ASSESSMENT OF PREVALENCE AND RISK FACTORS OF PERIPHERAL ARTERIAL DISEASE IN DIABETIC FOOT ULCER

G. Thulasikumar∗,1 and S. Vijayasarathy∗, 1

∗Department of Vascular Surgery, Govt. Stanley Medical College., ∗∗Department Of General Surgery, Govt. Stanley Medical College.

ABSTRACT Introduction: Diabetic foot ulcer (DFU) is very common yet challenging complication of diabetes worldwide. These ulcers are biologically compromised majorly by ischemia and neuropathy. Ischemia has gained recognition as a significant cause of DFU. The association of peripheral arterial disease (PAD) largely impacts the treatment outcomes of DFU regarding ulcer healing, lower limb amputations and mortality. The burden of PAD in DFU in South Indian population has not been assessed adequately in the recent years. A multidisciplinary approach to DFU and prompt diagnosis of ischemia will decrease the loss of limb and life. Objective The objective of the study was to assess the peripheral arterial disease and associated risk factors in patients with diabetic foot ulcer. Methods: A total of 100 patients were evaluated in this study after obtaining informed consent. The patients were subjected to detailed history and clinical examination which included distal pulse assessment, ankle-brachial index (ABI) and duplex scan to evaluate PAD. The data were subjected to statistical analysis to find out the association between parameters of interest. Results: The prevalence of PAD in DFU was found to be 36%. It was more prevalent in males and age>40 years and higher with increasing age. PAD was associated almost equally with plantar and dorsal ulcers, more often the whole of the foot was involved. There is a significant association of PAD with longer diabetic duration (p<0.0001) with mean disease duration of 10 years. Conclusion: Previous studies aimed to study the prevalence of PAD in diabetes irrespective of foot ulcer. The present study analysed various factors coexisting with DFU and PAD. The results conclude that peripheral arterial disease is a potential risk factor for major limb amputations.

KEYWORDS: Diabetic foot ulcer, peripheral arterial disease, ischemia, ankle brachial index

HOW TO CITE THIS ARTICLE

Thulasikumar G, Vijayasarathy S. Assessment of prevalence and risk factors of peripheral arterial disease in diabetic foot ulcer. Int J Surg Med. 2017; 3(3): 156-166. doi:10.5455/ijsm.diabetic-foot-ulcer-pad

Introduction

Peripheral arterial disease (PAD) is manifested by chronic limb ischemia commonly due to atherosclerosis of the peripheral arteries. Diabetes mellitus is an independent risk factor for this disease. Thus, a diabetic patient with PAD is at increased risk to develop an ischemic ulcer or gangrene than a non-diabetic patient.

Diabetic foot ulcer (DFU) is very common yet challenging
complication of diabetes worldwide. The International Working Group on the Diabetic Foot defines DFU as a full-thickness wound penetrating the dermis located below ankle in a diabetic patient.

These ulcers are biologically compromised majorly by ischemia and neuropathy. Ischemia is gaining recognition as a significant cause of DFU. Significant differences exist in clinical characteristics, pathophysiology and treatment of ulcers associated with peripheral arterial disease (PAD) and non-PAD ulcers. This has led to two different disease states namely DFU with PAD and without PAD.

Ankle-brachial-pressure index (ABI) is an important tool used at the bedside to provide a measure of perfusion to the ankle, although not reliable in the presence of calcified vessels. When combined with Doppler study, this could facilitate early diagnosis and treatment reducing the potential risk of limb amputation.

The association of PAD primarily impacts the treatment outcomes regarding ulcer healing, lower limb amputations and mortality. The burden of PAD in DFU in South Indian population has not been assessed adequately in the recent years. A prompt diagnosis of ischemia and multidisciplinary approach to DFU will decrease the loss of limb and life. This study aims to throw light on the same.

**Effect of Peripheral Arterial Disease in Diabetic population**

PAD is characterised by atherosclerosis of lower extremity arteries causing occlusive disease. It is a strong predictive factor for atherothrombotic disease in other vascular beds.

PAD involvement is mostly diffuse and particularly is more severe in tibial vessels. It usually involves long segment occlusions. In a non-diabetic individual, collateral vessels develop in response to occlusion of a major artery. This collateral formation is impaired in diabetes rendering the distal tissue more prone to severe ischemia.

Patient with PAD most commonly presents with a cramping pain in the calves, thighs or buttocks known as intermittent claudication. This pain relieved by rest and reappears with walking and exercise. Some patients present with extreme symptoms like rest pain, infected ulcer and gangrene. These limb-threatening symptoms are collectively termed as critical limb ischemia (CLI).

The high-risk factors for PAD are diabetes and smoking. The duration of diabetes, hypertension, hyperlipidemia and advanced age are the other established risk factors.

In diabetic patients, the occurrence of PAD increases with diabetic duration, advancing age and peripheral neuropathy.

Most patients are asymptomatic or do not report symptoms due to ignorance. For some, pain is blunted by the presence of neuropathy. Moreover, there is no uniformly agreed consensus on screening modalities. For these reasons, the assessment of the true prevalence of PAD in diabetic patients becomes difficult. Hence in the presence of diabetes, PAD is more likely to present at an advanced stage.

Two standard assessment tools are the presence of intermittent claudication and absence of distal foot pulses, both involving an element of insensitivity. For more accurate estimation of prevalence, the assessment should be based on reproducible and validated test like ankle-brachial index (ABI).

**Evaluation of PAD in DFU**

**Clinical evaluation** The clinical evaluation should start with a detailed medical history enquiring about the onset and progres-
Figure 1 (continue): Diabetic foot ulcer in various stages.
sion of the disease. Risk factors should be enquired about, and focus should be on identifying symptoms of claudication, rest pain and functional impairment. PAD patient may present in a diverse form from no symptoms to infected chronic ulcer and gangrene. Associated symptoms arising from atherothrombosis in other vascular beds like angina, stroke and abdominal ischemia should be noted. Alternative causes of claudication like spinal canal stenosis should be ruled out.

Physical examination should start with the attitude of limb and presence of deformity. Detailed inspection of the affected limb involves looking for the signs of vascular insufficiency. These include muscle wasting and loss of subcutaneous fat characterised by thinning of limbs with bony prominence. The skin becomes dry and fissured with reduced temperature. Nails are dystrophic, lusterless, brittle and contain transverse ridges. There is a loss of skin hair making the skin appear shiny. The interdigital spaces should be inspected for ulcers and fissures.

The ulcer should be examined in detail and classified on the level of infection and involvement of adjacent structures (Fig. 1).

This should be followed by an assessment of circulatory insufficiency like capillary refilling time, venous filling time (Harvey’s sign) and Buerger’s test. Buerger’s test involves assessing the leg elevation angle at which vascular compromise is obvious. Assessment of peripheral pulses is greater which involves charting of lower and upper limb pulses (Fig. 2). One has to auscultate these arteries and look for bruit. This has to be followed by an assessment of neighbouring joints for movements and deformity. A thorough evaluation of the motor system, sensory system of nerves and reflexes should be done. Finally draining lymph nodes should be examined. Non-invasive test: ABI ABI provides a comfortable, reasonably accurate and non-invasive assessment of occurrence of PAD. It also helps to assess the severity of the disease. It is a ratio in which the numerator is the highest of the three ankle systolic blood pressures in dorsalis pedis, anterior and posterior tibial arteries in the affected lower limb. The denominator is the highest of brachial systolic pressures measured in both the upper limbs. The pressures are measured by using handheld Doppler making it a very simple and quantitative tool to assess the patency of lower limb arteries.

However, in elderly, diabetic patients and chronic kidney disease, the peripheral arteries are calcified and are poorly compressible and hence may artificially elevate the values. This complicates the evaluation of PAD.

The tools required to calculate ABI include a hand-held Doppler probe of frequency 5–10 MHz and a sphygmomanometer with blood pressure cuff.

The ABI is measured by putting the patient in supine position for 5 min. Systolic blood pressure in the ankle is measured in the posterior tibial artery and dorsalis pedis and by placing the cuff just above the ankle. Systolic blood pressure in the arm is measured in the brachial artery by placing the cuff just above the elbow.

ABI>1.3 indicates the presence of poorly compressible arteries at the ankle level due to medial arterial calcification which occurs commonly in diabetes. This renders a diagnosis of PAD by ABI alone less reliable.

Since the digital arteries are less commonly affected by calcification, toe pressure measurements involving digital arteries are more reliable in the assessment of forefoot circulation in patients with diabetes. A toe-brachial index of <0.7 or toe pressure of <55mmHg strongly indicates PAD.

Evaluation of the flow signals from arteries in the foot us-
Table 1: Prevalence of PAD

|                | Count | Column N % |
|----------------|-------|------------|
| PAD NOPAD      | 64    | 64.0%      |
| PAD            | 36    | 36.0%      |

ing handheld Doppler revealing a monophasic or absent signal indicated severe ischemia.

Imaging modalities for PAD in diabetes

Doppler ultrasound:

Doppler ultrasound involves combining B-mode ultrasound and pulsed Doppler flow to assess anatomy and physiology of blood flow in specific arterial segments. The entire lower extremity arterial circulation is evaluated by sequential scanning of the abdominal aorta, iliac, femoral, popliteal and tibial arteries. CT angiography: It is a minimally invasive modality to diagnose PAD. It involves the use of iodinated contrast which is injected intravenously. For lower extremity, scanning is done from renal arteries to the distal foot. This is followed by 3D reconstruction of data. The advantage is that it provides high-resolution images of small vessels in the calf. The disadvantage being the use of radiation and potentially nephrotoxic contrast. Contrast-enhanced MR angiography: This is also a low invasive imaging technique for detecting PAD. Gadolinium is used as contrast. Digital subtraction angiography: Intra-arterial DSA is considered as the gold standard for imaging due to the high spatial resolution of arteries. Endovascular revascularization can be performed in the same sitting. The risks involved are arterial puncture, hematoma, extravasation and contrast allergy. Preferably DSA should be performed only when revascularization is planned.

OBJECTIVES

1. To know prevalence of peripheral arterial disease in diabetic foot ulcer.
2. To assess the associated risk factors.
3. To evaluate the appropriateness of triple test and need for routine Doppler in DFU to evaluate PAD.
4. To compare the results of previous similar studies on DFU with PAD.

MATERIALS AND METHODS

ETHICAL COMMITTEE APPROVAL:

- Obtained

PATIENT SELECTION:

- In-patients admitted with isolated diabetic foot ulcer were enrolled into the study after obtaining informed consent.
- They were randomly selected from the surgical wards on every 7th day.
- A total of 100 patients were sampled.
- Study area: Department of General Surgery and Vascular Surgery, Govt. Stanley Hospital, Chennai.

INCLUSION CRITERIA:

- Age group 35-65yrs.
- Both sexes.
- In-patient.
- Known diabetic.
- Isolated foot ulcer.

EXCLUSION CRITERIA:

- Outpatients.
- Known case of peripheral vascular disease during admission.
- Ulcer other than in foot.
- Vasculitis.

PERIOD OF STUDY:

6 months

METHODOLOGY

This is a cross-sectional study which involved type 2 diabetic patients with isolated foot ulcer (DFU). Their history and clinical parameters were noted and documented. A total of 100 patients were evaluated in this study. The patients were subjected to detailed history by administering questionnaires to assess the diabetic foot ulcer and associated risk factors. A thorough clinical examination was carried out followed by a specific test which included distal pulse assessment, ankle-brachial index (ABI) and duplex scan to evaluate PAD. Portable handheld Doppler was used to measuring ABI.

The data were subjected to statistical analysis to find out the association between parameters of interest.

DIAGNOSIS CRITERIA:

Diabetic foot ulcer: A full thickness wound breaching the dermis below the level of ankle in a diabetic patient.

Peripheral arterial disease: Any 2/3 criteria of the following:

1. ankle brachial pressure index (ABI) <0.9
2. absent distal foot pulses
3. abnormal Doppler flow/duplex scan

Fontaine classification:

- Stage I asymptomatic
- Stage IIa intermittent claudication >200m/mild
- Stage IIb intermittent claudication ≤200m/moderate-severe/incapacitating
- Stage III rest pain
- Stage IV ulceration/gangrene

Results

The prevalence of PAD in DFU was found to be 36% (Table 1, fig. 3). It was more prevalent in males and age >40 years and higher with increasing age (Table 2).

PAD was associated almost equally with plantar and dorsal ulcers, more often the whole of the foot was involved (p=0.008) (table 3, fig 4). There is a significant association of PAD with longer diabetic duration (p<0.0001) (table 6, fig 5) with mean disease duration of 10 years.

S. Vijayasarth et al./ International Journal of Surgery and Medicine (2017) 3(3):156-166
### Table 2: Distribution of DFU

|               | PAD | NO PAD | Total | P  |
|---------------|-----|--------|-------|----|
|               | Count | Row % | Count | Row % | Count | Column N % |
| Age           |       |       |       |       |       |            |
| <40           | 4     | 80.0  | 1     | 20.0  | 5     | 5.0        | 0.2 |
| 41-50         | 15    | 78.9  | 4     | 21.1  | 19    | 19.0       |
| 51-60         | 30    | 63.8  | 17    | 36.2  | 47    | 47.0       |
| >61           | 15    | 51.7  | 14    | 48.3  | 29    | 29.0       |
| Sex           |       |       |       |       |       |            |
| Male          | 44    | 65.7  | 23    | 34.3  | 67    | 67.0       | 0.6 |
| Female        | 20    | 60.6  | 13    | 39.4  | 33    | 33.0       |
| Education     | 10t   | 76.9  | 3     | 23.1  | 13    | 13.0       | 0.4 |
|               | 5th   | 100.0 | 0     | 0     | 1     | 1.0        |
|               | nil   | 61.6  | 33    | 38.4  | 86    | 86.0       |
| Religion      | christian | 2 | 33.3 | 4 | 66.7 | 6 | 6.0 | 0.06 |
|               | Hindu | 59    | 68.6  | 27    | 31.4  | 86    | 86.0       |
|               | Muslim | 3 | 37.5 | 5 | 62.5 | 8 | 8.0 |
| Socioeconomic status | low | 60 | 63.8 | 34 | 36.2 | 5 | 5.0 | 0.9 |
|               | middle | 4 | 66.7 | 2 | 33.3 | 19 | 19.0 |

### Table 3: Site of ulcer and PAD

|               | PAD | NO PAD | Total | P  |
|---------------|-----|--------|-------|----|
|               | Count | Row N % | Count | Row N % | Count | column N % |
| Side          |       |       |       |       |       |            |
| left          | 32    | 65.3  | 17    | 34.7  | 49    | 49.0       | 0.8 |
| right         | 32    | 62.7  | 19    | 37.3  | 51    | 51.0       |
| dorsum_plantar| dorsum | 53 | 65.4 | 28 | 34.6 | 81 | 81.0 | 0.5 |
|               | plantar | 11 | 57.9 | 8 | 42.1 | 19 | 19.0 |
| Location of foot | forefoot | 55 | 72.4 | 21 | 27.6 | 76 | 76 |
|               | hindfoot | 3  | 60.0 | 2  | 40.0 | 5  | 5 |
|               | midfoot  | 2  | 50.0 | 2  | 50.0 | 4  | 4 |
|               | whole foot | 4 | 26.7 | 11 | 73.3 | 15 | 15 | 0.008 |
Table 4 Trauma, footwear use and smoking in relation to PAD

|               | NO PAD |          | PAD |          | p  |
|---------------|--------|----------|-----|----------|----|
|               | Count  | Row N %  | Count| Row N %  |    |
| Trauma        | no     | 55       | 64.0 | 31       | 36.0| 0.9 |
|               | yes    | 9        | 64.3 | 5        | 35.7|    |
| Footwear use  | no     | 2        | 40.0 | 3        | 60.0| 0.2 |
|               | yes    | 62       | 65.3 | 33       | 34.7|    |
| Smoking       | no     | 28       | 65.1 | 15       | 34.9| 0.8 |
|               | yes    | 36       | 63.2 | 21       | 36.8|    |

Table 5 Comorbidities and PAD

|               | NO PAD |          | PAD |          | p  |
|---------------|--------|----------|-----|----------|----|
|               | Count  | Row N %  | Count| Row N %  |    |
| DM_Rx         | no     | 9        | 60.0 | 6        | 40.0| 0.8 |
|               | yes    | 54       | 64.3 | 30       | 35.7|    |
| Hypertension  | no     | 46       | 66.7 | 23       | 33.3| 0.4 |
|               | yes    | 18       | 58.1 | 13       | 41.9|    |
| CVA           | no     | 64       | 64.6 | 35       | 35.4| 0.2 |
|               | yes    | 0        | 0    | 1        | 100.0|   |
| CAD           | no     | 60       | 64.5 | 33       | 35.5| 0.7 |
|               | yes    | 4        | 57.1 | 3        | 42.9|    |
| Nephropathy   | no     | 61       | 64.9 | 33       | 35.1| 0.5 |
|               | yes    | 3        | 50.0 | 3        | 50.0|    |
| Retinopathy   | no     | 64       | 64.0 | 36       | 36.0|    |
|               | yes    | 0        | 0    | 0        | 0   | NA  |

Table 6 Diabetic duration and PAD

|               | NO PAD |          | PAD |          |      |
|---------------|--------|----------|-----|----------|------|
|               | Mean   | Median   | SD  | Mean     | Median| SD  |
| Diabetes duration| 7.30   | 5.0      | 5.80| 10.6     | 9.0   | 6.4  | 0.007 |
### Table 7 Distal pulses, Doppler flow and Fontaine grading in PAD

| PAD | NO PAD | PAD | P     |
|-----|--------|-----|-------|
|     | Count  | Row N % | Count | Row N % |     |
| Absent distal pulses | No | 64 | 84.2 | 12 | 15.8 | <0.001 |
| Yes | 0 | .0 | 24 | 100.0 | |
| Doppler flow | Normal | 55 | 100.0 | 0 | .0 | |
| No flow | 0 | .0 | 12 | 100.0 | |
| Monophasic | 0 | .0 | 4 | 100.0 | <0.001 |
| Biphasic | 7 | 25.9 | 20 | 74.1 | |
| Fontaine grade | .00 | 64 | 100.0 | 0 | .0 | |
| 1.00 | 0 | .0 | 7 | 100.0 | |
| Nephropathy | 2.00 | 0 | .0 | 10 | 100.0 | <0.001 |
| 3.00 | 0 | .0 | 8 | 100.0 | |
| Retinopathy | 4.00 | 0 | .0 | 11 | 100.0 | |

### Table 8 Neuropathy and venous disease associated with DFU

| PAD | NO PAD | PAD | P     |
|-----|--------|-----|-------|
|     | Count  | Row N % | Count | Row N % |     |
| Neuropathy | no | 48 | 66.7 | 24 | 33.3 | 0.4 |
| yes | 16 | 57.1 | 12 | 42.9 | |
| venous disease | no | 61 | 63.5 | 35 | 36.5 | 0.7 |
| yes | 3 | 75.0 | 1 | 25.0 | |
| PulseU#L# | no | 0 | .0 | 1 | 100.0 | |
| yes | 64 | 64.6 | 35 | 35.4 | 0.2 |
| Study                  | Year  | Occurrence of PAD | In diabetes | In diabetic foot ulcers |
|-----------------------|-------|-------------------|-------------|-------------------------|
| Shojaie Fard et al    | 2007  |                   |             | 30%                     |
| Probal K. Moulik et al| 2003  |                   |             | 41%                     |
| Ikem R et al          | 2010  |                   |             | 25.7% (>2 absent distal pulses) |
|                       |       |                   |             | 55.4% (ABI with handheld Doppler) |
| UKPDS                 | 2008  | 1.2% (at diagnosis) |             | 11% (after 6yrs)        |
| Mohan et al           | 1995  | South India       |             | 3.9%                    |
|                       |       |                   |             | X (10yrs)               |
|                       |       |                   |             | 3X (20yrs)              |
| Pendsey et al         | 1997  | Central India     |             | 3.9%                    |
|                       |       |                   |             | X (10yrs)               |
|                       |       |                   |             | 2X (>10yrs)             |
| Sahana et al          |       | Eastern India     |             | 34.4%                   |
|                       |       |                   |             | 46%                     |
With only ABI as diagnostic criteria, the occurrence of PAD was 28%, in another 7% cases ABI could not be assessed due to non-compressibility. Combining with Doppler study, the occurrence was 36%.

When >2 absent distal pulses by palpation alone were the criteria, occurrence of PAD was 24%. This may be due to human error, the presence of associated pedal oedema and presence of collaterals. Biphasic flow in Doppler was associated with only 74% of PAD (table 7, fig 6). This could be attributed to human error or hypodynamic circulation in septic patients.

**Discussion**

Previous studies aimed to study the prevalence of PAD in diabetic population irrespective of foot ulcer. This study aimed to assess the burden of PAD in specific subset (DFU) of diabetic patients, and the prevalence is 36%. A south Indian study (CUP) reported the prevalence of peripheral arterial disease as 11.8%.

Mohan et al. have reported on the prevalence of PAD in South Indian diabetics to be 3.9%. They compared their results with that of western studies, where the prevalence ranged between 22% and 45%. Another study from South India reported a lesser prevalence of PAD (13%) among Indians. A similar study from Greece reported the prevalence of 42%.

In a study among Central Indian population by Pendsey et al., Diabetic duration <10 yrs had 30% associated PAD, whereas when duration was >10 yrs, the association doubled to 60%. In our study, PAD prevalence was 36% which was higher in comparison to most of the other studies. This could be attributed to many causes including large percentage of patients with foot complications attending a tertiary care centres like our hospital, specific target population of DFU and triple assessment criteria.

**Conclusion**

The prevalence of PAD in DFU is high in South Indian population. The present study analysed the occurrence of PAD and various factors coexisting with DFU and PAD.
Increasing age and longer duration of diabetes are risk factors for peripheral arterial disease. High prevalence puts DFU at an increased risk of amputation.

The prevalence of PAD is found to be 36%. Patients with high-risk factors associated with PAD like male, age>40 yrs, ulcer involving whole of foot, with diabetic duration> 10yrs, should be dealt with a strong suspicion of PADs

The use of hand-held Doppler will aid early diagnosis reliably and cost-effectively. Moreover, triple assessment criteria involving distal pulse charting, ABI and Doppler study should be followed to diagnose a PAD at the earliest accurately.

Our data emphasise the need for further dedicated research to identify and target this high-risk population of DFU.

Authors’ Statements

Competing Interests

The authors declare no conflict of interest.

References

1. Rhee SY, Guan H, Liu ZM, Cheng SW, Waspadji S, Palames P, Tai TY, Suwanwalaikorn S, Kim YS; PAD-SEARCH Study Group. Multi-country study on the prevalence and clinical features of peripheral arterial disease in Asian type 2 diabetes patients at high risk of atherosclerosis.

2. A. Shojaie Fard, M. Esmaelzadeh, B. Larijani. Assessment and treatment of diabetic foot ulcer

3. Probal K. Moulik, Robert Mtonga, Geoffrey V. Gill. Amputation and Mortality in New-Onset Diabetic Foot Ulcers Stratified by Etiology. Diabetes Care 2003 Feb; 26(2): 491-494.

4. Ikem R, Ikem I, Adebayo O, Sooye D. An assessment of peripheral vascular disease in patients with diabetic foot ulcer. Diabetes Care. 2000 Sep;23(9):1295-300.

5. Premalatha G, Shanthirani S, Deepa R, Markovitz J, Mohan V. Prevalence and risk factors of peripheral vascular disease in a selected South Indian population: the Chennai Urban Population Study. Diabetes Care. 2000 Sep;23(9):1295-300.

6. Sh. Pendsey. PERIPHERAL VASCULAR DISEASE: AN INDIAN SCENARIO

7. Vijay Viswanathan, The Diabetic Foot: Perspectives From Chennai, South India

8. P Sahana, N Sengupta, S Chowdhury. High Prevalence Of Neuropathy And Peripheral Arterial Disease In Type 2 Diabetes In A Tertiary Care Centre In Eastern India. The Internet Journal of Endocrinology. 2010 Volume 6 Number 2.

9. Al-Maskari F, El-Sadig M. Prevalence of risk factors for diabetic foot complications. BMC Fam Pract 2007;8:59.

10. Rabia KI, Khoo EM. Prevalence of peripheral arterial disease in patients with diabetes mellitus in a primary care setting.

11. Guan H, Li YJ, Xu ZR, et al. Prevalence and risk factors of peripheral arterial disease in diabetic patients over 50 years old in China.

12. Newman AB. Peripheral arterial disease: insights from population studies of older adults.

13. Rhee SY1, Guan H, Liu ZM, Cheng SW, Waspadji S, Palmes P, Tai TY, Suwanwalaikorn S, Kim YS; PAD-SEARCH Study Group. Multi-country study on the prevalence and clinical features of peripheral arterial disease in Asian type 2 diabetes patients at high risk of atherosclerosis.

14. Bernstein EF, Fronke A: Current status of non-invasive tests in the diagnosis of peripheral arterial disease. Surg Clin North Am 62:473–487, 1982

15. Elhadd TA, Robb R, Jung RT, Stonebridge PA, Belch JF: Pilot study of prevalence of asymptomatic peripheral arterial occlusive disease in patients with diabetes attending a hospital clinic. Practical Diabetes Int 16:163–166, 1999

16. Hirsch AT, Criqui MH, Treat-Jacobson D, Regensteiner JG, Creager MA, Olin JW, Krook SH, Hunninghake DB, Comerota AJ, Walsh ME, McDermott MM, Hiatt WR: Peripheral arterial disease detection, awareness, and treatment in primary care. JAMA 286:1317–1324, 2001

17. Beckman JA, Creager MA, Libby P: Diabetes and atherosclerosis: epidemiology, pathophysiology, and management. JAMA 287:2570–2581, 2002

18. David G Armstrong. D.P.M., M.D., Kelman Cohen, M.D., Stephane Courric, Ph.D., Manish Bharara, PhD, and William Marston, M.D. Diabetic Foot Ulcers and Vascular Insufficiency: Our Population Has Changed, but Our Methods Have Not

19. Ricco JB et al. The diabetic foot: a review. J Cardiovasc Surg 2013; 54:755-62