REVIEW ARTICLE

Prevalence of Peripheral Artery Disease of the Lower Limbs in Patients with Diabetic Foot Ulcers: A Literature Review

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Abstract

Peripheral artery disease (PAD) is a common condition in diabetic patients. However, its prevalence is not well known in diabetic patients with a diabetic foot ulcer (DFU). We, therefore, aim to determine the prevalence of PAD in patients with DFU by identifying studies that have reported the prevalence of PAD in patients with DFU and provide a brief critical summary. This review shows that the prevalence of PAD in patients with DFU varies widely in studies according to the diagnosis criteria, but is generally higher than the prevalence known in the overall diabetic population and the general population.

Keywords: Peripheral Artery Disease; Diabetes; Diabetic Foot Ulcer; Prevalence

List of abbreviations: DFU: diabetic foot ulcer; PAD: peripheral artery disease

Introduction

Peripheral artery disease (PAD), defined as narrowing or blockage of the arteries that carry blood to the lower limbs, is a public health problem [1]. Nowadays, it is estimated that more than 200 million people have PAD worldwide with a high variability of symptoms. [2]. Its prevalence in the general population is also very variable according to the studies and the diagnostic tools used, but the literature generally agrees that it is strongly related to age. PAD is almost non-existent in the majority of young patients subjects (<40 years), but the prevalence would reach more than 10% (prevalence between 12 and 14%) of the population of people aged between 60 and 70 years, and up to 20% in people over 75 years [2,3].

PAD shares common risk factors with other major cardiovascular conditions, including coronary heart disease and cerebrovascular disease. Thus, smoking is one of its main risk factors, as is diabetes [3]. Even if there are few data summarizing the epidemiology of PAD in diabetic patients according to the diagnostic tools, based on current literature, the prevalence of PAD is 2 to 3 times higher in patients with diabetes than in the general population, and this increased risk can be very increased depending on the sex [3,4]. PAD is 3.5 times more common in men with diabetes and 8.6 times more common in women with diabetes than in people without diabetes [5].

Diabetic foot ulcer (DFU) is one of the major complications of diabetes and is defined as a loss of substance occurring in the lower limbs in people with diabetes, which generally happened progressively on several weeks. This is a specific entity, as at the level of physiopathology, it associates macroangiopathy, microangiopathy, and sometimes infection [6,7]. PAD is the macroangiopathic component of this condition and is unique in this context because of the neuropathy, which is part of the microangiopathy, patients are commonly asymptomatic for a long time, and this exposes them much more to a silent aggravation [8]. If PAD is well described in diabetic patients generally, this pathology remains little described in diabetic patients who already have a DFU. As the result, its prevalence is not well known in this population. We, therefore, conducted this brief literature review summarizing the studies that described PAD in patients with diabetes and DFU.

Methods

Search Strategy

We conducted a comprehensive search in MEDLINE / PubMed to identify potentially eligible studies. We used a combination of the following medical subject headings (MeSH) or key-words: « Peripheral Arterial Disease », « Vascular Diseases », « Diabetes Mellitus», «Diabetes Mellitus, Type 1», «Diabetes Mellitus, Type 2», «Diabetes», «Diabetic Foot»; « Foot Ulcer », « Skin Ulcer », « Leg Ulcer », « Ulcer », « Foot Ulcer », « Leg Ulcer », « Prevalence », « Frequency », « Epidemiology ». Titles and abstracts of all identified articles from the literature search were independently screened by two investigators, and the full texts of eligible articles were further evaluated for final inclusion. For duplicate publications, only the most comprehensive report including the largest sample size was considered.

Selection criteria

All population-based studies that reported the prevalence of PAD in adult patients with DFU, published between January 1, 2000, and March 31, 2021, and available on Pubmed / MEDLINE, were included. Only original research articles were considered. We excluded letters to the editors, commentaries, and studies published in a language other than English. Table 1 gives a summary of the search strategy and Figure 1 presents the summary of the selection process of the articles included in our review.

	Search	Results
#1	"Diabetes Mellitus"[Mesh] OR "Diabetes Mellitus, Type 2"[Mesh] OR "Diabetes Mellitus, Type 1"[Mesh] OR "Diabetic Foot"[Mesh] OR "Diabetes" [Tiab]	683207
#2	"Foot Ulcer"[Mesh] OR "Skin Ulcer"[Mesh] OR "Leg Ulcer"[Mesh] OR "Ulcer"[Mesh] OR "Foot Ulcer" [Tiab] OR "Leg Ulcer" [Tiab]	60451
#3	("Prevalence"[Mesh] OR "Epidemiology"[Mesh] OR "Frequency" [Tiab] OR "Prevalence" [Tiab] OR "Epidemiology" [Tiab]) AND ("Peripheral Arterial Disease"[Mesh] OR "Vascular Diseases"[Mesh] OR "Peripheral Arterial Disease" [Tiab])	1735291
#4	#1 AND #2	11949
#5	#3 AND #4	817
# 6	#5 Limit to - Humans, - English language, and - Period between January 1st 2000 and March 31st 2021.	723

Table 1: Number of studies found with different search equations

Data Extraction and Synthesis

We used an Excel file to collect information on the name of the first author, type of study, year of publication, sample size, the number of male participants, the proportion of type 2 diabetic patients, median or mean age of participants, PAD diagnostic criteria. When not directly provided, the crude prevalence of PAD in patients with DFU was calculated using primary data (number of patients with DFU, number of patients with PAD and DFU). We did not report the prevalence of PAD stratified by risk factors because of insufficient data in included studies. Data were extracted by an investigator (SN) and a second investigator (TG) rechecked for accuracy. The research results were compiled using Zotero Citation Management Software version 5.0.77.

Results

Our search initially identified a total of 723 potentially eligible studies; of which 680 were excluded after review of titles and abstracts. The full texts of the remaining 43 articles were thoroughly reviewed, and 38 were excluded at this level because PAD was not clearly reported in patients with PAD (27 studies) and because of irrelevance (11 studies) (Figure 1). The 5 articles finally selected were published between 2008 and 2019 [9-13]. The number of participants per study ranged from 50 to 1088. Table 2 gives the general characteristics of each included study. Table 3 below presents the prevalence of PAD in the 5 studies included in our review; as well as the diagnostic criteria used. The prevalence of PAD among DFU ranged from 20.00% to 48.13%.

Discussion

The objective of this literature review was to determine the prevalence of PAD in patients with DFU, by summarizing the studies that looked at PAD in diabetic patients with DFU. As main results, we can say that the prevalence of PAD in patients with DFU is variable depending on the diagnostic tools used, but in general much higher than the prevalence in the overall diabetic population [5,9-12]. Regarding diagnostic tools, the ankle brachial index (ABI) remains widely used in the literature for the diagnosis of PAD to the detriment of toe-brachial index and the toe systolic blood pressure.

We identified 5 studies that reported the prevalence of PAD in diabetic patients with DFU. The prevalences reported by these studies vary between 20% and 48.13%, with for the majority (4 studies out of 5), figures above 40% [9-12]. We can note, despite the great variability, a high prevalence in this population, much higher than the 12-14% described in the general population (non-diabetic people), and also much higher than the prevalence in the overall diabetic population. In fact, the prevalence of PAD is estimated to
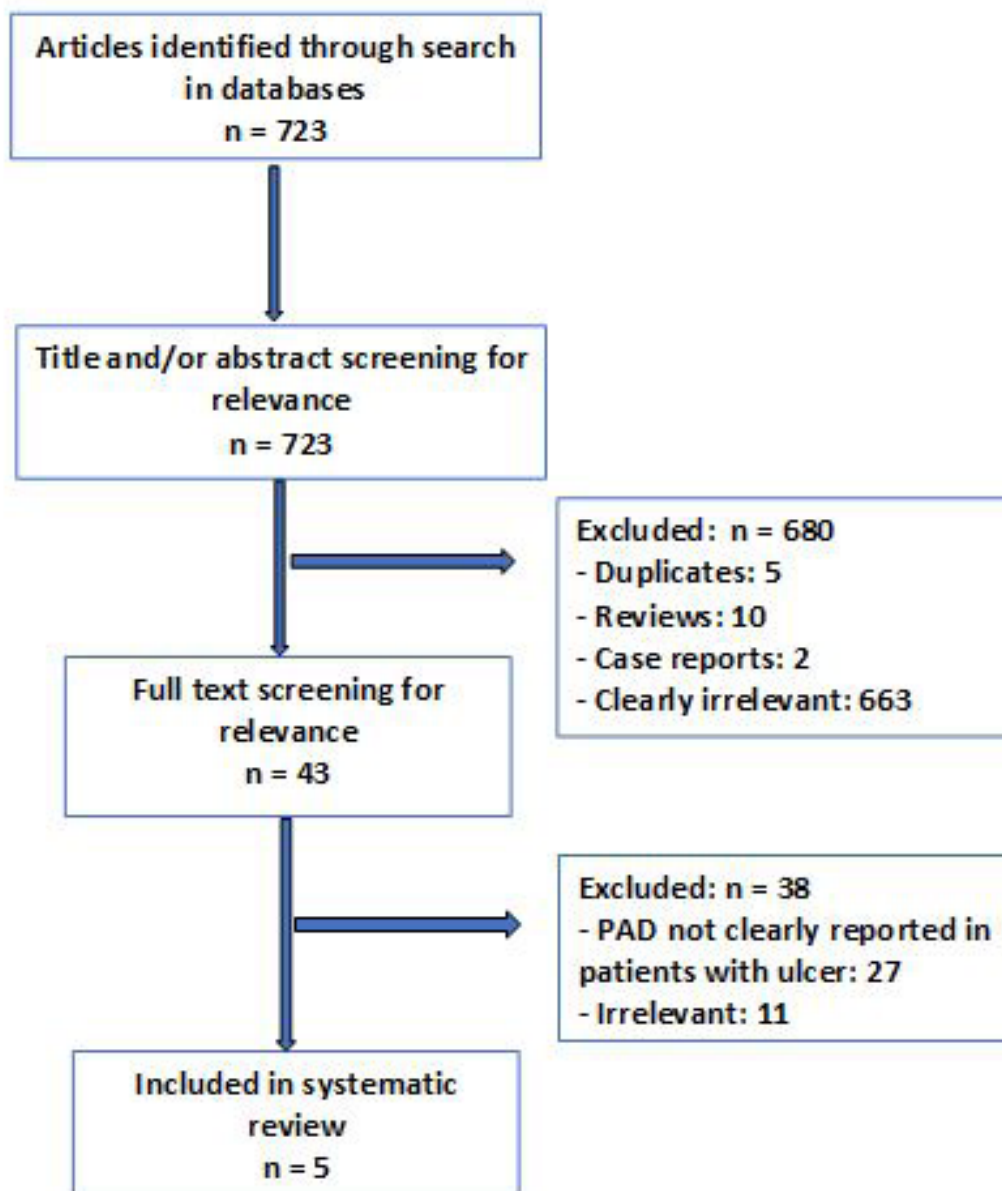
Figure 1: Study selection process

First author, Year	Number of participants with DFU	Men, n (%)	Mean/Median age (Years)	Proportion of patients with type 2 diabetes	Design of study
Megallaa, 2019	180	136 (75.6%)	NP	100%	Cross-sectional
Yufeng, 2015	669	435 (65%)	64	100%	Prospective cohort
Ye, 2013	61	35 (57.4%)	63.9	100%	Prospective cohort
Galkowska, 2009	50	39 (78%)	57.5	86%	Prospective cohort
Prompers, 2008	1088	703 (64.6%)	64.7	NP	Prospective cohort

DFU: Diabetic Foot Ulcer; NP: Not Provided

Table 2: General characteristic of included studies and participants

First author, Year	Number of cases, n (prevalence %)	Diagnostic criteria
Megallaa, 2019	36 (20.0%)	Abnormal ABI (no more precision).
Yufeng, 2015	322 (48.13%)	History of intermittent claudication, rest pain, history of previous lower limb vascular surgery, absent or reduced pedal pulses, ankle-brachial pressure index less than 0.9, or angiography showing significant stenosis in low extremity arteries.
Ye, 2013	26 (42.62)	History of intermittent claudication, a history of previous lower limb vascular surgery, or an ABI of <0.9 in a lower extremity
Galkowska, 2009	21 (42%)	ABI < 0.9
Prompers, 2008	505 (46.42%)	ABI < 0,9 and/or 2-foot pulse absent

ABI: ankle brachial index

Table 3: Prevalence of PAD among patients with DFU in included studies

be between 20% and 30% in the overall diabetic population [5,14]. In addition, the median or mean ages of the participants in the studies included in our review were all less than 65 years. It can therefore be envisaged, in agreement with certain authors, that the prevalence of PAD would be much higher in patients with DFU over 65 years of age [15].

The variability between the results obtained in the different studies could be explained by the type of study on one hand, but above all by the diagnostic tools used. If the abnormal ABI, or values less than 0.9 was an integral part of the definitions of the PAD in all the 5 included studies, it remains nonetheless true that its effectiveness for the diagnosis of PAD in diabetic population in general, is highly questionable [16–18]. Indeed, due to the calcification of the distal arteries (medial calcification or calcinosis) with sometime ABI > 1.4, very common in diabetic patients and making it difficult to take the systolic pressure at the ankle (by incompressibility of the arteries), several recommendations suggested to use either the toe-brachial index (normal cut-off value > 0.75, 0.70 or 0.67 depending on the study), or the toe systolic blood pressure for the diagnosis of PAD in diabetics, or to use a combination of several tools (ABI, toe-brachial index, toe systolic blood pressure, or transcutaneous measurement of oxygen pressure or Doppler waveform analysis of ankle arteries) [15,19,20].

However, this recommendation was not followed in any of the studies included in our review, despite the fact that they were all published between 2008 and 2019. We could therefore legitimately think that the prevalences reported in these studies are underestimated. and that the actual prevalences are much higher. Therefore, it appears that further studies with diagnosis criteria of PAD based on appropriate tools are absolutely necessary to determine the exact prevalence of PAD in diabetic patients with DFU.

To the best of our knowledge, this is the first literature review to summarize the studies that reported the prevalence of PAD in patients with DFU. The results may have clinical implications as they give an alert to put more attention for the early diagnosis and management of PAD in patients with DFU, in other to prevent its complications. However, this study has few limitations. First, we did not report the prevalence of PAD stratified by risk factors because of insufficient data in included studies. Second, the number of studies identified and included was small, highlighting the need of further studies to have strong conclusions. Finally, the diagnosis tool used in included studies were not the most reliable recommended in diabetic patients.

Conclusion

The prevalence of PAD in patients with DFU varies depending on the diagnostic tools used, but is generally much higher than the prevalence in the overall diabetic population and the general population. Despite the fact that its effectiveness is highly questionable in diabetic population due to medial calcinosis, which is common in this population, ABI remains widely used in the literature for the diagnosis of PAD to the detriment of other diagnostic tools, which may be more appropriate.

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

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