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One-year follow-up of patients screened for lower extremity arterial disease

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ABSTRACT

Background: We tested a screening algorithm of lower extremity arterial disease (LEAD) for general practitioners (GPs) with a 1-year follow-up examination. Besides, patients were referred for vascular specialists to verify the presence of LEAD with specific tools.

Method: 327 patients were followed-up. We recorded the differences in the anamnesis. Ankle brachial index was re-measured. Patients repeated walking-test. We compared our results to the specialist control.

Results: Specialists confirmed LEAD in 73.7%. 63.1% reported IC symptoms. Our screening algorithm had a sensitivity of 92%, and a specificity of 96%, positive and negative predictive values were 91% and 96%. Most LEAD-positive patients received LEAD-specific medications (94.2%) and antiplatelet therapy (91.7%). Improvement in walking test were shown in 96 cases (29.3%).

Conclusion: Our screening algorithm combined with specialist control has proven to be an easy-to-apply, and efficient methodology for GPs with excellent sensitivity and specificity in identifying individuals at risk of LEAD.

Keywords: LEAD, PAD, intermittent claudication, screening, murky zone, light zone

INTRODUCTION: BACKGROUND

Cardiovascular diseases are the leading cause of death in Europe, placing a significant social and economic burden on societies [1]. Lower extremity arterial disease (LEAD) generally develops as part of atherosclerosis and not as an isolated condition [2].

LEAD is a common condition, and its occurrence increases exponentially above the age of 55 and has a prevalence of nearly 20% above the age of 65 years [1-6]. It is key to note that most LEAD patients are asymptomatic, meaning that the illness will remain undiscovered unless targeted screening is carried out [7-9].

Early diagnosis of the condition is important, as the risk of experiencing cardiovascular (CV) or cerebrovascular events are two-four times higher for those who suffer from vascular diseases compared to the age matched healthy population [3,7,9,10]. 20% of patients with intermittent claudication (IC) symptoms suffer myocardial infarction (MI) or stroke within 5 years of the appearance of symptoms in which, 10-15% of these events ends in fatal outcome [11,12]. For this reason, the early diagnosis and treatment of this disease could result in a significant improvement in death prevention [2,3,10].

Ankle brachial index (ABI) is a routine examination in Hungarian primary health care; however, in our experience, it is carried out relatively rarely. This is especially important as the number of amputation cases in Hungary are manifold compared to that of international peers published in the literature [13,14]. The main reason behind this is because patients with LEAD-positivity generally remains undiagnosed at the level of primary care practitioners [15-19]. Guidelines could be particularly important in establishing the diagnosis, however according to a recent study there are several discrepancies between the different guidelines, especially concerning the diagnosis and treatment of asymptomatic patients [20]. There is a limited adherence concerning the risks and complications of LEAD, which further worsens the chance of early detection [12,17,21-25].

The number of epidemiologic studies on the occurrence of LEAD in Hungary is low. As part of the Hungarian hypertensive screening program (ÉRV–"For the protection of our blood vessels"), the prevalence of LEAD in patients who were being screened for hypertension were estimated to be 14.4%. The screening of 21,892 patients (average age: 61.45 years) was carried out in hypertension-centers where the examination was conducted by specialists [26,27].

During our 2015-2017 screenings, we grouped patients into two zones according to the uncertainty of the diagnosis based on the tools normally available in a general practitioner's (GP's) office. Patients were placed in the *light zone* if they could be diagnosed with great confidence using only the tools and

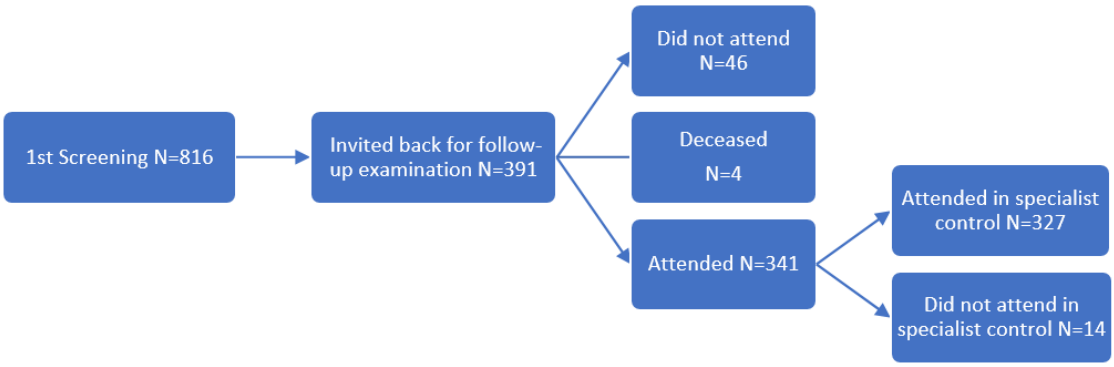

Figure 1. Flow chart of the patients of the 1st screening and the follow-up examination

equipment available in a GP's office. Clear LEAD-positive and clear LEAD-negative patients were both in this zone. A significant 23% were placed in the clear LEAD-positive group according our first examinations. On the other hand, patients for whom GP tools proved to be insufficient to obtain a definitive diagnosis were placed in the *murky zone.*

Nearly 25% of the examined patients were identified as *murky zone* patients, indicating the difficulties that GPs face when diagnosing LEAD [25]. Patients who only showed symptoms under strain and were healthy according to the ABI values, as well as those with non-compressible-arteries where the measured ABI values were over 1.4, were both placed in this zone. We named this groups *ABI-negative, symptomatic*, and *non-compressible-artery* groups.

The mentioned patient categories (clear-LEAD-positive; ABI-negative, symptomatic, and non-compressible artery groups) were subject to a second, follow-up screening one year after the first screening, except the patients placed in the clear-LEAD-negative group. Our main aim with this examination was to assess the percentage of changing or remaining of patients in the different groups following our control tests. In addition, we took the opportunity to consult for a second opinion from an angiologist or vascular surgeon (referred in the following: *specialist*) to corroborate the results of our screening algorithm to determine its sensitivity, specificity, positive and negative predictive values, as well as its applicability in primary health care settings.

Research on the incident of LEAD in general practices are scarce. Lower extremity arterial disease is a common disease in general practices in Hungary, although it is very rarely recognized. As a result, the number of complications due to LEAD is much higher in Hungary than in Western European countries. The aim of our research was to develop and test a cost and time efficient, and highly reliable screening methodology for general practitioners to help early detection and treatment of LEAD.

METHODOLOGY

For our first screenings between 2015 and 2017 we advertised the screening one month prior to the examination at GP offices, randomly chosen from the capital, major cities, and small villages [25]. The target demographic included men and women aged 50+. We screened every patient aged 50 and above with at least one major vascular risk factor or CV events in their personal or family medical history, as well as everyone aged 65 and above having their age as the only major risk factor. As we mentioned earlier, we categorized the screened patients to two zones and two-two subgroups according to their ABI values, presence of IC complaints, and the diagnostic difficulties for the GPs. We referred the results to the GPs, and we recommended risk-lowering medication therapies, as well as to refer the screened patients to a vascular specialist for further examinations [25].

Methodology of the Follow-Up Examination

We invited back 391 patients from the original cohort of 816 patients of the first screening for our follow-up examination, 1±0.23 years on average after the first screening appointments. We enrolled all the patients for a follow-up examination who were placed in one of the following categories during the first screening: *clear-LEAD-positive*, *ABI-negative-symptomatic*, and *non-compressible-artery groups*. Patients who were *clear-LEAD-negative* were not listed for follow-up. Of those patients who were listed, 46 did not turn up and 14 turned up but did not have a follow-up examination carried out by a vascular specialist. There were four cases of death in the examined population during this time. Therefore, we utilized data for our calculations from 327 patients. The evolution of patient numbers is shown in **Figure 1**.

Grouping details and patient data from the follow-up examination are presented in **Table 1**. Steps of the first and follow-up examination are shown in **Figure 2** and **Figure 3**.

At the follow-up examination, patients were first asked to fill in the Edinburgh claudication questionnaire (ECQ) again, which is a validated and frequently used tool for LEAD and IC screening [22]. By doing so, we examined changes in the symptoms of patients with clear signs of LEAD and those without them.

We recorded in the anamneses any differences that were observed in comparison to the examination one year before, paying special attention to CV events that have occurred since then, medication adjustments, and changes in main risk factors (smoking, diabetes, hypertension, hyperlipidemia) in particular, whether smoking had been given up or not.

We repeated the same measurements that were obtained during the first examination. We calculated the body mass index values for every patient. We took fasting state blood sugar and total cholesterol measurements from capillary blood, using testing strips (accu-check active equipment, >6.0 mmol/l as cut-off value for blood sugar). After five minutes of rest, we measured the systolic blood pressure in all four limbs (arteria brachialis, arteria tibialis posterior and arteria dorsalis pedis, respectively), using an eight MHz continuous-wave Doppler-ultrasound device (MultiDOPPY, Medicad, Hungary)

Table 1. Patients who attended the one-year follow-up examination, in their original grouping

Groups	Light zone		Murky zone	
	Clear-LEAD-negative	Clear-LEAD-positive	ABI-negative-symptomatic	Non-compressible-artery
ABI	0.9-1.4	<0.9	0.9-1.4	>1.4
Symptoms	Negative	Negative or positive	Positive	Negative or positive
Occurrence on the 1st screening (n=816) n (%)*	425 (52)	185 (23)	109 (13)	97 (12)
Distribution of patients in the follow-up examination**	0 (0)***	151 (46,1)	96 (29.3)	80 (24.6)
Men (%)	0 (0)	93 (61.6)	35 (36.5)	26 (32.5)
Women (%)	0 (0)	58 (38.4)	61 (63.5)	54 (67.5)
Average age (±SD)	Non-relevant	66.6±7.4	67.2±8	68±8.4

Note. *Occurrence during our first screening between 2015-2017; **Distribution of patients during our follow-up examination, one year after the first screening; & ***Patients categorized to the clear LEAD-negative group were not invited back for the follow-up examination

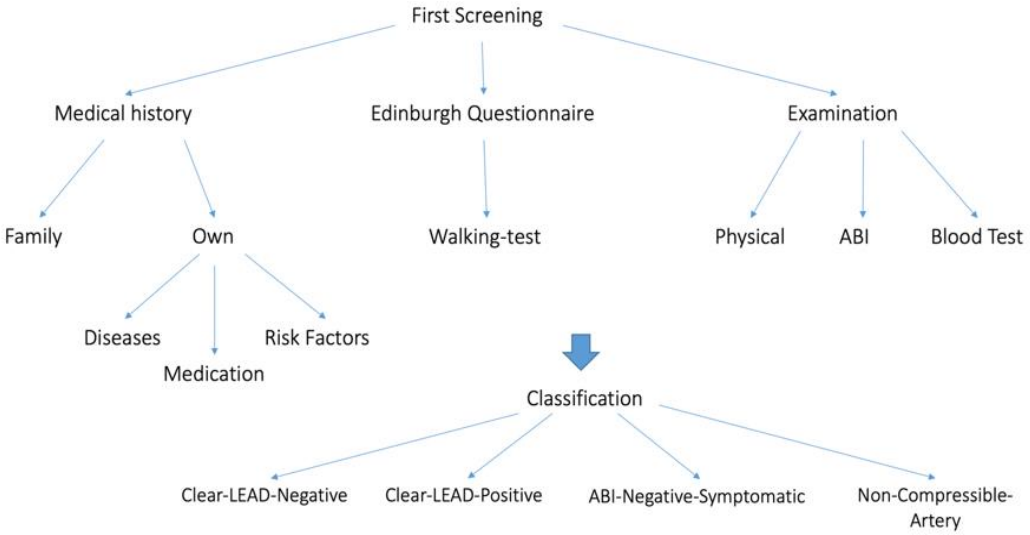

Figure 2. Methodology and phases of the first screening

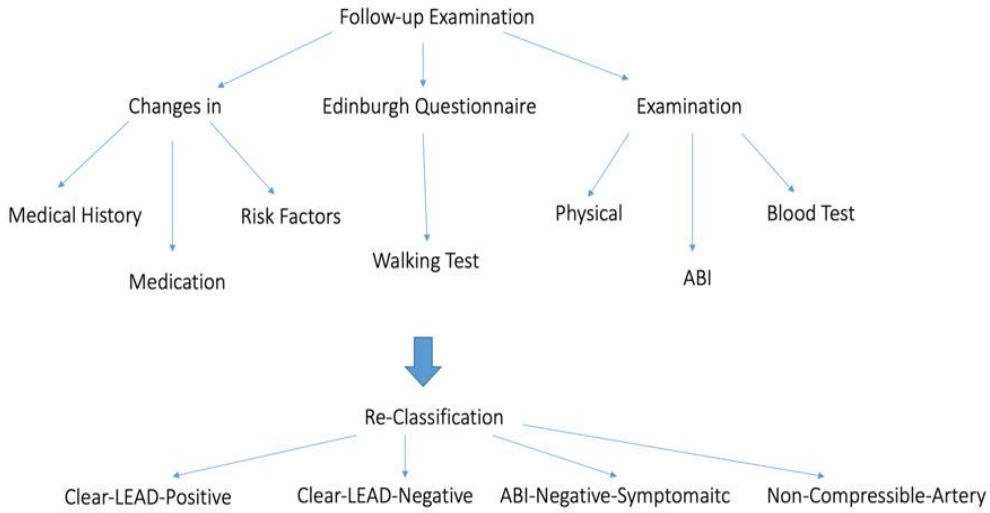

Figure 3. Methodology and phases of the follow-up examination

according to the current guidelines [7,9]. We used the data obtained to calculate the ABI once more.

Patients who showed signs of IC earlier according to the ECQ were asked for a repeated walking test. They were asked to walk on a previously measured track, at normal pace. We recorded the pain-free and maximum walking distance, noted any changes compared to before, and re-evaluated the patients' Fontaine classification. We made patients walk for a maximum of six minutes.

The Role of the Specialist Control

After our first screening we advised GPs to refer their patients to vascular specialists for further control examinations. Vascular specialists have much more sophisticated tools, so patients can have a much more accurate diagnosis in cases where the GP's tools would be insufficient for making a definitive diagnosis.

Table 2. Patients invited for follow-up examinations

	Invited for follow-up	Attended			Did not attend/deceased
	All	All	46/4	All	
All N (%)	391 (100)	341 (100)	341 (100)	341 (100)	46/4
Men N (%)	174 (44.5)	159 (46.6)	159 (46.6)	159 (46.6)	
Women N (%)	217 (55.5)	182 (53.4)	182 (53.4)	182 (53.4)	
Average age (years)	66.7±8	67.1±7.8	67.1±7.8	67.1±7.8	

Table 3. Group changes based on our follow-up examination

Original groups*	Results of the 1st screening	Results of the follow-up examination			
		Clear-LEAD-positive	Clear-LEAD-negative	ABI-negative, symptomatic	Non-compressible-artery
Clear-LEAD-positive N (%)	151 (100)	122 (80.8)	29 (19.2)	0 (0)	0 (0)
ABI-negative, symptomatic N (%)	96 (100)	8 (8.3)	31 (32.3)	57 (59.4)	0 (0)
Non-compressible-artery N (%)	80 (100)	0 (0)	25 (31.3)	0 (0)	55 (68.7)
All patients N (%)	327 (100)	130 (39.8)	85 (26)	57 (17.4)	55 (16.8)

Note. *The cohort of patients, who show up at the follow-up examinations

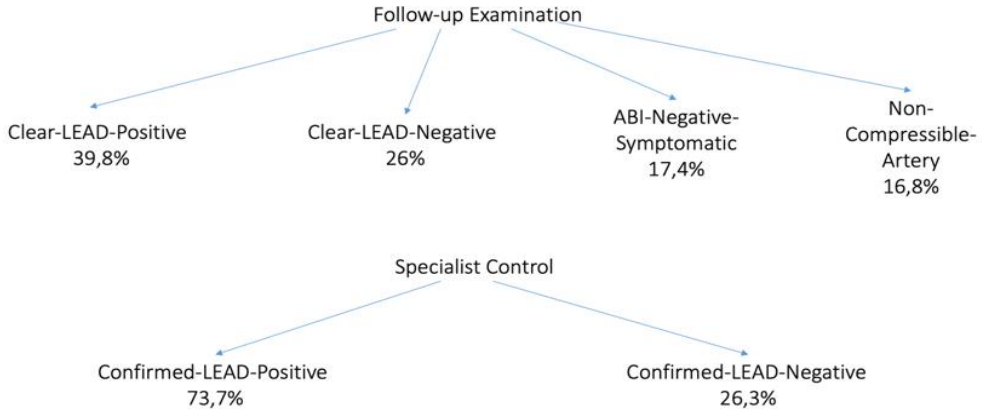

Figure 4. Changes in the classification after the follow-up examination and specialist control

For our calculations we only used the data of patients, who were referred to a vascular specialist to prove the existence or non-existence of the presence of LEAD. Thus, in the final diagnosis, the opinion of the vascular specialist was considered the gold standard for comparing the results of our follow-up examination. We recorded whether the patients had been examined by a specialist, whether the preliminary diagnosis by the GP was corroborated or refuted, and whether LEAD-specific medication was prescribed. After the specialist control we re-grouped patients to two main categories: *confirmed-LEAD-positive* and *confirmed-LEAD-negative.*

From comparing the results of our follow-up examination with the results of the specialist control we were able to evaluate the sensitivity, specificity, and positive and negative predictive values of our screening method, and thus its applicability for screening LEAD in primary healthcare. All participants received a written informed consent before involvement in the study. Everyone signed and agreed the participants' consent, which was performed according to the Helsinki Declaration. Our study has been approved by all the authors and the Research Ethics Committee of the Semmelweis University (285/2015).

RESULTS

We invited back 391 patients, from whom 341 show up. We had to exclude 14 among the appeared patients, because of the lack of specialist control. We evaluated the data of 327 patients (47% male, 53% female). The average age was 67.1±7.8 years. These data are summarized in **Table 2**.

Changes in the Original Groups after the Follow-Up Examination

In **Table 3**, we summarized the changes of patients in the original groups after our follow-up examination. According to our follow-up, 26% of the cohort of patients moved to the clear-LEAD-negative group. It is worth to mention, that more than 8% of the ABI-negative-symptomatic group moved to the clear-LEAD-positive group, based on the deterioration of their ABI values. We will explain the reasons in the discussion.

Changes in the Original Cohort after the Specialist Control

GPs referred the patients to vascular specialist, to determine with the more specific tools, if the patients are affected by LEAD or not. After the specialist control we re-grouped patients to two main categories: *confirmed-LEAD-positive* and *confirmed-LEAD-negative.* Changes in the classification after the follow-up examination and specialist control were summarized in **Figure 4**.

Results of the specialist control are summarized in **Table 4**. We compared the results of the specialist control with the results of our follow-up examination to evaluate the sensitivity, specificity, and positive and negative predictive values of our screening method. This results also summarized in **Table 4**.

Table 4. Group changes based on specialist control and reliability indicators

	All examined cases	Confirmed-LEAD-positive	Confirmed-LEAD-negative	False negative	False positive	Positive predictive value	Negative predictive value	Sensitivity	Specificity
	Occurrence in the original cohort N (%)	N (%)	N (%)						
All patients N (%)	327 (100)	241 (73.7)	86 (26.3)	22	23	0.91	0.96	0.92	0.96
Clear-LEAD-positive N (%)	151 (46.2)	125 (82.8)	26 (17.2)	7	4	0.97	0.79	0.95	0.87
ABI-negative-symptomatic N (%)	96 (29.3)	72 (75)	24 (25)	9	2	0.97	0.73	0.89	0.92
Non-compressible-artery N (%)	80 (24.5)	44 (55)	36 (45)	6	17	0.72	0.86	0.88	0.68

Table 5. Risk factor and medication changes in the confirmed LEAD-positive group compared to the results of the 1st screening

	Clear-LEAD-positive	ABI-negative-symptomatic	Non-compressible-artery	Confirmed-LEAD-positive*
	1st screening (N=186)	1st screening (N=110)	1st screening (N=99)	Specialist control (N=241)
Risk factors	**All**	**All**	**All**	**All**
Smoking N (%)	84 (45)	32 (29)	20 (20)	89 (36.9)
Smoking cessation (N)	0	0	0	3
Hypertonia N (%)	161 (87)	89 (81)	79 (80)	214 (88.8)
Diabetes N (%)	67 (36)	39 (35)	36 (37)	127 (52.7)
Hyperlipidaemia N (%)	128 (69)	66 (60)	47 (80)	175 (72.6)
Obesity N (%)	129 (69)	82 (75)	81 (82)	174 (72.2)
Ischemic heart disease N (%)	48 (26)	52 (47)	38 (38)	96 (39.8)
Chronic kidney disease N (%)	9 (5)	11 (10)	9 (9)	14 (5.8)
Stroke N (%)	16 (9)	14 (13)	2 (2)	29 (12)
MI N (%)	21 (11)	25 (23)	6 (6)	31 (12.9)
Intermittent claudication N (%)	137 (74)	110 (100)	28 (28	152 (63.1)
CI Men N (%)	74 (54)	39 (35)	9 (32)	83 (54.6)
CI Women N (%)	63 (46)	71 (65)	19 (68)	69 (45.4)
Became complaint-free (N)	Non-relevant	Non-relevant	Non-relevant	47

Note. MI: Myocardial infarction; CI: Intermittent claudication; *Confirmed-LEAD-positive cases in the cohort of the 327 patients of the follow-up examination, according to specialist control

Table 6. Changes in medication

	Clear-LEAD-positive	ABI-negative-symptomatic	Non-compressible-artery	All (confirmed-LEAD-positive)
	1st screening (N=186)	1st screening (N=110)	1st screening (N=99)	Specialist control (N=241)*
Medication	**All**	**All**	**All**	**All**
Antihypertensive	147 (79)	92 (84)	71 (71)	212 (88)
Lipid-lowering	58 (31)	42 (38)	23 (23)	170 (70.5)
Antidiabetic	54 (29)	32 (29)	22 (22)	81 (33.6)
Antiplatelet therapy	72 (39)	45 (41)	28 (28)	221 (91.7)
LEAD-specific	41 (22)	34 (30)	8 (8)	227 (94.2)
Diuretics	5 (3)	15 (14)	7 (7)	38 (15.8)

Note. *Specialist control: Confirmed-LEAD-positive cases according to a vascular specialist's examinations

Specialist control confirmed LEAD-positive diagnosis in 73.7% of the patients. 52.3% were male and the average age was 67.3±8.0 years. 63.1% of the patients reported IC symptoms.

The highest number of patients was confirmed in the clear-LEAD-positive group (82.8%), the lowest in the non-compressible artery group (55%). Compared with the results of our follow-up examination, we got high sensitivity (0.92), specificity (0.96), positive (0.91), and negative (0.96) predictive values. We had the highest sensitivity in the clear-LEAD-positive group (0.95), the highest specificity in the ABI-negative-symptomatic group (0.92). The positive predictive values were equally high in the clear-LEAD-positive and ABI-negative-symptomatic groups (0.97), the negative predictive value was the highest in the non-compressible-artery group (0.86). We had the lowest sensitivity (0.88) and specificity (0.68) in the former group.

Risk Factors and Medication in the Confirmed-Lead-Positive Group Compared to the Original Groups

We summarized the changes in risk factors and medication of the patients after the specialist control in **Table 5** and **Table 6**.

There was a significant increase in the overall prescription of risk-lowering therapies: due to the confirmed diagnosis of LEAD, 94.2% received prescription for LEAD-specific medication, 70.5% for lipid-lowering therapy, and 91.7% for antiplatelet therapy, which were prescribed following the specialist control.

Table 7. Changes in walking test results and Fontaine-classification, LEAD-specific medication

The occurrence of intermittent claudication (IC) between the follow-up patients N (%)	152 (63,1) *
The walking distances increased** (N)	96
The walking distances decreased (N)	64
No changes in the walking distances (N)	23***
Became complaint-free for the control (N)	12
By what percentage did walking distances increase on average for improving patients? (%)	11,5
By what percentage did walking distances decrease on average for deteriorating patients? (%)	5,9
Daily walking exercise beside medication**** (N)	21
LEAD-specific medication All (N)	227
Cilostazol N (%)	169 (74,4)
Pentoxyohyllin N (%)	58 (25,6)
Fontaine-stages (N) 1st screening/follow-up examination	224/241
I	24/88
II a	81/43
II b	110/99
III	3/5
IV	6/6

Note. *199 patients attended from the 1st screening who previously had IC complaints; **Pain-free and maximum walking-distances; ***In five cases continuous pain remained, in 13 cases there are still no complaints at a calm pace; **** Not supervised

Active smoking was present in 36.9% between the patients of the confirmed-LEAD-positive group. The most common risk factor remained hypertension with 88.8%, diabetes was present in nearly 33%, and hyperlipidaemia and obesity with 73-73%. IC was present with 63% of the patients.

Changes in IC Symptoms

The majority of patients (63.1%) complained of symptoms of IC based on the ECQ. Changes in walking test results and Fontaine-classification are summarized in **Table 7**.

An improvement in walking test results were shown in 96 cases (walking distances increased and 12 patients became complaint-free). However, a decrease in walking distance was observed in 64 cases and no change occurred in 23 cases. 21 patients practiced walking-exercises regularly in addition to medication. Prescribed medications were generally (74.4%) cilostazol-containing LEAD-specific medicine. The number of patients in Fontaine IIa and IIb classes decreased while Fontaine I patients increased reciprocally. Patients in Fontaine III also increased, whereas Fontaine IV numbers remained unchanged.

DISCUSSION

Between 2015 and 2017, during the first round of screening involving 816 patients, we found that the prevalence of LEAD was 23% in the examined population, which corresponds to the published data in the literature [3,25,28-32].

According to previous studies the incidence of LEAD is higher among men [2,3,30], but a recent study draws attention to the fact, that the number of affected women could be nearly equal to this [30,32]; however, because the asymptomatic appearance of LEAD is higher among women, they often remain unrecognized due to a lack of symptoms [33]. After the specialist control, 73.7% of patients fell into the confirmed LEAD-positive group, where there were roughly equal number of women and men.

Reliability of the Screening Method

Based on the screening algorithm that we developed, GPs referred a significant number of patients for specialist control after receiving the results of the first screening. Comparing the results, for patients in the light zone who were classified as *clear-LEAD-positives*, the specificity, sensitivity and predictive values of the screening test were exceptionally high. The low number of false-negative patients in the clear-LEAD-positive group also demonstrates the applicability and practicability of this screening algorithm. The high *specificity* and *sensitivity* of the screening algorithm in this group confirmed our hypothesis that the use of this screening methodology enabled GPs to identify vulnerable patients who has low ABI values with high accuracy.

We observed similarly high values in the two groups of the murky zone. In our first publication, we highlighted that the actual number of patients who were diagnosed as LEAD-positive solely based on ABI measurements could be less than that of the truly LEAD-positive cases [25]. This hypothesis was confirmed by our findings. In the ABI-negative-symptomatic group specialist controls confirmed LEAD-positivity status in 75% of the patients despite the fact that they only experience symptoms under higher stress (as a result of a small or nearly invisible constriction), thus having to move them into the confirmed LEAD-positive group. The specificity and sensitivity of the screening were 90% on average for patients who were in the *ABI-negative-symptomatic group*. The false-negative value here indicates that patients who initially turned out to be false-negative based on the follow-up examinations but were later diagnosed as confirmed LEAD-positive following specialist control. An explanation for this could be that those patients in the follow-up examinations who were initially diagnosed as LEAD-positive by a specialist after the first screening had already received LEAD-specific medications which reduced or even fully eliminated the symptoms by the time the follow-up examination happened. This again emphasizes the importance of approaching the process of diagnosing LEAD with multiple methods, as diagnosis based solely on ABI can be misleading and leave patients mistakenly categorized as negative despite their symptoms, which can ultimately result in patients unable to receive adequate treatment [17,23,34,35].

The other group in the murky zone included patients with *non-compressible artery*. It was previously mentioned that in their case, the available resources for GPs were insufficient to decide if the calcification had narrowed the lumen of the artery or not. During the specialist control, 55% of these patients were moved to the confirmed LEAD-positive group. The number of

false-positive patients were the highest in this group. And the specificity, sensitivity and predictive values of the screening test were the lowest in this group. This indicates that there could be more difficulties for GPs to correctly diagnose LEAD in this subgroup. Although this screening algorithm was unable to provide a definitive diagnosis in these cases, however, it could raise the GPs' suspicion and thus refer these patients to a specialist for further examination. Therefore, the screening aids in identifying the patients at risk and the follow-up of these patients are especially important [36,37].

Changes in Medication and Risk-Lowering Therapies

According the present guidelines, in the prevention and treatment of LEAD risk lowering therapies are especially important [1,7,9,38]. As one of the most important achievements of our screenings, a significant proportion of patients have been prescribed risk-reducing therapies by the GPs or other specialists (angiologist, cardiologist, diabetologist) between the first screening and the follow-up examinations.

Based on the results of the follow-up examination 91.7% in the confirmed LEAD-positive group received antiplatelet therapy, compared to 27% registered during the first screening. There was even a more significant increase in the prescription of LEAD specific medication: this increased from 11% to 90.4%. The prescribed were the cilostazol-containing medications.

Occurrence of Risk Factors in the Confirmed-LEAD-Positive Group

Our results concerning the occurrence of major risk factors among patients with LEAD were consistent with the results of similar studies [11,30,32,39].

Patients in the confirmed LEAD-positive group still had a reasonably high rate of active smokers. Previous studies highlighted the difficulty quitting smoking for at patients with LEAD [40-43]. Despite the advice to quit smoking, there were only a negligible number of cases that gave up smoking after the first screening.

Hyperlipidemia was proved as one of the most important risk factors for developing LEAD worldwide [3,30,32,44,45]. It was present in 72.6% of patients in the confirmed-LEAD-positive group after control by the specialist (in contrast, only 11.4% of these patients had diagnosis for this disease after the first screening). At the time of the follow-up examination, 70.5% of patients received lipid-lowering therapy, as opposed to only 27% receiving treatment after the first screening.

Hypertension remained the most common risk factor among confirmed-LEAD-positive patients, however, according to two recent studies its connection is weaker to LEAD, than to coronary artery disease [30,32,38]. Thus, all LEAD-positive patients with hypertension received treatment with antihypertensives. However, these therapies were only new for a very small portion of patients as most patients already have pre-existing treatment regimen for hypertension.

Diabetes has one of the strongest connections for developing LEAD with severe complications [30,46-48]. Current recommendations therefore recommend antidiabetic therapy to prevent severe complications [1,7,9]. The presence of diabetes could accelerate the development of non-compressible arteries, which could increase the risk of a future amputation [36,37]. The occurrence of diabetes mellitus was increased. The reason for this increase is that among these cases, 22% were newly diagnosed diabetics. Following the first screening, 23% of patients received anti-diabetic therapy and this figure was increased by nearly 11% after the follow-up examination.

Obesity is another key risk factor of LEAD [10,49]. Nearly three-quarters of the examined population were obese while the highest rate of obesity was seen among patients originally belonged to the non-compressible-artery group.

Changes in IC Symptoms and Fontaine Classification

Due to the increased number of risk-reducing therapies and LEAD-specific medication prescriptions, the functional status of patients also showed a marked improvement over the time-period between the two screening appointments.

63.1% of patients reported IC symptoms based on the ECQ. Compared with the first screening, increased pain-free and maximum walking distance were recorded in a significant number, where 12 of them became symptom-free as a result of medication therapy. Walking distances decreased in 64 cases, the reason for that could be the lack of proper medication therapy, or the effect of the persistent major risk factors.

Supervised exercise therapy could improve walking distances and has a primary importance in the treatment of LEAD [50-54]. However, due to pain, most of these patients do not adhere to the practice of walking [55]. In addition, a small percentage of this population achieved the minimum recommended levels of physical activity. 21 patients did additional walking exercises on a daily basis, however there was no opportunity to supervise it by specialist care. Thus, the results of this should be treated with caution.

In regard to the Fontaine classification, the number of patients in stages IIa and IIb decreased, while patients in stage I increased reciprocally. This positive change could be attributed to the increased walking distance achieved through medication therapies. According to our expectations, the greatest improvements were measured with patients taking cilostazol-containing medications, which is consistent with the results of other previous studies in the literature [26,56-59].

CONCLUSIONS

The two-round screening method combined with specialist control has proven to be an easy-to-apply and easily reproducible screening method for GPs. In addition, it has an excellent specificity and sensitivity. The majority of patients received new risk-reducing medications following specialist visits, where their symptoms have decreased or disappeared as a result. Screening results obtained by GP circumstances were mostly identical with the control results by specialists. Despite the difficulty of establishing a definitive diagnosis for murky zone patients due to a lack of sufficient tools, screening in such patients can still provide clues about the possibility of an underlying vascular illness where the GP may refer the patient to a specialist for further examination and thus, facilitate an earlier diagnosis and slow down the progression of the disease. Considering this, this screening methodology could be exceptionally useful and beneficial for screening LEAD in a GP setting, where early recognition along with prompt and adequate treatment could decrease the presence of risk factors and improve the quality of life and long-term prospective for patients.

Limitations

Because of the voluntary nature of the screening, it is possible, that the more health-conscious patients appeared on our screenings. Moreover, the screening cannot be said to be nationally representative, as most of our examinations focused on the region of Northern Hungary, which is one of the most infrastructurally backward regions of the country. These two facts could explain the higher proportion of LEAD-positive patients.

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