



Internal iliac artery stenosis: diagnosis and how to manage it in 2015

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OPEN ACCESS

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Specialty section:

This article was submitted to Vascular
Medicine, a section of the journal
Frontiers in Cardiovascular Medicine

Received: 08 April 2015

Accepted: 18 August 2015

Published: 01 September 2015

Citation:

Mahé G, Kaladji A, Le Faucheur A
and Jaquinandi V (2015) Internal iliac
artery stenosis: diagnosis and how to
manage it in 2015.
Front. Cardiovasc. Med. 2:33.
doi: 10.3389/fcvm.2015.00033

Lower extremity arterial disease (LEAD) is a highly prevalent disease affecting 202 million people worldwide. Internal iliac artery stenosis (IIAS) is one of the localization of LEAD. This diagnosis is often neglected when a patient has a proximal walking pain since most physicians evoke a pseudoclaudication. Surprisingly, IIAS management is reported neither in the Trans-Atlantic Inter-Society Consensus II nor in the report of the American College Foundation/American Heart Association guidelines. The aims of this review are to present the current knowledge about the disease, how should it be managed in 2015 and what are the future research trends.

Keywords: internal iliac artery stenosis, management, methods, surgery, peripheral artery disease

Lower extremity arterial disease (LEAD) is a highly prevalent disease mainly caused by atherosclerosis, a systemic disease process that alters the normal structure and function of the vessels (1). Thus, LEAD risk factors are well identified: non-modifiable risk factors such as age, gender, and heredity; and modifiable risk factors such as smoking, hypertension, diabetes, and dyslipidemia (2).

It is common to define proximal LEAD and distal LEAD depending on the ischemia area supplied by the damage artery (3). Twenty to 50% LEAD patients are asymptomatic (4). When the claudication is present, the distal LEAD is typically characterized by calf pain and relies on either common iliac lesion and/or external iliac artery and/or femoropopliteal lesions (2). Contrary to distal LEAD, the proximal LEAD is characterized by lower back, hip, buttock, or thigh pain and relies on either common iliac and/or isolated internal iliac lesions (2, 3, 5, 6).

Internal iliac artery stenosis (IIAS) is one of the possible localizations of atherosclerosis on the arterial tree. This disease is often missed in the diagnosis process when a patient has a proximal walking pain. Indeed, a pain that appears during walking and involves the lower back, hip, buttock, or thigh suggests either proximal claudication or proximal pseudoclaudication (2). Claudication is a vasculogenic pain whereas pseudoclaudication results from diseases such as lumbar spinal stenosis, hip osteoarthritis, venous congestion, or bone metastasis, sciatica, and so on (7–9) (**Figure 1; Table 1**).

Unfortunately, due to nearly similar symptoms, the vascular origin is largely neglected when a patient has a proximal limb pain since most physicians evoke a pseudoclaudication (9).

Several explanations can be proposed. First, claudication was historically defined by a fatigue, discomfort, or pain occurring in calves during effort due to exercise-induced ischemia and which is relieved with rest (10). Second, ankle-brachial index (ABI) is used as the standard for the diagnosis of LEAD (11). Indeed, LEAD is defined by an ABI ≤ 0.90 (11), but the latter can remain within normal limit in case of isolated IIAS (12) or superior gluteal artery lesions (13). Finally, IIAS management is reported neither in the Trans-Atlantic Inter-Society Consensus II (TASC II) nor in the report of

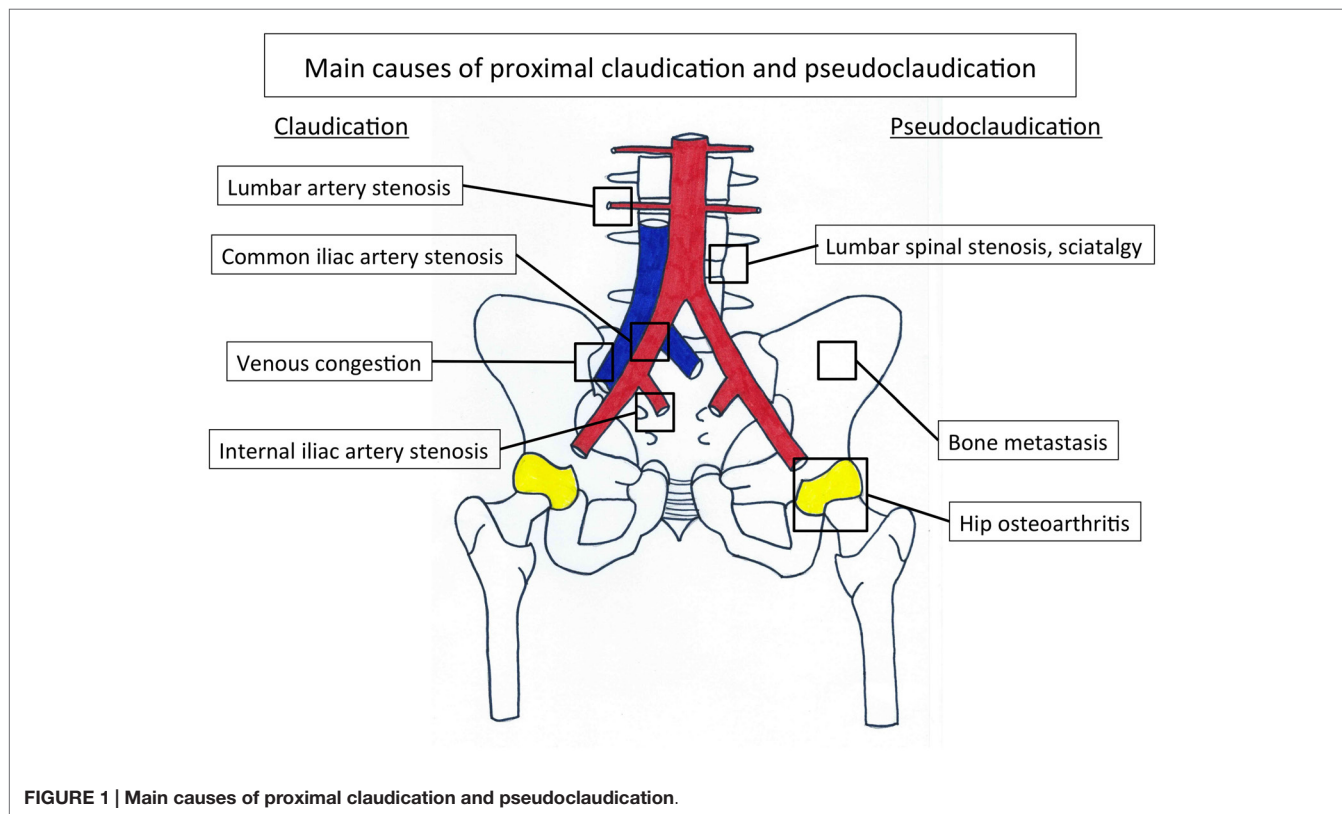


FIGURE 1 | Main causes of proximal claudication and pseudoclaudication.

TABLE 1 | Differential diagnosis of internal iliac artery stenosis.

Potential disease	Location of pain or discomfort	Characteristic discomfort	Exercise-induced discomfort	Effect of rest	Effect of body position	Other characteristics
Arterial atherosclerotic disease (intermittent claudication)	Buttock, hip, lower back, thigh	Cramping, aching, fatigue, weakness, or frank pain	Yes	Rapid relief with rest	None	Presence of cardiovascular risk factors
Spinal stenosis	Buttock, hip, thigh	Cramping, aching, fatigue, weakness or tingling or clumsiness	Variable	Relieved by sitting or changing position	Relief by lumbar spine flexion (sitting or stooping forward)	History of back problems
Hip osteoarthritis	Buttock, hip, thigh	Aching	Variable	Not rapid relief (and may be present at rest)	More comfortable sitting	Related to activity level, weather changes
Bone metastasis	At the bone level	Aching	Variable	Not rapid relief (and may be present at rest)	Avoid direct pressure on bones	History of cancer
Venous congestion	Thigh, groin	Tightness, bursting	After walking	Subsides slowly	Relief by elevation	History of deep veins thrombosis at the inferior cava or iliac level; presence of varicoses

Adapted from Hirsh et al. (2) and White C (9).

the American College Foundation/American Heart Association (AHA) guidelines (4, 11).

Incidence and Prevalence of IIAS

Incidence and prevalence of IIAS have not been established in general population. Although isolated IIAS is probably rare,

IIAS is often associated with common iliac artery stenosis. The prevalence of proximal claudication is 5–14% in patients with mild-to-moderate distal LEAD (5, 14), appears high among patients with patent aortobifemoral bypasses (15), approximately 28%, and nearly 35% of patients after bilateral internal iliac artery (IIA) embolization prior to endovascular aneurysm repair (16).

Symptoms and Functional Impairment

The main symptom is the lower back, hip, buttock, or thigh claudication defining the proximal claudication, a fatigue, discomfort, or pain occurring in specific muscle groups alimenting by IIA during effort due to exercise-induced ischemia and which is relieved with rest (2, 6). However, the presentation of proximal claudication is often atypical and may mimic other non-vascular diseases that may induce misleading diagnoses (5, 9) (**Figure 1**). Moreover, the pain may appear at rest when IIAS is severe, and can lead even to gluteal necrosis (17). Finally, IIAS induces different functional impairments: walking impairment that leads to work disability, and sexual impairment as erectile dysfunction (16, 18). These two impairments reduce the patient quality of life (19–21). To avoid these impairments, although it is challenging with conventional non-invasive tests, it is of interest to diagnose the disease in order to diminish the delay of diagnosis, which is currently of 2 years, when the disease is not associated with distal LEAD (14).

Strategies and Evidences

Clinical Evaluation

Patients typically report a gradual decrease of their walking capacity, which is evaluated by the maximal walking distance (2). Claudication traditionally stops within 10 min after the end of walking (22, 23). The maximal walking distance often impairs either with the increase of the arterial stenosis or the deterioration of the functionality of the collateral network, which both diminish blood flow delivery to muscles irrigated by the IIA (6). The maximal walking distance can be evaluated by different methods: medical interview, questionnaires (24), standardized treadmill evaluation which is recommended (11), 6-min test when patients are unable to walk on a treadmill (11), and recently GPS technology (25).

Physical examination should rule out a pseudoclaudication (9). Hip osteoarthritis is associated with pain typically in the groin provoked by internal or external rotation of the hip (8). The hip pain often radiates in the knee, whereas lumbar spinal stenosis is associated with discomfort that radiates beyond the spinal area into the buttocks (7). Furthermore, active lumbar extension may induce discomfort that is relieved with flexion. Finally, pain due to bone metastasis is aggravated by direct pressure on bones.

Different questionnaires have been developed to help clinicians to distinguish vascular claudication from pseudoclaudication. The most used are the World Health Organization (WHO)/Rose Questionnaire, the Edinburgh claudication questionnaire, and the San Diego questionnaire (22, 26, 27) [Readers will find these entire questionnaires in the same article published in *Vascular Medicine* (28)].

Pulse palpations, auscultation of lower limbs, and abdomen looking for a vascular breath have to be done on patient (2).

The ABI measurement defined as the highest systolic pressure in the dorsalis pedis or posterior tibial artery divided by the highest arm pressure measurement can be helpful, although it may be insensitive in the case of isolated internal iliac lesions (11, 12).

The penile pressure measurement has been suggested to be an alternative method to diagnose proximal arteries stenosis (29).

Penile-brachial index (PBI), defined as penile pressure over the highest systolic brachial ratio, is rarely used in routine investigations, and its accuracy is 69.3% (95% confidence interval: 58.6–78.7) for the detection of an arterial stenosis or occlusion on at least one side as compared with the arteriograms (30). Therefore, a normal PBI (>0.60) cannot rule out the presence of lesions on the internal iliac arteries (30).

Classical Imaging

Duplex ultrasound (DUS) of the vascular abdominal circulation may help to evoke the diagnosis (11) (**Table 2**). Indeed, the sensitivity and specificity of DUS to assess aorto-iliac disease (stenoses) when compared with arteriography are 91% and 93%, respectively (31). However, no study has evaluated the sensitivity and specificity of DUS in the specific assessment of IIAS. Sensitivity and specificity obtained for the aorto-iliac disease are probably higher than those expected in the assessment of IIAS because the IIA is deeper and more difficult to evaluate with DUS. Some authors have also suggested assessing indirectly the IIA by studying the gluteal artery with DUS but the results have to be confirmed on larger population (32).

Computerized-tomodensitometric angiography (CTA) and magnetic-resonance angiography (MRA), “semi-invasive” exams, can be an option for the diagnosis of IIAS especially when a patient is candidate for revascularization (**Figure 2**) (11).

Digital subtraction angiography, an invasive technique remains the gold standard for the diagnosis of IIAS with oblique projections to avoid missing the diagnosis of IIAS (11). Indeed, the external iliac artery hides the IIA at the level of gluteal canal on antero-posterior views (33). Moreover, as suggested by the American College of Cardiology (ACC) and the AHA, when conducting a diagnostic lower extremity arteriogram in which the significance of an obstructive lesion is ambiguous, trans-stenotic pressure gradients should be obtained (2). The cut-off of mean resting gradient to determine whether or not the stenosis is significant is discussed ranging from 5 (34) to 10 mm Hg (35). The peripheral fractional flow reserve (p-FFR), which is defined as the ratio of the mean pressure distal to the stenosis to the mean aortic pressure at hyperemia, could also be a valuable test (36–38).

Functional Assessment of IIAS During Walking

Both exercise transcutaneous oxygen pressure (Exercise-TcPO₂) and exercise near-infrared spectroscopy (NIRS) measurements performed on treadmill have been proposed to estimate exercise-induced ischemia at the buttock level (3, 37, 39, 40). Exercise-TcPO₂ reflects skin oxygenation whereas NIRS reflects muscles oxygenation. Nevertheless, at the buttock level at least, the skin and muscles below are vascularized by the same arterial trunk, the internal artery. Compared in the same study, NIRS and Exercise-TcPO₂ provided, respectively, 55% (range, 41.6–67.9%) and 82% (range, 69.6–90.5%) accuracy (95% confidence interval) to predict the presence of arteriographically proven lesions (41). The Exercise-TcPO₂ has 79% sensibility and 86% specificity to detect significant lesions (stenosis ≥75%) in the arterial tree of the pelvic circulation when the cut-off point is lower than –15 mm Hg (3) (**Figure 3**). The Exercise-NIRS provides a non-invasive method of measuring tissue oxygen saturation [StO(2)].

TABLE 2 | Different tests that can be used to diagnose the internal iliac artery stenosis.

	Non-invasive test					Invasive test		
	ABI/Post-exercise ABI	Continuous-wave Doppler waveforms	Penile-brachial index	DUS	CTA/MRA	Exercise-NIRS	Exercise-TcPO ₂	Digital subtraction angiography
Arteries assessed (direct or indirect assessment)								
Aorta	Yes/Indirect	Yes/Direct	Yes/Indirect	Yes/Direct	Yes/Direct	Yes/Indirect	Yes/Indirect	Yes/Direct
Common iliac artery	Yes/Indirect	Yes/Direct	Yes/Indirect	Yes/Direct	Yes/Direct	Yes/Indirect	Yes/Indirect	Yes/Direct
Internal iliac artery	No	No	Yes/Indirect	Yes/Direct	Yes/Direct	Yes/Indirect	Yes/Indirect	Yes/Direct
External iliac artery	Yes/Indirect	Yes/Direct	No	Yes/Direct	Yes/Direct	Yes/Indirect	Yes/Indirect	Yes/Direct
Limb artery	Yes/Indirect	Yes/Direct	No	Yes/Direct	Yes/Direct	Yes/Indirect	Yes/Indirect	Yes/Direct
Type of assessment	Functional	Functional	Functional	Functional and morphological	Morphological	Functional	Functional	Morphological
Patient's condition	at rest	at rest	at rest	at rest	at rest	during exercise	during exercise	at rest
Availability	Every center	Every center	Specialized center	Every center	Every center	Specialized center	Specialized center	Every center
Cost	+	+	+	++	+++	++	++	+++

ABI, ankle-brachial index; DUS, duplex ultrasound; CTA, computerized-tomodensitometric angiography; MRA, magnetic-resonance angiography (MRA); Exercise-TcPO₂, exercise transcutaneous oxygen pressure; NIRS, exercise near-infrared spectroscopy.

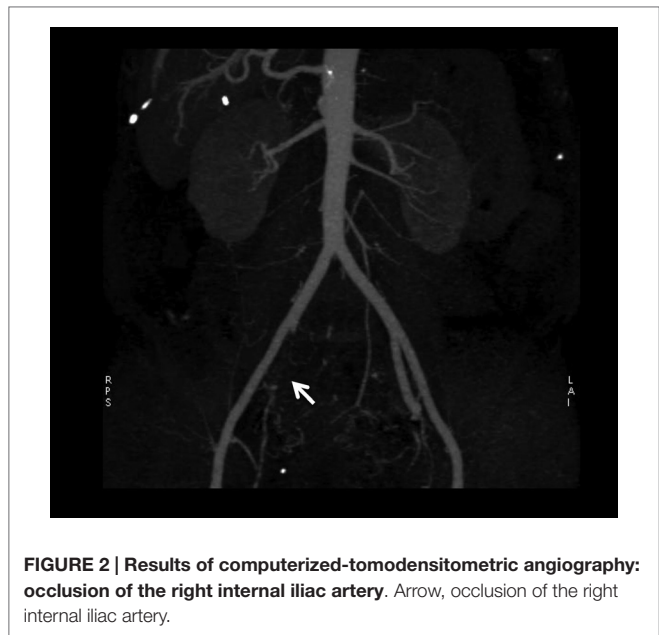


FIGURE 2 | Results of computerized-tomodensitometric angiography: occlusion of the right internal iliac artery. Arrow, occlusion of the right internal iliac artery.

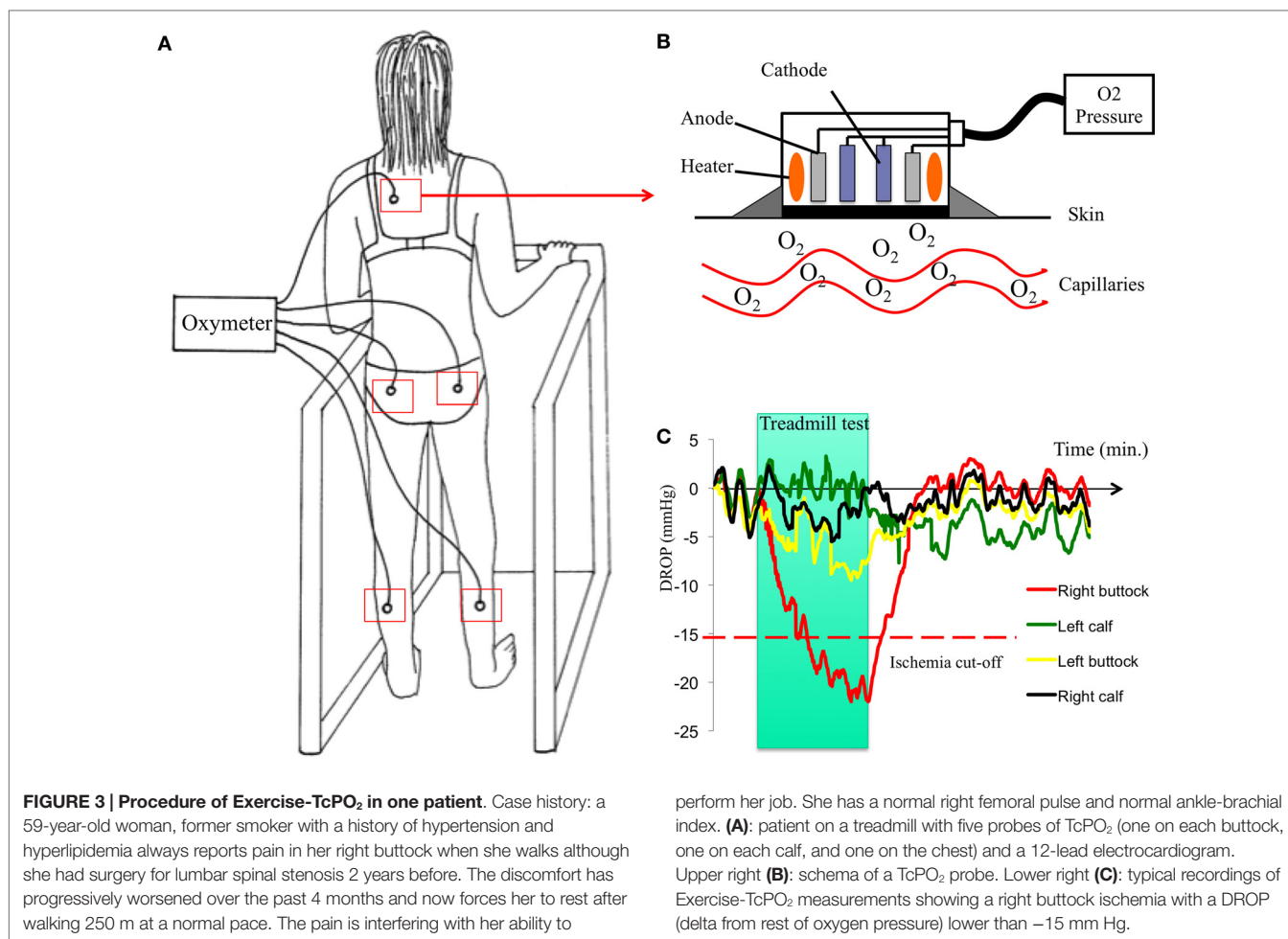
Different parameters have been proposed using different treadmill protocols (39, 42, 43). Time to 50% of StO(2) recovery to baseline [T(50)] >70 s yielded a sensitivity of 89% and a specificity of 85% for PAD (42). To predict a significant lesion on the arteries toward the hypogastric circulation, a recovery time >240 s was considered as a cut-off value (39).

Management

There is no specific management of IIAS (4, 11). The medical management is the same as for LEAD. To reduce adverse cardiovascular events such as stroke and acute myocardial infarction, lifelong therapy should include elimination or modification of atherosclerotic modifiable risk factors such as smoking, hypertension, diabetes mellitus, and dyslipidemia (11). Daily exercise and favorable diet limiting the atherosclerotic process are recommended (9, 11). Revascularization indication depends on the patient functional impairment (e.g., normal work or other activities important for the patient) after a lack of adequate response to exercise therapy and well-conducted medical treatment (11). The morphology of the lesion is also an important criterion for the choice of the revascularization (4, 11).

Lifestyle Intervention and Atherosclerotic Risk Factors Modifications

Smoking cessation is needed because continuing smoking compared with smoking cessation was found to increase the risk of death, myocardial infarction, and amputation (44). Patients who are smokers or former smokers should be asked about tobacco use status at every visit and be assisted to stop (11). The WHO study group has proposed that guidelines for the prevention of cardiovascular disease include a diet low in fat (<30% of calories) and saturated fatty acids (<10% of calories) and devoid of trans fatty (saturated) acids. Salt intake should be reduced to 5 g/d (90 mmol/d). Consumption of a broad range of fruits, vegetables (>400 g/d corresponding to five intakes per day) is



encouraged (45). Thus, dietary assessment has to be done in clinical practice with specific validated tool (46).

Patients with proximal claudication could benefit from home-based exercise program or supervised exercise training with at least three sessions of 35 to 45 min per week for a minimum of 12 weeks (11, 47). Therefore, physical activity has to be highly recommended (45).

Medical Treatment

In addition to lifestyle changes, antiplatelet agents as aspirin in daily doses of 75–325 mg is recommended as safe and effective therapy to reduce the risk of myocardial infarction, stroke, and vascular death (48). Clopidogrel (75 mg per day) can be an alternative antiplatelet therapy since it appears to be more effective than aspirin in preventing ischemic events in patients with symptomatic LEAD without increasing bleeding events (CAPRIE study) (49).

Lipid-lowering drugs are also recommended for all LEAD patients to achieve a goal of LDL cholesterol level less than 100 mg per dL, and when risk is very high, a LDL cholesterol target of less than 70 mg/dL is preferable (11). However, the ACC/AHA guidelines published in 2013 have stopped to recommend a cholesterol target since clinical trial data do not indicate what the

target should be. According to these guidelines, in case of atherosclerotic cardiovascular disease, a high intensity statin should be used for patients aged ≤ 75 years old or a moderate intensity statin for patients aged > 75 years old (50). In the Heart Protection Study trial, simvastatin (a hydroxymethyl glutaryl (HMG) coenzyme-A reductase) has significantly reduced the risk of major vascular event by 22% (95% confidence interval: 15–29) in LEAD patients as compared to placebo (51). Antihypertensive drugs should be administered to LEAD patients with hypertension to achieve a goal of < 140 mm Hg systolic over 90 mm Hg diastolic (in non-diabetic patients) or < 130 mm Hg systolic over 80 mm Hg diastolic (diabetic patients and patients with chronic renal disease) (11). The angiotensin-converting enzyme inhibitors (ACEI) should be preferred in asymptomatic or symptomatic LEAD to reduce the risk of adverse cardiovascular events since ramipril 10 mg/day diminished the risk of myocardial infarction, stroke, or vascular death in patients with LEAD by approximately 25% (52). Ramipril resulted also in significant increases in pain-free and maximum treadmill walking times compared with placebo (53). In practice, the introduction of ACEI should be done over 1 month by increasing the dose slowly and monitoring the creatinine clearance.

In diabetic patients, antidiabetic drugs should be administered to reach a goal of Hemoglobin A1c below 7% to reduce

microvascular complications and improve cardiovascular outcomes (11).

Others drugs as cilostazol or pentoxifylline can be used in patients with LEAD to improve the walking distance (11).

Revascularization

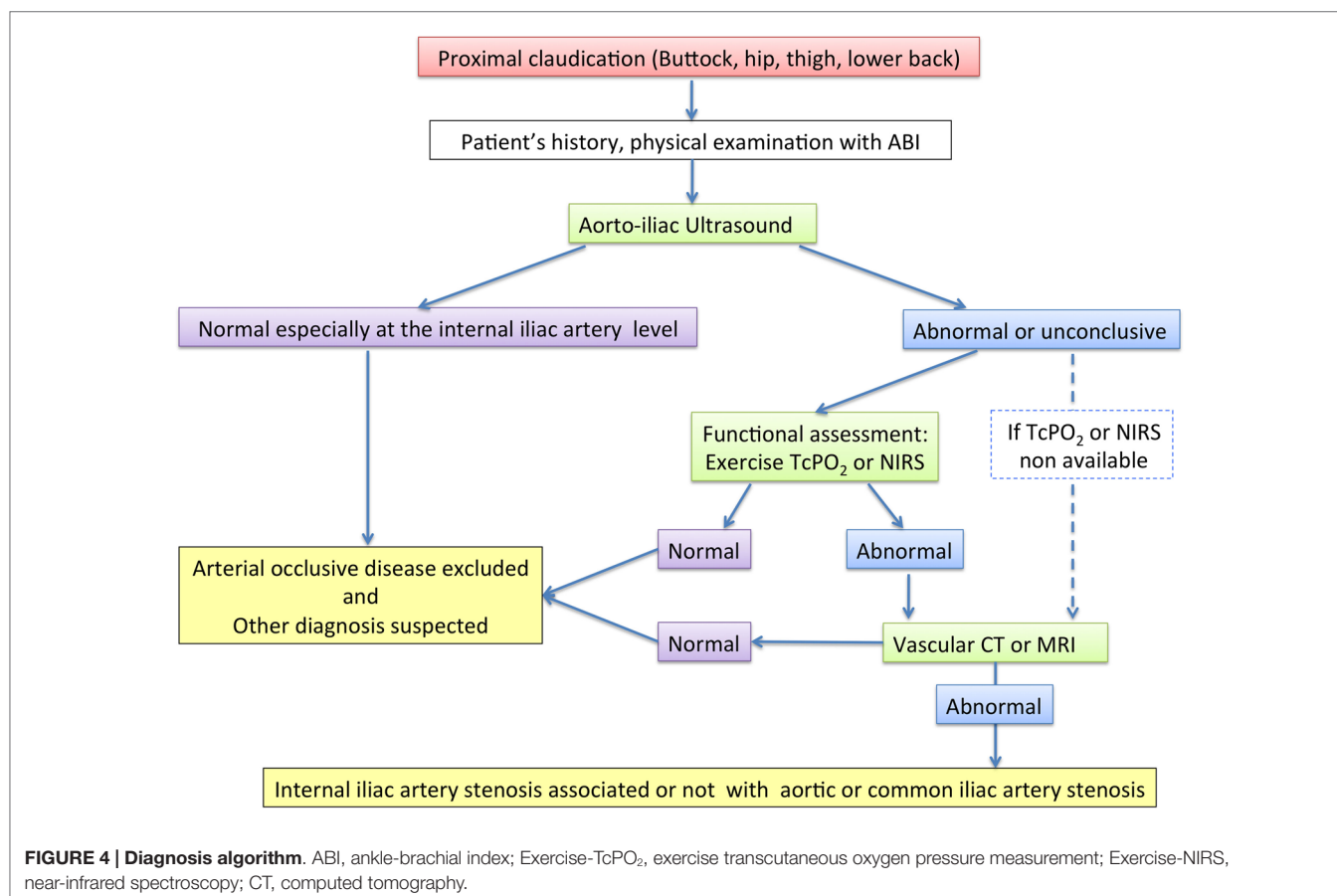
Revascularization can be proposed to patients who have an important walking impairment and after no improvement after medical treatment and supervised exercise training (4, 11). In case of isolated IIAS, endovascular treatment is the most used procedure since surgical revascularization is both technically more demanding and brings along a higher risk to the patient (54, 55). Contrary to stenosis concerning the common iliac artery or external iliac artery, there is neither randomized comparison of primary stent placement versus percutaneous transluminal angioplasty (PTA) nor comparison with surgery for IIAS (35, 56). Several studies have assessed the endovascular treatment (PTA alone or stenting) on short series of patients. Thompson et al. have shown that the procedures either for PTA alone or stenting were safe without any complication in nine patients with buttock claudication: seven out of nine had pain relief after 1 month of follow-up (54). Another study, including 21 patients followed during 14.7 ± 5.7 months, found that all patients had complete alleviation of the buttock claudication and a significant increase of the walking distance from 85 m to 225 m after the endovascular treatment (PTA alone or stenting) (55). In 2013, Prince et al. have shown that endovascular treatment of

IIAS has a high technical success rate (i.e., absence or stenosis after procedure lower than 30%) and a low complication rate (in 3 out of 34 patients). In their study (34 patients included), 79% of patients had complete or partial pain relief of symptoms (57). Morse et al., Smith et al., Adlakha et al., and Huetink et al. have also reported different symptomatic cases of IIAS that were successfully treated by endovascular procedures (58–61). Batt et al. have also shown good results for the angioplasty of the superior gluteal artery lesions (13, 62). Paumier et al. have suggested that in case of common iliac artery stenosis, aorto-iliac bypasses with a reimplantation of IIA should be discussed (63). The same group performed another study in 40 patients, in whom a direct revascularization of the IIA was performed concomitant to aorto-or iliofemoral bypasses. Proximal claudication after revascularization disappeared in 23 out of 27 patients who had previous proximal claudication (64). The patency rate of the IIA was 89% at 1 year and 72.5% at 5 years (64).

Areas of Uncertainties

Algorithm of Diagnosis

To date, no algorithm has been proposed to perform the IIAS diagnosis taking account the cost of the exams and their possible results to help for the diagnosis. Studies are lacking about the sensitivity and specificity of several exams such as ultrasound exam, CTA, or MRA on the specific IIAS evaluation. Herein, we propose our diagnosis algorithm (Figure 4).



Percutaneous Transluminal Angioplasty Alone or Stenting

Randomized comparison of primary stent placement versus angioplasty concerning common iliac artery or external iliac artery had shown that there were no substantial differences in technical results and clinical outcomes of the two treatment strategies both at short-term and long-term follow-up (2 years) (35). Since angioplasty followed by selective stent placement is less expensive than direct placement of a stent, the choice of primary stenting or not has to be studied for the IIAS.

Assessment of other Atherosclerotic Localizations

An electrocardiogram, carotid, and aortic DUS should be discussed because LEAD is associated half the time with other atherosclerotic localizations (65).

Guidelines

An expert multidisciplinary committee organized by the ACC and the AHA have reported comprehensive guidelines for

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the management of LEAD in 2013 (11). Surprisingly, neither this committee nor the TASC II working group mentioned the way of managing IIAS (4, 11). In 2014, the Society for Cardiovascular Angiography and Intervention (SCAI) has published an expert consensus statement about aorto-iliac arterial management (34). In this statement, the experts considered as:

- appropriate care to treat a patient with moderate to severe symptoms of buttock of hip claudication or major tissue loss (Rutherford Classification: 2–6) with IIA $\geq 50\%$ stenosis and/or resting mean translesional gradient ≥ 5 mm Hg;
- may be appropriate care to treat a patient with IIAS $\geq 50\%$ with vasculogenic impotence.

Conclusion

This review shows that when a patient has a proximal walking pain, physician should look for IIAS. We also found that literature is very sparse and that guidelines and recommendations have to be addressed to know how to manage IIAS.

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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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