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ORIGINAL RESEARCH ARTICLE

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Correlation between toe brachial index and walking ability in peripheral arterial disease with type 2 diabetes mellitus

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Abstract

Background The primary symptom of peripheral arterial disease (PAD) is intermittent claudication and the most common non-invasive diagnostic method is ankle brachial index. Peripheral arterial disease is usually accompanied by various other co-morbidities like type 2 diabetes mellitus, hypertension, and hypercholesterolemia. Literature suggests that when peripheral arterial disease is accompanied by type 2 diabetes mellitus, the ankle-brachial index can be falsely elevated due to medial calcification of the arteries. Therefore, an assessment of microcirculation using the toe brachial index is needed to diagnose PAD in these individuals. It has been well established that walking ability and ankle-brachial index are correlated in peripheral arterial disease. However, there is a dearth of literature on whether there is a correlation between toe brachial index (TBI) and walking ability. Therefore, the objective of the study is to find the correlation between toe brachial index and walking ability in type 2 diabetes mellitus with peripheral arterial disease. A total of 1485 participants were screened for the study, among which 133 met the inclusion criteria. Informed consent was obtained and the included participants were assessed for their demographic details. Toe brachial index was performed with the help of Doppler and 6-min walk test was performed to measure the claudication in the participants.

Results In the present study of 133 participants, we found a strong positive correlation between toe brachial index and 6-min walk distance ($r = 0.911$ p value < 0.05). The walking ability is directly proportional to the TBI, i.e., the lesser the values of TBI, the lesser the walking distance covered in peripheral arterial disease with type 2 diabetes mellitus.

Conclusion The present study concludes that there is a strong positive correlation between toe brachial index and 6-min walk distance.

Keywords Type 2 diabetes mellitus, Peripheral arterial disease, 6-min walk distance, Toe brachial index, Claudication pain

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Background

Intermittent claudication is one of the major symptoms of peripheral arterial disease (PAD). This is defined as cramping pain in the calf muscle which leads to difficulty in walking larger distances [1]. The worldwide prevalence of PAD with age-matched is around 12%, affecting roughly around 8 to 12 million people [2]. It has also been observed that age is directly proportional to PAD. As the age increases the prevalence of PAD increases simultaneously when accompanied with other co-morbidities like hypertension, type 2 diabetes mellitus (T2DM), hypercholesterolemia, and so on. The prevalence of PAD is 2–3 times more advanced in people with diabetes as compared to non-diabetes [3]. The prevalence reported in North India was 1.49% in 2018 and in South India was 8.56% in 2019 [4, 5]. The varying prevalence across the globe is due to its asymptomatic nature and other due to its diagnostic availability. A majority of the individuals are unable to appreciate the symptoms at the initial stages and are usually reported late leading to poor blood supply to the lower limb which could be followed by ulcer and gangrene [6].

The major symptom experienced by the individual is the cramping pain in the lower limb otherwise known as claudication pain while walking. It is due to reduced blood supply to the lower limb which is caused due to atherosclerosis. Atherosclerosis is defined as plaque formation in the artery which leads narrowing of the vessels and this results in obstruction to the blood flow in the lower limb. The cramping pain noticed by the individuals makes them incompetent to walk larger distances. Six-minute walk distance (6MWD) is one of the easiest and readily available tests that can be performed on these individuals to assess their walking ability with an intraclass correlation coefficient (ICC) for peripheral arterial disease of 0.94. The distance covered by the individual and initiation of pain is referred to as claudication pain [1, 2].

The diagnostic method for PAD is classified as invasive and non-invasive methods. The non-invasive method includes ankle-brachial index, toe-brachial index, and Doppler ultrasound. The invasive method includes computed angiography and MRI angiography [7]. The non-invasive method is the most frequently used method for the diagnosis of PAD. At times when PAD is accompanied by T2DM, there is medial calcification of the lower limb arteries which gives falsely elevated ankle brachial index values. In such cases, the toe brachial index is considered a better diagnostic method for PAD with T2DM. TBI does not involve the major lower limb arteries but it takes pressure from the great toe which suppresses the drawback caused by ABI in T2DM individuals. The presence of reduced blood supply to the lower limb is responsible for the reduced systolic pressure at the toe, this results in reduced values of TBI compared to normal individuals. A systematic review done in 2016 found that the sensitivity and specificity of the TBI for PAD ranged from 45 to 100% and 16 to 100% respectively [8].

The reduced walking ability in PAD is due to reduced blood supply to the lower limb which is indicated by reduced values of ABI. This shows that reduced walking ability is linked to the reduced values of ABI [9]. Even though it is considered that TBI records the pressure at the capillary level and is considered more accurate in PAD with T2DM, there is a dearth of literature on TBI correlated to 6MWD. So, the objective of the study was to find the correlation between TBI and 6MWD in T2DM with PAD.

Materials and methods

This was a cross-sectional study which was conducted in the diabetic foot clinic of a tertiary hospital in coastal Karnataka. After the approval from the institutional ethics committee, the study was initiated. The inclusion criteria were individuals in the age group of 30–70 years with diagnosed diabetes according to the American Diabetes Association (ADA) [10] and no neurological/musculoskeletal disorders. The exclusion criteria were individuals with any active foot ulcer; individuals who underwent any recent cardiac or vascular surgical intervention, and neurological or musculoskeletal disorders influencing the blood pressures of both upper and lower limbs.

In the present study based on the inclusion and exclusion, a total of 133 participants were recruited. Based on a calculation with an error of 0.05, a power of 0.8, and a correlation strength of 0.25, a minimum sample size was 123 considering 10 dropouts. So, total sample size was 133 ($N = [(Z\alpha + Z\beta)/C]2 + 3$).

The procedure was explained to the participants and the informed consent was obtained.

Detailed demographic details for all the participants which included age, body mass index, duration of diabetes, and medication history were noted at the time of examination. Because of the calcification of arteries seen in diabetes, the ABI is falsely elevated in these individuals. As TBI is considered a better method of assessing PAD in T2DM, the study used TBI as an outcome measure. A cut-off of 0.7 and below is considered abnormal. The patient was advised to take the medicine according to the schedule and to avoid any intake of caffeine 2 h prior to the test as it could hinder the blood pressure values. With the help of Kody's Hadeco smartdop 30EX Doppler, TBI with the help of handheld Doppler was performed for all the participants in a long sitting position with back supported in the first half of the day. The patient was

instructed to rest for 10 min before the start of the test. The procedure of the test was explained to the participants and they were made aware of the noise the device could make. A toe pressure cuff was tied on the great toe of the dominant leg a photoplethysmogram (PPG) sensor was attached to measure the toe systolic pressure and an arm cuff was tied at the arm 1 inch above the cubital fossa of the dominant side to measure the systolic pressure of the arm. The probe was kept at the measurement area and was moved to locate the area where the maximum sound was heard. After placing the probe in the correct position, a waveform was seen on the software screen and the systolic pressure was measured. Both toe systolic pressure and brachial pressures were obtained from the Doppler machine and thus TBI was calculated as explained in Fig. 1. The sensitivity and specificity of handheld Doppler are 42.8% and 97.5% respectively [11].

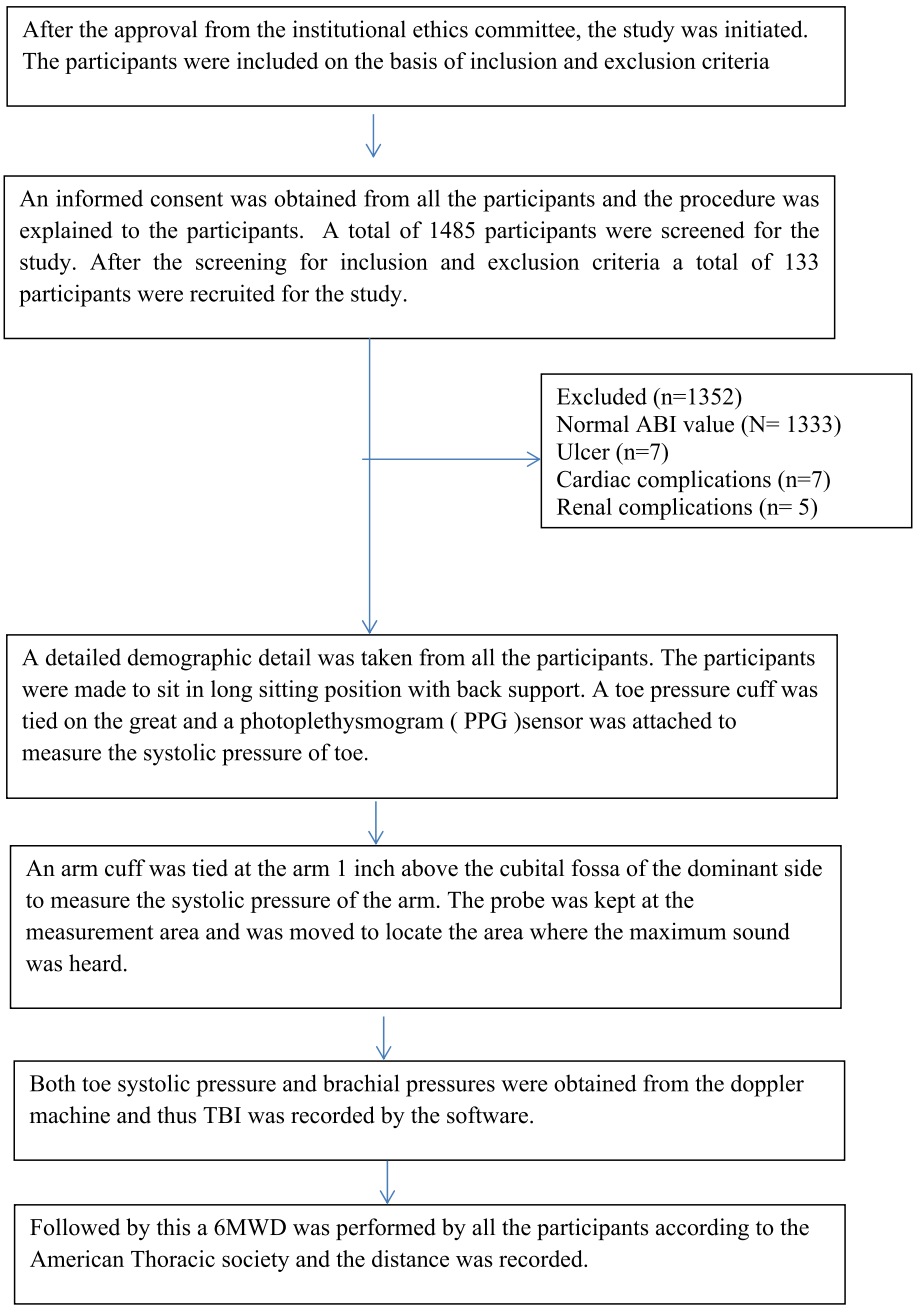

Fig. 1 Flow chart of methodology

After completion of the TBI measurement, with the standard procedures of the 6-min walk test stated by the American Thoracic Society, the 6-min walk test was explained to the participants [12, 13]. Peripheral arterial disease pain scale was explained to the participants and were advised to walk till the claudication pain was appreciated. The claudication pain scale consists of scoring from 0 to 5 where 0 corresponds to no pain and 5 corresponds to severe pain that cannot be walked through [14]. The test was either terminated when the 6 min were over or when the participant felt the maximum pain before 6 min of walking, whichever was reported first by the participant was taken into account. The distance was measured with the help of the number of laps completed and was noted. The data was then analyzed (Fig. 2).

Statistical analysis

EZR (Easy R) software was used to perform the statistical analysis of the data. Descriptive data and frequency were reported for the demographic variables. The data was tested for normal distribution with the help of the Shapiro–Wilk test and the data following normal distribution was reported in mean and standard deviation. Pearson's correlation coefficient was used to find the relation between TBI and 6MWD.

Results

After the inclusion and exclusion criteria for the study, 133 participants were recruited for the study. Table 1 shows the demographic details of the participants. Table 2 shows the drug history of the participants. Note that all 133 participants could finish the 6MWD with moderate pain. Pearson's correlation coefficient shows a strong correlation between TBI and 6 MWD with $r = 0.911$ and p value < 0.05 (Table 3). Table 4 shows the classification of TBI and the distance covered by the participants.

Table 1 Demographic and biochemical parameters of the participants

S.no	Variable	Mean ± SD
1.	Age in years	61.48 ± 9.64
2.	BMI in Kg/m^2	25.56 ± 4.15
3.	FBS in mg/dL	157.05 ± 17.21
4.	Glycated hemoglobin in %	8.56 ± 0.76
5.	Duration of diabetes in years	14.22 ± 6.78
6.	TBI	0.55 ± 0.11
7.	6MWD in meters	311.49 ± 57.10

Term glossary: *BMI* body mass index, *FBS* fasting blood sugar, *TBI* toe brachial index, *6MWD* 6-min walk distance

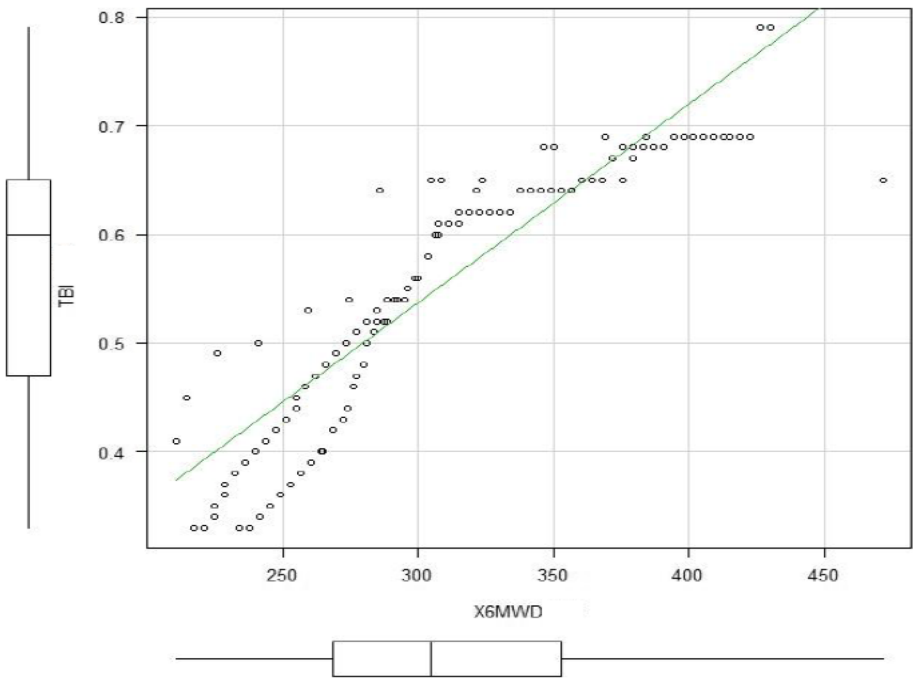

Fig. 2 Correlation between TBI and 6 MWD

Table 2 Drug history of participants

S.no	Variables	Number of participants *n* = 133(%)
1.	Oral hypoglycemic drugs	80 (60.15)
2.	Insulin	42 (31.58)
3.	Oral hypoglycemic drug + insulin	11 (8.27)
4.	Anti-platelets	83 (62.4)
5.	Statins	72 (54.13)

Table 3 Pearson's correlation coefficient between TBI and 6MWD

Variable	Correlation coefficient	*P* value
TBI versus 6MWD	0.911	< 0.05

Term glossary: *TBI* toe brachial index, *6MWD* 6-min walk distance

Table 4 Distance covered in 6MWD in relation to TBI

TBI	Claudication distance (m)
< 0.7 (*n* = 66)	264.39 ± 26.14
> 0.7 (*n* = 67)	357.90 ± 37.86

Term glossary: *TBI* toe brachial index, *6MWD* 6-min walk distance

Discussion

In the present study, we have reported a strong positive correlation between 6MWD and TBI in individuals with T2DM and PAD. This implies that the lower values of TBI are correlated to the lesser distance walked by the individual. 6MWD is one of the easiest forms of walking ability tests for PAD with T2DM. Usually for PAD individuals, a treadmill test is performed to evaluate the walking ability, but 6MWD is considered a better way to assess the walking ability as it represents the walking in the daily life on a plain surface and is inexpensive to perform. Also, it allows the participant to walk in a corridor and if found difficult can slow down or even temporarily rest without stopping the protocol. This makes the individual more confident in performing the test and can more importantly provide meaningful clinical difference [12]. Also, this helps in designing the exercise home protocol for the individual without causing any financial burden to the individual.

TBI can be considered as an early detector in individuals diagnosed with PAD with T2DM as it describes the blood circulation at the capillary level. In individuals diagnosed with T2DM, TBI can help in the diagnosis of PAD as it bypasses the medial calcified arteries which might give falsely elevated values of ABI and can mislead the diagnosis. Thus, TBI is considered more accurate in individuals diagnosed with PAD and T2DM [9, 10].

The possible mechanism involved in reducing walking ability in these individuals could be due to atherosclerosis which is plaque formation in the arteries which is responsible for the reduced blood supply to the lower limb. This leads to increased oxygen demand but insufficient supply to the lower limb. PAD is also known to be responsible for the endothelial dysfunction. There is reduced nitric oxide availability in the skeletal muscles and this is responsible for arterial vasoconstriction and disturbed blood flow to the lower limb [15, 16]. This is accompanied by changes in the skeletal muscles. There is reduced muscle mass and altered ATP production which leads to further structural changes of the lower limb muscle. This all could lead to reduced walking ability by the individual thereby reducing the quality of life [17]. The changes in the skeletal level and the reduced blood flow are responsible for the claudication pain experienced by the individual. The skeletal component is observed by reduced walking ability and the reduced systolic pressure in TBI is due to reduced blood flow in the lower limb.

T2DM is defined as hyperglycemia in the body that increases sugar levels which could be either a genetic factor or could be due to environmental factors. The first line of treatment for T2DM is considered lifestyle modification which includes exercise, physical activity, and diet modification [18]. However, due to the involvement of PAD, the walking ability is already reduced thereby increasing the blood glucose level and further reducing the quality of life. On one side, PAD makes it difficult to walk and on the other side, T2DM requires an aggressive exercise regime to reduce the blood glucose level contradicting the condition.

The involvement of both PAD and T2DM implies the reduced walking ability in these individuals, thereby reduced 6MWD is reported in our study. This reduced walking ability is due to a lack of blood supply to the lower limb. Walking involves continuous pumping of the blood in the calf muscle, which implies that the force with which the contraction has to happen should be greater as the blood has to be pumped back to the coronary system against gravity. Due to atherosclerosis, there is difficulty in pumping the blood because of narrowed arteries of the lower limb. This can be diagnostically identified in terms of TBI, which highlights the correlation between TBI and 6MWD.

The limitation of the study is the sample size and a concise geographic area which cannot be generalized to a larger population and the lack of adjusting the confounding factors like age, gender, duration of diabetes, and claudication history. Future studies highlighting the

confounding factors with a larger sample size can be done for better outcomes of the study.

The present study concluded that there is a strong positive correlation between TBI and 6MWD. The findings of the current study highlight the importance of reduced walking distance as an indicator of reduced TBI.

Abbreviations

T2DM	Type 2 diabetes mellitus
PAD	Peripheral arterial disease
ABI	Ankle-brachial index
TBI	Toe brachial index
6MWD	6-Minute walk distance
BMI	Body mass index
FBS	Fasting blood sugar

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Authors' contributions
All authors contributed to the study's conception and design. Material preparation, data collection, and analysis were performed by Arora E and Yadav H. The first draft of the manuscript was written by Arora E and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Ethical approval for the study was taken before the recruitment of the participants. Every participant was explained the protocol before recruitment and informed consent was obtained.

Consent for publication
The informed consent had the consent for publication of data. No personal data was disclosed in the study.

Competing interests
The authors declare that they have no competing interests.

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References

1. Lane R, Harwood A, Watson L, Leng GC. Exercise for intermittent claudication. Cochrane Database Syst Rev. 2017;12(12):CD000990.
2. Shu J, Santulli G. Update on peripheral artery disease: epidemiology and evidence-based facts. Atherosclerosis. 2018;275:379–81.
3. Soyoye DO, Abiodun OO, Ikem RT, Kolawole BA, Akintomide AO. Diabetes and peripheral artery disease: a review. World J Diabetes. 2021;12(6):827.
4. Makkar BM, Sharma JK, Jaggi S, Soota K, Gupta V, Khurana G. Low prevalence of peripheral arterial disease in type 2 diabetes patients in North India. Diabetes. 2018;67(Supplement_1).
5. Arora E, Maiya AG, Devasia T, Bhat R, Kamath G. Prevalence of peripheral arterial disease among type 2 diabetes mellitus in coastal Karnataka. Diabetes Metab Syndr. 2019;13(2):1251–3.
6. Criqui MH, Matsushita K, Aboyans V, Hess CN, Hicks CW, Kwan TW, McDermott MM, Misra S, Ujueta F. Lower extremity peripheral artery disease: contemporary epidemiology, management gaps, and future directions: a scientific statement from the American Heart Association. Circulation. 2021;144(9):e171–91.
7. Nirala N, Periyasamy R, Kumar A. Non invasive diagnostic methods for better screening of peripheral arterial disease. Ann Vasc Surg. 2018. https://doi.org/10.1016/j.avsg.2018.03.018.
8. Tehan PE, Santos D, Chuter VH. A systematic review of the sensitivity and specificity of the toe–brachial index for detecting peripheral artery disease. Vasc Med. 2016;21(4):382–9.
9. Høyer C, Sandermann J, Petersen LJ. The toe-brachial index in the diagnosis of peripheral arterial disease. J Vasc Surg. 2013;58(1):231–8.
10. Donohue CM, Adler JV, Bolton LL. Peripheral arterial disease screening and diagnostic practice: a scoping review. Int Wound J. 2020;17(1):32–44.
11. Alavi A, Sibbald RG, Nabavizadeh R, Valaei F, Coutts P, Mayer D. Audible handheld Doppler ultrasound determines reliable and inexpensive exclusion of significant peripheral arterial disease. Vascular. 2015;23(6):622–9.
12. American Thoracic Society. ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med. 2002;166:111–7.
13. Chen X, Stoner JA, Montgomery PS, Casanegra AI, Silva-Palacios F, Chen S, Janitz AE, Gardner AW. Prediction of 6-minute walk performance in patients with peripheral artery disease. J Vasc Surg. 2017;66(4):1202–9.
14. Harwood AE, Pymer S, Ingle L, Doherty P, Chetter IC, Parmenter B, Askew CD, Tew GA. Exercise training for intermittent claudication: a narrative review and summary of guidelines for practitioners. BMJ Open Sport Exerc Med. 2020;6(1):e000897.
15. McDermott MM, Guralnik JM, Criqui MH, Liu K, Kibbe MR, Ferrucci L. Six-minute walk is a better outcome measure than treadmill walking tests in therapeutic trials of patients with peripheral artery disease. Circulation. 2014;130(1):61–8.
16. Muller MD, Reed AB, Leuenberger UA, Sinoway LI. Physiology in medicine: peripheral arterial disease. J Appl Physiol. 2013;115(9):1219–26.
17. Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, Ostolaza H, Martín C. Pathophysiology of type 2 diabetes mellitus. Int J Mol Sci. 2020;21(17):6275.

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