a significant difference between pre and post the intervention of the lower extremity joint movement on left limb ABI value (p = 0.00) and the ABI value on the right limb (p = 0.00) in patients suffering from DM under 10 years. In the left limb and right limb of patients suffering from DM over 10 years, there was a significant difference of ABI value between pre and post the intervention of lower extremity joint movement (p = 0.00).

Table 6: The difference in ankle-brachial index values before and after lower extremity joint movements based on time suffered from DM

Ankle-brachial index	Mean		p-value
	Pretest	Posttest	
Left extremity (<10 years)	0.93	1.02	0.00
Right extremity (<10 years)	0.92	1.01	0.00
Left extremity (>10 years)	0.89	0.98	0.00
Right extremity (>10 years)	0.88	0.96	0.00

ABI: Ankle-brachial index, DM: Diabetes mellitus.

Discussion

The ABI value refers to the length of suffering from DM before joint movement exercises and all respondents have moderate circulation disorders in the upper and lower extremities. Rosenson, Fioretto, and Dotson stated that long-suffering from DM and glycemic control, increased HbA1c, was associated with an increased risk of cardiovascular morbidity and mortality and decreased ABI values each decrease in HbA1c was followed by a significant decrease in microvascular and macrovascular complications. Increased glucose in the blood causes increased blood viscosity, so blood flow was reduced and an increase in platelet aggregation will spur the formation of microthrombus and microvascular blockage; this was associated with the development of microvascular and macrovascular complications among DM people [20].

Many factors could affect the value of ABI, research conducted by Hoe *et al*., there was a relationship between decreased ABI with age (mean = 54.9%), duration of diabetes, history of hypertension, increased HbA1c, serum creatinine, and history of retinopathy [21]. Increased HbA1c and poor glucose control were risk factors for complications of vascular peripheral disease. Blood viscosity depends on the presence of blood cells and plasma proteins including nutrients such as glucose, amino acids, fats, and waste products such as keratin and bilirubin. The state of hyperglycemia that lasts a long time in patients with T2DM causes pathological changes in blood vessels, endothelial cell dysfunction and abnormalities of smooth muscle cells was a consequence of a long period of hyperglycemia. This results in a decrease in the vasodilator in the endothelium, resulting in narrowing the lumen of blood vessels.

Jude, eleftheriadou, and tentolouris stated that vascular disease in diabetic patients occurs due to angiopathy and abnormal metabolic conditions that affect arteries. Abnormal metabolism that greatly affects the occurrence of chronic hyperglycemia, insulin resistance, and dyslipidemia makes arteries susceptible to atherosclerosis which will continue in blood vessel disease in T2DM patients, namely, microvascular and macrovascular. Microangiopathy was characterized by the involvement of blood vessels at the level of arterioles and capillaries which causes thickening and makes it more permeable to plasma solutes [22].

The longer a person experiences T2DM, the greater the risk of complications. This research was in line with Chen *et al*. study that stated that there was a relationship between the length of suffering from T2DM to the value of ABI, T2DM patients over 10 years are more at developing peripheral arterial disease risk [23]. The length of time a person suffers from T2DM can aggravate complications of T2DM due to an increase in blood glucose levels that long lead to damage to the lumen of blood vessels so that more and more tissue damage occurs and one of them was impaired circulation of blood vessels. Blood glucose control was very important in decrease microvascular complications risk among T2DM patients; the epidemiological analysis showed that long-term hyperglycemia was also associated with macrovascular complications [24].

This study found that there was an increase in ABI value after the lower extremity joint movement exercises. This was in line with research conducted by Barone Gibbs *et al*. in 140 patients with T2DM without complications given intervention in the form of aerobic exercise showed that there was a significant change in the value of ABI, where the exercise resulted in an increase in ABI value accompanied by a decrease in HbA1c and was shown to increase endothelial function so that blood flow to the peripheral to be better. Smooth blood circulation conditions will inhibit thickening of the capillary membrane, increasing the size and number of capillary endothelial cells, so that the lumen of the blood vessels remains adequate [11].

Joint exercise similar to lower extremity joint movement was a stimulation of the gastrocnemius muscle; effective contraction of the calf muscles can increase calf muscle strength and calf pumping muscles which will facilitate the venous return and can improve circulation of the vessels venous blood. Joint exercise has been proven to increase the efficiency of calf muscle pumps. O'Brien *et al*. stated that home-based exercises such as the ROM ankle were very effective and had an effect on healing ulcer veins; this was related to the function of the calf muscle pump. The inactive calf muscle pump was considered as one of the most causes of chronic venous insufficiency which leads to leg veins ulceration [25].

Joint motion training was an isotonic exercise that was performed to mobilize all joints through movement with full reach and was one of the nursing interventions to overcome the nursing problem of joint mobility impairment [26]. Berman *et al*. stated that isotonic exercises such as active ROM exercises can increase muscle tone, mass, and strength while maintaining joint flexibility and circulation. During isotonic exercise, heart rate, and cardiac output increase to increasing blood flow of the body. The joint exercise that was carried out routinely and continuously in patients with diabetes can prevent complications in the future. Lower extremity joint movement exercises, such as diabetic foot exercises, can affect vascularity of the lower extremities and maintain normal ABI values [18].

Strength of the study were (1) in the measurement of value ABI, the procedures performed were based on procedures established by Wound, Ostomy, and Continence Nurse Society so as to produce a value accurate, (2) researchers have been trained by experts in measuring ABI values, and (3) determine the sample with power analysis. Limitation in this study was that this study did not examine blood glucose levels, HbA1c, triglycerides, and cholesterol, did not use a control group as a comparison, and did not specify the sample with a decrease in ABI values in T2DM patients with different cases.

Conclusions

Exercise of the lower extremity movement can increase the value of ABI. It is important for DM patients to know early on the measurement of ABI values to assess the presence of impaired peripheral vascular function and to exercise regularly to improve blood flow to improve health and prevent disability.

References

1. Raghavan S, Vassy JL, Ho YL, Song RJ, Gagnon DR, Cho K, *et al*. Diabetes mellitus-related all-cause and cardiovascular mortality in a national cohort of adults. J Am Heart Assoc. 2019;8(4):e011295. https://doi.org/10.1161/jaha.118.011295
2. International Diabetic Federation. IDF Diabetes Atlas. 6th ed. Available from: https://www.idf.org/e-library/epidemiology-research/diabetes-atlas/19-atlas-6th-edition.html
3. Riskesdas K. Hasil Utama Riset Kesehatan Dasar RISKESDAS; 2018. p. 1-200. Available from: https://www.depkes.go.id/resources/download/info-terkini/materi_rakorpop_2018/Hasil%20Riskesdas%202018.pdf
4. Papatheodorou K, Banach M, Bekiari E, Rizzo M, Edmonds M. Complications of Diabetes 2017. J Diabetes Res. 2018;2018:3086167. https://doi.org/10.1155/2018/3086167
   PMid:29713648 PMCid:PMC5866895
5. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of Type 2 diabetes mellitus and its complications. Nat Rev Endocrinol. 2018;14(2):88-98. https://doi.org/10.1038/nrendo.2017.151
   PMid:29219149
6. Mehraj DM. A review of Wagner classification and current concepts in the management of diabetic foot. Int J Orthop Sci. 2018;4(1n):933-5. https://doi.org/10.22271/ortho.2018.v4.i1n.133
7. Maggi DL, Dal Piva de Quadros LR, de Oliveira Azzolin K, Goldmeier S. Ankle-brachial index: Nurses strategy to cardiovascular disease risk factors identification. Rev Esc Enferm USP. 2014;48(2):223-7. https://doi.org/10.1590/s0080-623420140000200004
   PMid:24918879
8. 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. Circulation. 2012;126(24):2890-909. https://doi.org/10.1161/cir.0b013e318276fbcb
   PMid:23159553
9. Hammad TA, Strefling JA, Zellers PR, Reed GW, Venkatachalam S, Lowry AM, *et al*. The effect of post-exercise ankle-brachial index on lower extremity revascularization. JACC Cardiovasc Interv. 2015;8(9):1238-44. https://doi.org/10.1016/j.jcin.2015.04.021
   PMid:26292588
10. Barone Gibbs B, Dobrosielski DA, Althouse AD, Stewart KJ. The effect of exercise training on ankle-brachial index in Type 2 diabetes. Atherosclerosis. 2013;230:125-30. https://doi.org/10.1016/j.atherosclerosis.2013.07.002
    PMid:23958264 PMCid:PMC3775271
11. Shaunmigan A, Thenmozhi P. Effectiveness of Allen Buerger

exercise in preventing peripheral arterial disease among people with Type II diabetes mellitus. Int J Pharm Bio Sci. 2015;6(2):966-70.

12. Francia P, Anichini R, De Bellis A, Seghieri G, Lazzeri R, Paternostro F, *et al*. Diabetic foot prevention: The role of exercise therapy in the treatment of limited joint mobility, muscle weakness and reduced gait speed. Ital J Anat Embryol. 2015;120(1):21-32.
13. Kumari A, Rai K, Kumari V, Sarin J. A study to assess the effectiveness of Buerger Allen exercise on foot perfusion among patients with diabetes mellitus admitted in selected hospital of Ambala, Haryana. Int J Heal Sci Res. 2019;9(1):112.
14. American Diabetes Association. Standards of Medical Care in Diabetes-2015 Abridged for primary care providers. Diabtes Care. 2015;38(1):17-9 http://doi.org/10.2337/dc15-S006

    PMid:25537701.
15. Cavalcante BR, Farah BQ, Barbosa JP, Cucato GG, Chehuen M, Santana FD, *et al*. Are the barriers for physical activity practice equal for all peripheral artery disease patients? Arch Phys Med Rehabil. 2015;96(2):248-52. http://dx.doi.org/10.1016/j.apmr.2014.09.009

    PMid:25281872
16. Hawkins M, Chasan-Taber L, Marcus B, Stanek E, Braun B, Ciccolo J, *et al*. Impact of an exercise intervention on physical activity during pregnancy: The behaviors affecting baby and you study. Am J Public Health. 2014;104(10):e74-81. https://doi.org/10.2105/ajph.2014.302072

    PMid:25122031 PMCid:PMC4167076
17. Potter PA, Perry AG. Fundamental of Nurse. Mosby: Elsevier; 2013. p. 2-5.
18. Berman A, Snyder S, Frandsen G. Kozier&Erb's. Fundamentals of Nursing: Concepts, Process, and Practice. New Jersey: Pearson; 2016. p. 1542.
19. Department of Rehabilitation Services the Ohio State University Wexner Medical Center. Ankle Range of Motion Exercise; 2012. Available from: https://www.patienteducation.osumc.edu/documents/anklerom.pdf [Last retrieved on 2015 Dec 28].
20. Rosenson RS, Fioretto P, Dodson PM. Does microvascular disease predict macrovascular events in Type 2 diabetes? Atherosclerosis. 2011;218(1):13-8. http://dx.doi.org/10.1016/j.atherosclerosis.2011.06.029

    PMid:21763654
21. Hoe J, Koh WP, Jin A, Sum CF, Lim SC, Tavintharan S. Predictors of decrease in ankle-brachial index among patients with diabetes mellitus. Diabet Med. 2012;29(9):e304-7. https://doi.org/10.1111/j.1464-5491.2012.03705.x

    PMid:22587456
22. Jude EB, Eleftheriadou I, Tentolouris N. Peripheral arterial disease in diabetes a review. Diabet Med. 2010;27(1):4-14. https://doi.org/10.1111/j.1464-5491.2009.02866.x

    PMid:20121883
23. Chen YW, Wang YY, Zhao D, Yu CG, Xin Z, Cao X, *et al*. High prevalence of lower extremity peripheral artery disease in Type 2 diabetes patients with proliferative diabetic retinopathy. PLoS One 2015;10(3):e0122022. https://doi.org/10.1371/journal.pone.0122022

    PMid:25822410 PMCid:PMC4379174
24. Vella S, Petrie JR. Macrovascular disease: Pathogenesis and risk assessment. Med (United Kingdom). 2015;43(1):1-6. http://dx.doi.org/10.1016/j.mpmed.2014.10.012
25. O'Brien J, Edwards H, Stewart I, Gibbs H. A home-based progressive resistance exercise program for patients with venous leg ulcers: A feasibility study. Int Wound J. 2013;10(4):389-96. https://doi.org/10.1111/j.1742-481x.2012.00995.x

    PMid:22697811
26. Bulechek GM, Butcher HK, Dochterman JM, Wagner CM. Nursing Intervention Classification. 6th ed. The United States of America: Mosby Elsevier; 2013.