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Research Article

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Evaluation of Peripheral Arterial Disease as a Development Factor of Peripheral Neuropathy in Diabetic Patients

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Abstract

Peripheral arterial disease incidence is getting higher in the last years. This is explained due to higher life expectancy of the population, smoking persistence and the high incidence of obese, hypertension e diabetes. In diabetic patients specifically, cardiovascular disease is one of the main cause of morbimortality and the peripheral arterial disease has a huge importance on it. And as known, one of the principal complications of diabetes is the peripheral neuropathy, which may be more aggressive due to peripheral arterial disease in diabetic patients. That is the background for this paper.

Keywords: Peripheral arterial disease; Diabetes; Neuropathy; Peripheral neuropathy

Introduction

The global prevalence of peripheral arterial disease (PAD) is unclear, it is estimated that there are between 8 and 12 million people affected in the United States, corresponding to 4.3% of the population [1,2]. There is a clear and strong association with the increase in the age and it is expected that the incidence of the disease increases in the next years, with the greater life expectancy of the population, the persistence of smoking and the epidemic of hypertensive, obese and diabetic patients; risk factors for atherosclerosis that is the main cause of plaque formation in the arteries and consequent reduction of arterial flow in the lower limbs. The Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II) brings as the main risk factors for PAD, smoking and diabetes mellitus (DM) [3].

The classic symptomatology for PAD is intermittent claudication and occurs as an initial presentation of the disease in 10 to 35% of cases. Atypical pains in the legs can occur in 40 to 50% of cases; as well as asymptomatic patients (20 to 50%) at the time of diagnosis. In only 1 to 2% of cases, critical ischemia with risk of limb loss is the initial presentation of the disease [2].

Because of this multiplicity of clinical presentation, the measurement of the ankle-brachial index (ABI) is the priority method to establish the diagnosis of PAD [2,4]. An ABI less than or equal to 0.90 has a high sensitivity and specificity for the identification of the PAD, and it may be compared the arteriography that would be the gold standard.1 It is recommended to screen for PAD in patients over 65 years of age independent of other cardiovascular risk factors and in patients over 50 years of age with history and DM [2].

Cardiovascular disease is the main cause of morbidity and mortality in diabetic patients and directly or indirectly is the main factor for the high cost that the disease has on the health system [5].

There are several studies in the literature that establish a direct association between DM and PAD [1-3]. In general, intermittent claudication is twice as frequent in diabetic patients when compared to patients who do not have the disease. It is believed that with each 1% increase in glycated hemoglobin (HbA1C) measurement there is a 26% increase in the patient's chance of developing peripheral arterial disease [6].

Several evidences suggest a direct relationship between insulin resistance and cardiovascular risk through a fundamental role in the development of hyperglycemia, dyslipidemia, hypertension and obesity. All of these are great "villains" for the formation of atherosclerotic plaques leading to cardiovascular diseases like coronary insufficiency and PAD. It is estimated that the risk of developing PAD in individuals with insulin resistance increases by 40 to 50% [3].

When we associated DM with PAD, we perceived a greater aggressiveness of the disease when compared to non-diabetic patients. There is an extremely early involvement of medium- and large-caliber arteries (with an initial tendency of involvement for medium-caliber arteries, such as leg arteries [7]) associated with a large complicating factor that is the development of peripheral neuropathy (PN). These associated factors increase the risk of a patient with diabetes being subjected to amputation in the lower limb by 5 to 10 times when compared to non-diabetic patients [3].

One of the main complications affecting diabetic patients is peripheral neuropathy [5]. There are two theories to explain the development of PN in the diabetic patient: (a) vascular theory, where vasa nervorum microangiopathy occurs that would lead to local ischemia causing nerve damage and (b) biochemical theory, where nerve damage occurs due to the increase of toxic substances such as sorbitol and fructose and depletion of myonisitol [8,9].

Such changes lead to a gradual loss of tactile and painful sensitivity, making the feet vulnerable to trauma (loss of protective sensitivity). They also lead to atrophy of the intrinsic musculature of the foot, causing imbalance between the flexor and extensor muscles, triggering osteoarticular deformities. These deformities alter the dynamics of points of greater pressure in the feet, increasing the susceptibility to ulcerations [8,9].

Clinical examination is the most effective, simple and low cost diagnostic method for the diagnosis of PN. It is essential to perform a proper clinical history, where the patient can refer to sensitive symptoms such as burning, pricking, needling, numbness, feeling of cold and / or heat, cramps and pain. At physical examination we can see the atrophy of the intrinsic musculature of the feet and osteoarticular deformities; as well as the evaluation of the plantar protective sensitivity, through the 10 g monofilament test, tactile, thermal and vibratory sensitivity evaluations and the aquileu reflex [5,8]. It is expected to make the diagnosis as early as possible so that one can act in the manner more adequate and consequently to avoid the appearance of ulcers, local worsening with onset of infection and even amputation of the area [8]. To do so, annual clinical screening is recommended for all diabetic patients [5].

It is rarely necessary to use invasive tests for diagnosis, and clinical examination is fundamental for diagnosis; but there are limitations such as the subjectivity inherent in the tests, the lack of cooperation and/or understanding of the patients. Another factor to consider is the fact that clinical tests detect peripheral neuropathy in the presence of symptoms; a fact that may be late for earlier treatment and consequent better prognosis.

As one of the currently accepted causes of PN is of microangiopathic origin, we try to detect, in this study, a correlation between these entities that can act in the development of PN through the hostile environment that a patient with PAD presents; through chronic and gradual deficit of the blood supply to the lower limbs.

Objective

To evaluate the importance of Peripheral Arterial Disease as a developmental factor of Peripheral Neuropathy in patients with Diabetes Mellitus.

Method

The patients treated at the Angiology and Vascular Surgery outpatient clinic of the Municipal Polyclinic of the Continent, belonging to the Florianópolis City; within the Public Health System (SUS) in medium complexity for the region of Greater Florianópolis.

We evaluated 26 individuals, divided into 3 groups:

- Group 1: control; without DM and without PAD, totalizing 9 individuals.

- Group 2: patients with DM and without PAD, totaling 10 individuals.

- Group 3: DM and DAOP patients, totaling 7 individuals.

In these 3 groups, presence or absence of NP was evaluated.

Inclusion criteria

Included in the study were:

- Patients with type 2 DM who fit the diagnostic criteria recommended in this study (groups 2 and 3);

- Patients with PAD stages 0, 1, 2 and 3 of Rutherford and with ABI <0.90 (group 3);

- Patients over 18 years of age (for all 3 groups);

- Volunteers who agree to participate as a control group and are over 18 and healthy.

Exclusion criteria

The following were excluded from the study:

- Patients with PAD stages 4, 5 and 6 of Rutherford, that is, patients with decompensation of the disease, which characterizes a vascular urgency and are not attended in an outpatient setting;

- Patients with ABI>1.4 for any group;

- Impossibility to measure ABI, to perform tests for peripheral neuropathy.

3.3 Diagnosis of Diabetes Mellitus

The diagnosis of DM was defined according to the guidelines of the American Diabetes Association (ADA) [5]. Glycated hemoglobin (HbA1C) greater than or equal to 6.5% was used as the diagnostic criterion.

Diagnosis of peripheral obstructive artery disease

The diagnosis of PAD was defined according to the recommendations of the ACC / AHA Guidelines [2] and TASC II [3] through the completion of ABI for diagnostic confirmation [2]. A patient presenting ABI less than 0.90 diagnosed PAOD [2,3].

Diagnosis of peripheral neuropathy

The diagnosis of peripheral neuropathy was defined in two ways:

Semmes-Weinstein test (10 g monofilament test): It consists of pressing, with the tip of a nylon (monofilament) yarn of 10 grams, some areas of the surface of the foot in order to test the sensitivity to this pressure [9].

The three points to be researched were:

- in the plantar region; in the distal phalanx of the hallux;

- in the plantar region, at the head of the first metatarsus;

- in the plantar region, at the head of the fifth metatarsus.

Scales for diagnosis of diabetic distal polyneuropathy: neuropathic symptom score (NSS): 1. Have you experienced pain or discomfort in your legs?

(A) If NO, interrupt the evaluation (B) If YES, continue evaluation

2. What kind of sensation bothers you?

(Describe the symptoms if the patient does not name any of these).

(A) Burning, numbness and tingling – 2 points

(B) Fatigue, cramps and pruritus – 1 point

3. What is the most frequent location of this (symptom described)?

(A) Foot – 2 points

(B) Calf - 1 point

(C) Other location - 0 point

4. Is there any time of day when this (symptom described) increases in intensity?

(A) During the night – 2 points

(B) During the day and at night – 1 point

(C) Only during the day - 0 point

5. Did this (symptom described) already wake you up at night?

(A) Yes - 1 point

(B) Not - 0 point

6. Any maneuvers that you are able to reduce this symptom (described)?

(Describe the maneuvers to the patient if he does not name any of these).

(A) Walk – 2 points

(B) Stand – 1 point

(C) Sit or lie down - 0 point

Score: 3 and 4 - mild symptoms, 5 and 6 - moderate and 7 to 9 severe symptoms [10,11].

Neuropathic compensation score (NCS): NCS is derived from examination of the achileus reflex and the vibratory, painful and thermal sensitivity of the hallux bilaterally.

The sensory modalities should be scored with (0) if present or (1) if reduced / absent; and the reflexes as (0) if normal or if present with reinforcement or (2) if absent, for each side. Score: 3 to 5 - mild neuropathic signs; 6 to 8 - moderate and severe neuropathic signs and 9 and 10 - severe neuropathic signs.

Diagnostic criteria for peripheral neuropathy: The minimum acceptable criteria for the diagnosis of peripheral neuropathy, using NSS and NCS, are:

- moderate signs with or without symptoms or

- mild signs with moderate symptoms.

Mild signs alone or with mild symptoms are not considered adequate for the diagnosis of peripheral neuropathy.

Statistical analysis

After collecting the data pertinent to the research, these were stored in a computerized database and analyzed in software such as the SPSS® (Statistical Package for Social Sciences®) of IBM®.

Ethical aspects

This research was submitted to the Ethics and Research Committee of the City of Florianópolis (data collection site) and also to the Ethics and Research Committee on Human Beings of UFSC. For all the patients, the Informed Consent Term was presented for this study, and the inclusion of the patient will only occur if the patient accepts their participation in the research. Anonymity has always been maintained.

Results

As general data we observed, of the 26 individuals evaluated, 17 men and 9 women, with a mean age of 61.4 ± 7.5 years (Tables 1-6). We had an HbA1c of 6.6% ± 0.73 and an ITB of 0.94+-0.12. Table 1 shows the same data and their variations by groups.

	Group 1 (n=9)	Group 2 (n=10)	Group 3 (n=7)
Sex (M / F)	06-Mar	08-Feb	03-Apr
Age	62.2 ± 5.0	63.0 ± 8.33	58.2 ± 9.21
HbA1C	5.78 ± 0.23	7.16 ± 0.41	7.07 ± 0.39
ABI	0.99 ± 0.06	1.01 ± 0.09	0.77 ± 0.03
p>0.05.			

Table 1: Demographic, clinical and laboratory data of the groups: As for the diagnosis of peripheral neuropathy through the Semmes-Weinstein test, we observed a similar incidence between groups 2 and, see Table 2.

	Group 1 (n=9)	Group 2 (n=10)	Group 3 (n=7)
Positive	0 (0%)	4 (40%)	3 (42,9%)
Negative	9 (100%)	6 (60%)	4 (57,1%)
p>0.05.			

Table 2: Semmes-Weinstein test: Regarding the diagnosis of peripheral neuropathy through the questionnaires, we have the following data.

	Group 1 (n=9)	Group 2 (n=10)	Group 3 (n=7)
Negative (0-2)	9 (100%)	2 (20%)	2 (28,6%)
Mild (3-4)	0 (0%)	5 (50%)	2 (28,6%)
Moderate (5-6)	0 (0%)	3 (30%)	2 (28,6%)
Severe (7-9)	0 (0%)	0 (0%)	1 (14,2%)
p>0.05.			

Table 3: Neuropathic Symptom Score (NSS).

	Group 1 (n=9)	Group 2 (n=10)	Group 3 (n=7)
Negative (0-2)	9 (100%)	4 (40%)	3 (42,8%)
Mild (3-5)	0 (0%)	6 (60%)	2 (28,6%)
Moderate (6-8)	0 (0%)	0 (0%)	2 (28,6%)
Severe (9-10)	0 (0%)	0 (0%)	0 (0%)
p>0.05.			

Table 4: Neuropathic Compensation Score (NCS).

	Group 1 (n=9)	Group 2 (n=10)	Group 3 (n=7)
Presence	0 (0%)	3 (30%)	3 (42,8%)

Absence	9 (100%)	7 (70%)	4 (57,2%)
p>0.05.			

Table 5: Peripheral Neuropathy diagnosis (NSS + NCS).

	Group 1 (n=9)	Group 2 (n=10)	Group 3 (n=7)
Presence	0 (0%)	5 (50%)	3 (42,9%)
Absence	9 (100%)	5 (50%)	4 (57,1%)
p>0.05.			

Table 6: Reflects the final diagnosis, both by the Semmes-Weinstein test and the questionnaires, showing a higher percentage in group 3. Peripheral Neuropathy final diagnosis

Discussion

The cardiovascular system is a complex system and must be evaluated with numerous subsystems that interact with each other (mainly with the autonomic nervous system) [12].

In our study we observed the importance of the questionnaires for evaluation of peripheral neuropathy, although it may be a confounding factor, most of the patients were able to differentiate the symptoms of PN and PAD. And we can clearly see a tendency to observe PAD as an aggravating factor / development of peripheral neuropathy in diabetic patients.

Brownrigg et al evidenced an association between PN (which was evaluated only with reduced sensitivity to the 10g monofilament test) and increased cardiovascular risk in diabetic patients without previous history of such events, recommending population measures to reduce morbidity and mortality [13].

The effect of the AADDITION Denmark Study on the reduction of NP and PAD in diabetic patients at 6 years of follow-up was not observed [14]. It is one of the few studies in the literature that points out such a finding.

The Kyong Shin study assessed patients with PAD and PN through the questionnaires also used in this research and also with electrophysiological study, evidencing alterations in PN scales and electrical conduction studies, pointing out a special role for the NSS and NCS questionnaires in the evaluation of PN in PAD patients; the same criterion used in this study [15].

Once again reinforced the use of the scales. That is, PN had a higher incidence in the subgroup with PAD than with DM, showing that the deficit of the blood supply chronically to a region may leave a ground for worsening PN in diabetic patients. We emphasize the importance of early clinical examination in diabetic patients, as well as the questionnaires for neuropathy and the monofilament test. With this, we hope to reduce the morbidity and mortality rate in this population.

As a limiting factor in our study, we have a small sample of patients studied, due to the limitations of access of these patients to the specialized outpatient clinic. With a larger sample, we could have statistical significance in the cross data.

Another limiting factor to be highlighted is the bias of the questionnaires. Occasionally the answers can be confusing or even misinterpreted. One point that could help to solve this limitation would be the electroneurophysiological study in the lower limbs, but with a high cost for the health system.

Conclusion

An increase in the incidence of peripheral neuropathy was observed in the subgroup of diabetic patients with peripheral arterial disease compared to the group of patients with diabetes alone. This data is extremely important because we try to prevent or detect both entities early (PAD and PN) so that we can reduce morbidity and mortality in these groups.

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