REVIEW ARTICLE

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Endofibrosis as a cause of peripheral artery disease: a comprehensive review and proposal of two novel algorithms for diagnosis and treatment

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INTRODUCTION

Endofibrosis is a rare condition affecting blood vessels, occurring mainly among young healthy athletes. This condition arises as progressive stenosis of the iliac arteries, which attenuates the blood circulation of the limb, thus leading to pain during movement. Iliac artery compression was first described in 1984 among professional cyclists[1]. Some authors have reported that up to 10–20% of top athletes are affected[2,3]. Endofibrosis is one of the rare causes of peripheral artery disease, in which the exact prevalence is unknown, possessing no any accurate data.

This comprehensive review is purposed to sum up the current knowledge of endofibrosis and ensure concise information about its etiology, and diagnostic and treatment modalities. In addition, two cases including imagery are purposed to be presented to illustrate the perioperative findings.

METHODS

Input data for endofibrosis have been limited. Our search was carried out in Cochrane, PubMed, EMBASE, and UpToDate databases using keywords "endofibrosis," "iliac artery compression," and "cyclists." A total of 233 articles were selected. Of these, 183 articles had not been relevant for the study. Also, 30 case or original studies with minimal groups of the patients were excluded from the study. The remaining 20 articles had been included in our review.

Epidemiology and etiology

Endofibrosis is characterized by iliac artery stenosis, with a predilection for the external iliac artery (EIA). It mostly affects athletes, of which 80% of the cases are performance cyclists, but runners, football players, cross-country skiers, and others can also be affected[4]. The disease occurs in men 8–10 times more often than in women.

Stenosis often occurs due to anatomic, mechanic, and postural causes[5]. Repeated hip hyperflexion causes trauma to the vessel wall and hypertrophy of the psoas muscle, leading to the psoas compression of the artery, thereby causing stenosis[6]. The affected vessel restricts the blood supply to the limb, and the leg becomes ischemic, which leads to pain during sports activities.

Symptoms

Patients with endofibrosis are often entirely asymptomatic during routine activities, with difficulties appearing only at the maximal limb stress. It can manifest as femoral claudication, limb weakness, numbness, or, less frequently, swelling[7].

Diagnosis

Early diagnosis is the cornerstone of successful treatment. Although the top athletes have their own doctors, these physicians might have minimal experience with endofibrosis. In addition, the available literature data suggest that the vascular surgeon is the most relevant physician for this phenomenon. A detailed

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personal history, signs and symptoms, low ankle-brachial index (ABI), and Doppler sonographic examination of the lower limb arteries are essential to determine the correct diagnosis of endofibrosis[8]. Lim et al.[9] highlighted the importance of the ABI measurements before and within 1 min after an exercise activity. The authors described a significant attenuation in the blood pressure by 21–40 mmHg in patients with endofibrosis. Furthermore, the specific cycle ergometer-based protocols are more appropriate for the diagnosis of endofibrosis than a standard treadmill[9].

Pathological ABI values appear in 85% of patients with endofibrosis after exercise, with the sensitivity being high[10]. If the ABI value drops by 0.5 within the first minute of the exercise, the sensitivity is 80–85% (but the specificity was not reported)[11]. If the drop of ABI is by 0.66 or more after 1 min of physical exercise, the sensitivity increases to 90%, with a specificity of 87%[12]. At this end, the importance of abundance for pathological ABI data is an emerging knowledge for physicians.

Color Doppler sonography is the method of choice in diagnosing endofibrosis, mostly due to its noninvasive nature and high sensitivity of up to 85%[13]. The results are relatively normal during rest examination; however, after provocative maneuvers, such as examination in hip flexion or immediately after exercise, the results become pathological. Peak systolic velocity (PSV) is significantly higher in the symptomatic limb, which supports the high sensitivity of this method in diagnosing endofibrosis[4]. Other available imaging modalities include digital subtraction angiography (DSA), computed tomography angiography (CTA), and magnetic resonance imaging (MRI)[14]. Our novel proposal for the diagnostic algorithm of this entity, according to the available literature, is depicted in Figure 1.

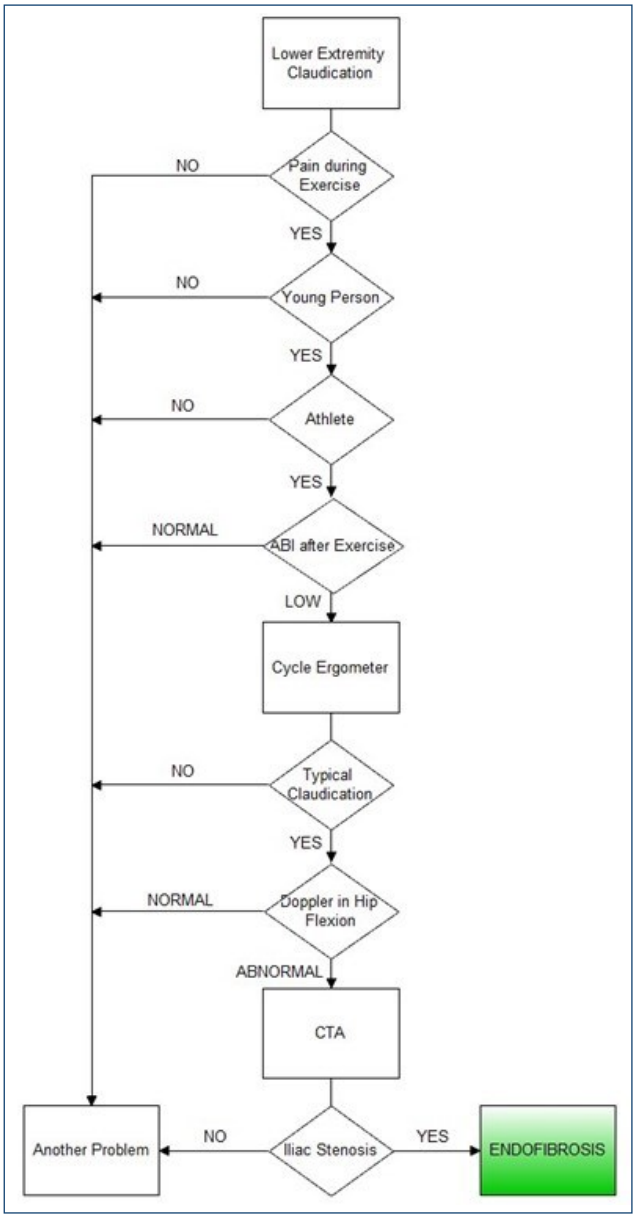

Figure 1. Proposal for the diagnostic algorithm.

Our experience

To date, there are no official guidelines on how to treat a patient with endofibrosis. Based on our research and international evidence-based medicine, our second proposal in this work, our novel proposal for the treatment algorithm of this phenomenon, is depicted in Figure 2. If the patient diagnosed with endofibrosis is a professional athlete, then he should undergo surgery. Even though the patient is not a professional athlete but very limited in life, he should also undergo surgery. In case with no significant limitation in life, the patient should stop the provocative activity and follow the rules for atherosclerosis risk reduction. Regarding surgery, endofibrosectomy and thrombectomy with a venous patch, in case of fibrotic stenosis, and with a venous bypass, in case of chronic obliteration of EIA, are the best options. In this surgical process, the iliac artery is usually attached to the surrounding structures, and surgeons need to release the artery so that they can operate.

Two cases of endofibrosis, both professional cyclists, had been managed in the Vitkovice Hospital. The first case, a 29-year-old woman, possessed the rapid and sudden onset of symptoms, including pain in the right leg, numbness, and paresthesia. She was originally diagnosed with embolism. Later, she was diagnosed with endofibrosis. During surgery, the EIA was released from the psoas muscle and then thrombectomy, endofibrosectomy, and patch reconstruction with a great saphenous vein (GSV) were performed. Histopathological examination of the excised artery revealed the preserved endothelium, in places with a fibrin

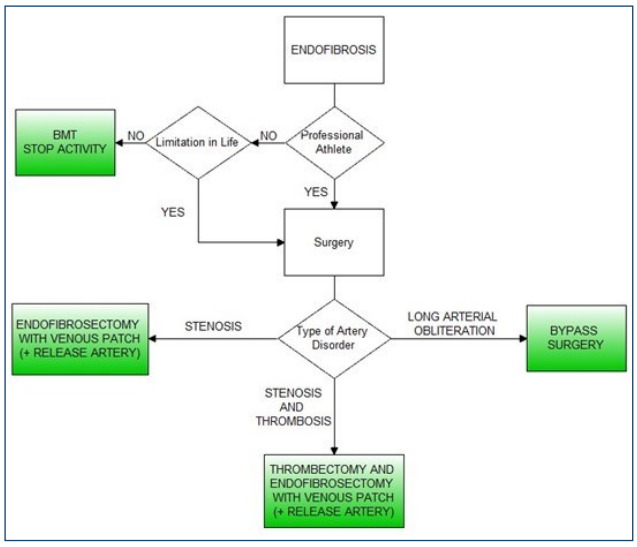

Figure 2. Proposal for the treatment algorithm.

Figure 3. External iliac artery with a thrombus, endofibrotic tissue (left, center), and thrombus from external iliac artery (right).

thrombus. The media appeared to be normal and the patient returned to cycling within 2 months (Figure 3). The second case, a 31-year-old woman, presented with post-exercise pain in the left leg. Her ABI level was revealed at a normal range at rest (1.0) and dropped to 0.42 after exercise. The Doppler sonography exhibited a normal triphasic waveform at rest, replaced with the pathological monophasic waveforms after an exercise activity. Her CTA confirmed the EIA stenosis, and the diagnosis of endofibrosis was established. The patient underwent a surgical procedure involving the release of EIA and endofibrosectomy with a GSV venous patch. The patient returned to cycling in 6 weeks. The current follow-up is 48 and 29 months, respectively. The current primary patency is 100%, and both cases are still professional cyclists without limitations.

DISCUSSION

A protocol, describing the diagnosis and management of endofibrosis of the iliac artery, was published in 2016. Experts have agreed that the recommended best medical treatment may not be sufficient in terms of the therapeutic approach for the entity. As a method of choice, surgical modalities should be recommended for patients in whom endofibrosis leads to a reduced quality of life. They also agreed that endovascular therapy has not been placed in the treatment of endofibrosis[8]. Schep et al.[4] recommended that if the patient is not a professional athlete, they should give up sports; this change in lifestyle should be combined with conservative treatment. Although the etiology of endofibrosis is not related to atherosclerosis, it is recommended that patients should follow the general rules for atherosclerosis risk reduction[15].

Only a short-term effect is described in patients undergoing angioplasty. In most cases, the symptoms recurred within 8 weeks[16]. Giannoukas et al., on the contrary, reported that angioplasty is less invasive, with faster recovery and less tissue damage than surgical treatment[17]. Arterial dissection and recurrence of symptoms are the most common complications, and stent implantation is not recommended because of the risk of migration or fracture[7].

The outcomes of most studies favor surgical therapy. Of note, in case of diagnosed endofibrosis, some authors recommend endarterectomy (endofibrosectomy) with a venous patch[18-20], whereas others prefer resection of the affected EIA and a venous iliofemoral bypass graft from the GSV[13]. It is not recommended to use a prosthetic patch due to the risk of infection and pseudoaneurysm formation. Feugier et al.[21] included a total of 56 women and 435 men treated between 1991 and 2013 with an absolute majority of cyclists (87%). Endofibrosectomy was performed in 322 limbs and venous iliofemoral bypass in 202. One case, aged 28 years, died of iliac artery rupture 3 weeks after the surgery due to a premature return to sport. A sum of 97% of the cases returned to the original sport on average after 3.2±1.5 months. Five years after the surgery, the symptoms improved in 96% of the patients. The primary patency of endofibrosectomy and iliofemoral bypass after 5 years was 94 and 98%, respectively, and the secondary patency was 100% for both types of reconstruction.

We propose that, based on the outcomes of the literature review, iliac endofibrosis should always be considered a possibility in the case of claudication in athletes. Early diagnosis, per se, will attenuate unnecessary examinations, prevent disease progression, and offer early treatment. As such, the patient's history, stress test, Doppler sonography, and, possibly, other imaging modalities are essential tools instrumental

in the diagnosis of endofibrosis[22]. Reviewed publications suggest that the cases who are not top athletes should start with a conservative approach and abstain from exercise causing difficulty, thus reducing the risk factors of atherosclerosis. On the contrary, surgical treatment is a primary recommendation for professional athletes. In general, it is recommended to avoid endovascular procedures and the use of artificial materials in surgical treatment. However, specific recommendations and guidelines for the management of this phenomenon are still missing. Endofibrosis, per se, is described as a progressive disease, and the regeneration process remains controversial with the cases frequently suffering for an unnecessarily long period of time[23,24]. As such, professional athletes, in particular, cyclists, with this entity should be considered in an occupational disease condition[25].

CONCLUSION

So far, there are no complete guidelines that we should follow up on, which leads to relatively late diagnosis. As endofibrosis is a progressive disease, patients often suffer for an unnecessarily long time[23]. It would be advantageous to create a registry of cases treated for endofibrosis and to develop prospective studies with long-term follow-up. This could in effect lead to preparing international guidelines valid for the diagnosis and management of this disease. It is also worth considering that in the case of professional athletes or (in particular) cyclists, endofibrosis should be classified as an occupational disease[24]. In this article, we have also demonstrated the use of surgical procedures that agree with the up-to-date literature knowledge in two patients.

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AUTHORS' CONTRIBUTIONS

TM: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Resources, Validation, Visualization, Writing – original draft. **IS**: Investigation, Methodology, Software, Supervision, Validation, Visualization, Writing – review & editing. **DT**: Data curation, Formal Analysis, Investigation, Methodology, Resources, Validation, Visualization. **AP**: Investigation, Methodology, Project administration, Validation, Visualization. **DS**: Investigation, Methodology, Software, Supervision, Validation, Visualization, Writing – review & editing. **MM**: Data curation, Formal Analysis, Investigation, Project administration, Visualization, Writing – original draft. **PV**: Methodology, Project administration, Resources, Supervision, Visualization. **VP**: Methodology, Project administration, Resources, Supervision, Visualization.

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