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Original Research Article

Prospective observational study evaluating the predictive value of ankle branchial pressure index on the outcomes of diabetic foot ulcers

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ABSTRACT

Background: The study was conducted to determine the diagnostic accuracy of ankle branchial pressure index (ABPI) in predicting major amputation and duration of wound healing in diabetic foot ulcers.
Methods: 105 participants (30-85 years) admitted in general surgery inpatient with diabetic foot ulcers during 18 months were enrolled in the present prospective observational study. Institutional ethics committee approved the study and written informed consent was obtained from all study participants. Data was analyzed using R and the tests of significance were chi square test and ANOVA. Area under curve (AUC) of receiver operator characteristic (ROC) was used to describe the diagnostic accuracy of ABPI. $P<0.05$ was considered statistically significant.
Results: The mean ABPI of study participants was 0.7 with 23.8% participants having normal ABPI. Lower ABPI was associated with longer duration of ulcer healing ($p=0.003$). All participants with ABPI <0.3 required more than 120 days for wound healing ($p<0.001$) and required above knee amputation ($p<0.001$). AUC ROC of ABPI and major amputation is 0.987 with 92.9% sensitivity and 98.9% specificity. Significantly higher proportion of participants with ABPI ≤0.48 underwent major amputation. The AUC of ROC of ABPI on duration of wound healing was 0.953 with 84.9% sensitivity and 98.1% specificity.
Conclusions: ABPI can be used as a routine tool in all patients with diabetic foot ulcers for screening peripheral arterial disease so that the decision for amputation can be made early during diabetic foot ulcers.

Keywords: Diabetic foot ulcers, Ankle brachial pressure index, ABPI, Peripheral arterial disease, ROC

INTRODUCTION

Reduced insulin secretion, its action or a combination of both results in the chronic metabolic disorder known as diabetes mellitus (DM).[1] In the last three decades, the global burden and prevalence in adults has increased fourfold and two fold respectively.[2] Low and middle income countries have shown to have higher increase in prevalence and related complications which impose a major financial burden on healthcare sector. Though often referred to as the diabetic capital of the world, India has the second largest population of diabetics.[3] The prevalence of DM is high among South Indian states, and Kerala has been reported to have among the highest prevalence rates in the country. Among the complications of DM, foot ulcers are the most common yet preventable complication. The annual incidence of diabetic foot ulceration globally is 9.1 to 26.1 million and the Indian prevalence of diabetic foot ulcers is considerably lower than western population and is ~3%.[4] Almost 15-25% diabetic patients develop foot ulcers at least once in their life time and the prevalence is dependent on age and ethnicities.[5] Though Indians are not considered ethnically as a high risk population for foot ulcers, the explosive increase in DM and being home to the second largest population of diabetics and lower standard of healthcare

in rural areas diabetic foot ulcers remain a matter of concern. Poor foot care and glycemic control, presence of neuropathy, peripheral arterial disease (PAD), calluses and foot deformities, ill-fitting footwear, poor circulation and dry skin are some of the contributing risk factors for foot ulcers.[5] Areas that encounter repetitive trauma and pressure sensations are the areas that develop ulceration.[6] Neuropathy results in the development of callus which is the initial phase in the pathophysiology of diabetic foot ulcers. Deformities due to motor neuropathy, sensory loss resulting in trauma due to sensory neuropathy and reduced secretions and resultant dryness due to autonomic neuropathy contributes to development of diabetic foot ulcers. Infections superimposing these ulcers due to small vessel atherosclerosis and peripheral arterial disease delays the healing process. Being the cause of the highest healthcare burden among diabetics, the prevention and treatment of foot ulcers remain a considerable challenge.[7] Lower limb ischemia and vascularity determines healing in diabetic foot ulcers and plays as a major role in predicting lower limb amputations. Vascularity of the lower limb is assessed by clinical examination, hand held and color doppler or angiographic studies. Ankle branchial pressure index (ABPI) is calculated by dividing ankle systolic pressure with brachial systolic pressure using handheld or color doppler. The normal ABPI is 1.11 (0.1) and it ranges from 0.2-1 in patients with intermittent claudication, 0-0.65 in patients with ischemia at rest and less than 0.3 in those with impending or active gangrene. The decision of amputation in patients diabetic foot ulcers is usually delayed due to the time consuming first line management, surgical debridement. The decision of amputation is reached when there is no sign of healing after multiple debridement's or when angiography or doppler reveals reduction in lower limb vascularity. Angiography is considered the gold standard but due to the high cost and limited use in patients with renal failure, ABPI becomes a viable investigation in decision making in a resource poor setting. The present study aims at evaluating the diagnostic value of ABPI in aiding early decision making in diabetic foot ulcers.

METHODS

The present prospective observational study enrolled 105 participants aged 30-85 years admitted in general surgery department with diabetic foot ulcers (Wagner class 1-5) in a time period of 18 months between March 2012 to September 2013. Terminally ill, who received outpatient treatment and ulcers resultant of Hansen's disease and filariasis were excluded. The study was approved by institutional ethics committee and written informed consent was obtained from all study participants. The total duration of ulcer was obtained from history (duration of lesion prior to hospital admission and duration of lesion from the time of admission to stage of healed ulcer or scar). Ulcer completely covered by healthy granulation tissue and neo-epithelization in the peripheral regions of the ulcer either during hospital stay or during follow up visits was considered as healed ulcer. We did consider the variations in width, size and depth of the ulcers. A completely healed stump or scar was considered as endpoint in participants who underwent amputation. All participants received standard of care with betadine, hydrogen peroxide or normal saline and appropriate antibiotics depending on the culture and sensitivity report. Topical papain, polypropylene glycol, skin graft, debridement, disarticulation and amputation were as per the discretion of the treating surgeon. The outcomes measured were the healing of ulcer with different treatment modalities. ABPI of the affected limb was measured using hand held doppler and a value less than 0.9 was presumed to have PAD. Data was analyzed using free software R and are expressed as proportions and as mean standard deviation (SD) after rounding off to the nearest decimal. The association between various parameters were determined using chi square test, one-way ANOVA and receiver operator characteristic (ROC) curve was used to demonstrate the predictive value of ABPI. $P<0.05$ was considered statistically significant.

RESULTS

63.8% (n=61) participants were males and 41.9% (n=44) were females. The mean age of diabetic foot among male participants was 63.8 (9.1) and among female participants was 58.1 (10) years respectively.

Table 1: ABPI of study participants.

ABPI	N (%)
<0.3	4 (3.8)
0.3-0.49	10 (9.5)
0.5-0.89	66 (62.9)
≥0.9	25 (23.8)

Table 2: Association between duration of healing and ABPI.

Time for ulcer healing (days)	ABPI (<0.3)	ABPI (0.3-0.49)	ABPI (0.5-0.89)	ABPI (≥0.9)
	N (%)	N (%)	N (%)	N (%)
<30	0	0	27 (25.7)	25 (23.8)
30-89	0	0	36 (34.3)	0
90-119	0	10 (9.5)	3 (2.9)	0
≥120	4 (3.8)	0	0	0

Significant association was observed between groups ($p<0.001$) indicating all participants with ABPI <0.3 who required more than 120 days for ulcer healing.

The mean ABPI was 0.7 (0.2) and only 23.8% (n=25) had normal ABPI (Table 1) and the association between duration of healing and ABPI is demonstrated in (Table 2). The duration of ulcer healing was significantly longer as ABPI reduced using one-way ANOVA (Table 3). Significant association was observed between ABPI and method of treatment required (p<0.001) (Table 4).

Significant association was observed between groups probably indicating the higher proportion of participants with ABPI <0.3 who underwent above knee amputation or the higher proportion of participants with normal ABPI who required dressing and debridement alone for ulcer healing.

The area under the curve (AUC) of ROC determining the predictive value of ABPI on major amputation is 0.987 with 92.9% sensitivity, 98.9% specificity, 7.1% false negative rates, 1.1% false positive rates, 92.9% predictive value of the positive test, 84.5% positive likelihood ratio and 98.1% accuracy. Significantly higher proportion of participants with ABPI ≤0.48 underwent major amputation and significantly lower proportion of participants with ABPI >0.48 underwent major amputation. The AUC of ROC of the predictive value of ABPI on duration of wound healing was 0.953 with 84.9% sensitivity, 98.1% specificity, 15.1% false negative rates, 1.9% false positive rates, 97.8% predictive value of a positive test, 44.2% positive likelihood ratio and 91.4% accuracy. Significantly higher proportion of participants with ABPI ≤0.67 required ≥30 days for wound healing and significantly higher proportion of participants with ABPI >0.67 required <30 days for wound healing.

Table 3: Comparison of the duration of ulcer healing between groups categorized according to ABPI.

ABPI	N	Mean duration of wound healing (SD) days	P value
<0.3	4	153.3 (49.5)	0.003*
0.3-0.49	10	107.3 (3.4)	<0.001*
0.5-0.89	66	41.1 (22.6)	<0.001*
≥0.9	25	16.5 (3.4)	<0.001*

*Indicates significant difference between groups using one-way ANOVA.

Table 4: Association between ABPI and treatment required.

Treatment	ABPI (< 0.3)	ABPI (0.3-0.49)	ABPI (0.5-0.89)	ABPI (≥0.9)
	N (%)	N (%)	N (%)	N (%)
Dressing alone	0	0	0	2 (1.9)
Dressing and debridement	0	1 (1)	23 (21.9)	20 (19)
Dressing, debridement and split skin thickness graft	0	0	9 (8.6)	3 (2.9)
Toe amputation	0	0	28 (26.7)	0
Fore foot amputation	0	0	6 (5.7)	0
Below knee amputation	0	9 (8.6)	0	0
Above knee amputation	4 (3.8)	0	0	0

DISCUSSION

Foot ulceration is one of the leading causes of hospital admission in DM and is the most common non-traumatic cause of lower limb amputation. The presence of peripheral neuropathy and peripheral vascular disease are important causative factors for development of diabetic foot ulcers and the presence of lower limb ischemia and reduced vascularity are most important prognostic factors in diabetic foot ulcer healing. Preservation of the maximal length of the viable extremity and minimizing the morbidity and mortality is very significant in lower limb amputation since overly distal amputation can result in lower rates of healing due to inadequate blood supply which might require further surgical procedures. Also repeated amputation is associated with higher rates of mortality and morbidity hence should be avoided whenever possible. Overly proximal amputation can result in lower rates of ambulation without appropriate prosthesis and in an ethical point of view it is incorrect.[8] Owing to these factors, selection of a proper amputation level is crucial in diabetic foot ulcers. The clinical diagnosis of the most important predictor in diabetic foot ulcers, ischemia is difficult since autonomic neuropathy can give a perception of warmth in the extremity. Lack of autonomic tone in capillaries results in shunting of blood from arteries to veins leading to warmth, bounding pulses and dilated veins. This could be misinterpreted and the absence of ischemia. The lack of claudication pain due to autonomic neuropathy delays the clinical diagnosis often. The usual scenario in patients with diabetic foot ulcers with PAD is an initial phase of multiple debridement's with poor wound healing eventually leading to the only option, amputation. The initial stage of multiple debridement's require prolonged hospitalization and associated complications and economic burden which would suggest early institution of amputation.[9] Males accounted to 64% of participants which could be due to the higher prevalence of DM among males in our setting.[10] This can also be attributed to the higher risk of diabetic foot ulcers among males which has been previously reported.[11] Among diabetics age above 80 years, foot ulcers are more common in females and the risk increases by a minimum of two fold in the presence

of calluses and claw toe.[11] Physical activity is considered protective among women while the use of insulin, presence of sensory complaints is associated with higher risk among men. The lower proportion of elderly participants in our study could also be a reason for the lower proportion of female participants in our study.

The mean age of male participants with diabetic foot was higher than female participants, though the reverse is expected. This finding can only be explained on the basis of the location of the hospital which is in a rural area where the access to the hospital is still difficult to elderly females, however high the literacy rate is. High prevalence of diabetic foot ulcers was observed in the ages between 50-69 years, higher proportion of male participants were at higher age compared to female participants. This is also contrary to previous reports and published literature. This can only be explained on the basis of the lower hospital access to elderly females. ABPI among study participants was significantly low (0.7) which is considered moderate PAD.[12] Only 24% participants had normal ABPI, while 76% participants had lower than normal ABPI. The mechanisms of development of PAD are similar to that of coronary and carotid vascular disease. Hyperglycemia, dyslipidemia, insulin resistance and increased free fatty acid production in DM produces vascular inflammation, increased leukocyte adhesion, coagulation and chemotaxis by increased release of C reactive protein. Increased levels of tumor necrosis factor-α and interleukin-6 in DM activate nuclear factor-κβ producing thrombus, promote leukocyte migration and adhesion, increase plaque instability and rupture. The other pathogenic processes include endothelial cell dysfunction, reduced nitric oxide production, inhibition of vasodilation by increase in reactive oxygen species, increase in advanced glycation end products (proinflammatory) which induces leukocyte chemotaxis, adhesion, and transformation into foam cells. Vascular smooth muscle cell derangement, increase in tissue factor production which is proatherogenic and procoagulatory, increased production of fibroblast growth factor and transforming growth factor-α increases extracellular matrix production, impairment in synthesis of collagen destabilizes atherosclerotic plaque, coupled with apoptosis of vascular smooth muscle cells increases the risk of plaque rupture and thrombosis. Increased production of endothelin-1, angiotensin II, and prostanoids lead to vasoconstriction and platelet dysfunction, enhanced uptake of glucose increases oxidative stress and decrease NO production, upregulation of P-selectin, glycoproteins (Ib, IIb/IIIa) promote platelet adhesion and aggregation. Calcium dysregulation increase platelet aggregation and hypercoagulability while increase in levels of tissue factor and factor VII production enhances coagulability. Decreased antithrombin and protein C synthesis, rheology, elevation in blood viscosity, increase in fibrinogen production increases the coagulability of blood. Other pathogenic processes include impairment in arteriogenesis, inhibition of shear stress sensing mechanisms and decrease in monocyte and growth factor signaling. All these pathogenic mechanisms contribute to increase in atherothrombosis causing reduced plaque stability, increased chances of plaque rupture and restenosis.[13]

All participants with ABPI less than 0.3 required more than 120 days for ulcer healing while all participants with ABPI of more than or equal to 0.9 required less than 30 days for ulcer healing ($p<0.001$). Participants with ABPI less than 0.3 had significantly higher duration of wound healing (~150 days) compared to all other participants ($p=0.003$). All the participants with ABPI less than 0.3 required above knee amputation while none of the participants with ABPI more than or equal to 0.9 required any amputation ($p<0.001$). AUC of ROC on the predictive value of ABPI on major amputation is 0.987 with high sensitivity (~93%) and specificity (99%) with low false positive (1%) and false negative rates (7%) indicating that ABPI is an exceptional diagnostic test in predicting major amputations in diabetic foot ulcers. AUC of ROC on the duration of wound healing was 0.953 with lower sensitivity (~85%) and specificity (98%), higher false negative (15%) and false positive (2%) rates still a reliable tool on predicting the duration of wound healing in diabetic foot ulcers. The outcome of coexistent PAD in patients with diabetic foot ulcers is dependent on various other factors such as co-morbidities, infection, neuropathy, immunological factors and poor glycemic control.[14,15] Hence, we recommend a careful history, physical examination with ABPI in the poor socioeconomic strata or angiography in affording patients. ABPI is a valuable tool for predicting the outcomes and duration of wound healing in patients with diabetic foot ulcers.

CONCLUSION

We recommend the use of ABPI as a routine tool in all patients with diabetic foot ulcers for screening PAD and angiography in those with lower ABPI so that the decision for amputation can be made early which would save a considerable amount in healthcare expenditure towards hospital admission, surgical debridement and dressing and eventual amputation.

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