The Role of Magnetic Resonance in the Diagnosis of Chronic Exertional Compartment Syndrome*

O papel da ressonância magnética no diagnóstico da síndrome compartimental crônica do exercício

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Abstract

Chronic compartment syndrome is a common and often underdiagnosed exercise-induced condition, accounting on average for a quarter of cases of chronic exertional pain in the leg, second only to the fracture/tibial stress syndrome spectrum. It traditionally occurs in young runner athletes, although more recent studies have demonstrated a considerable prevalence in low-performance practitioners of physical activity, even in middle-aged or elderly patients. The list of differential diagnoses is extensive, and sometimes it is difficult to distinguish them only by the clinical data, and subsidiary examinations are required. The diagnosis is classically made by the clinical picture, by exclusion of the differential diagnoses, and through the measurement of the intracompartmental pressure. Although needle manometry is considered the gold standard in the diagnosis, its use is not universally accepted, since there are some important limitations, apart from the restricted availability of the needle equipment in Brazil. New protocols of manometry have recently been proposed to overcome the deficiency of the traditional ones, and some of them recommend the systematic use of magnetic resonance imaging (MRI) in the exclusion of differential diagnoses. The use of post-effort liquid-sensitive MRI sequences is a good noninvasive option instead of needle manometry in the diagnosis of chronic compartment syndrome, since the increase in post-exercise signal intensity is statistically significant when compared with manometry pressure values in asymptomatic patients and in those with the syndrome; hence, the test can be used in the diagnostic criteria. The definitive treatment is fasciotomy, although there are less effective alternatives.

Keywords
- compartment syndromes
- exercises
- stress fractures
- magnetic resonance

Resumo

A síndrome compartimental crônica é uma condição comum e frequentemente subdiagnosticada, induzida pelo exercício, que corresponde em média a um quarto dos casos de dor crônica na perna relacionada ao exercício, e que perde em frequência

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apenas para o espectro fratura/reação ao estresse tibial. Tradicionalmente ocorre em jovens atletas corredores, embora estudos mais recentes tenham demonstrado uma prevalência considerável em praticantes de atividade física de baixo rendimento, mesmo em pacientes de meia idade ou idosos. A lista de diagnósticos diferenciais é extensa, e por vezes é difícil fazer a distinção apenas pelos dados clínicos, sendo necessários exames subsidiários.

Classicamente, o diagnóstico é feito pelo quadro clínico, pela exclusão dos diferenciais, e pela medida pressórica intracompartimental. Embora a manometria por agulha seja considerada o padrão-ouro no diagnóstico, seu uso não é universalmente aceito, visto que existem algumas limitações importantes, além da disponibilidade restrita do equipamento com agulha no Brasil. Recentemente, novos protocolos de manometria têm sido propostos a fim suplantar a deficiência dos tradicionais, com algum deles inclusive recomendando o uso sistemático da ressonância magnética (RM) na exclusão dos diagnósticos diferenciais. O uso de sequências de RM sensíveis a líquido pós-esforço é uma ótima opção não invasiva à manometria por agulha no diagnóstico da síndrome compartimental crônica, uma vez que o aumento da intensidade de sinal pós-exercício é estatisticamente relevante quando comparados os valores pressóricos de manometria em pacientes com a síndrome e assintomáticos; portanto, o exame pode ser usado no critério diagnóstico. O tratamento definitivo é a fasciotomia, embora existam alternativas menos eficazes.

Palavras-chave
- síndromes compartimentais
- exercícios
- fraturas de estresse
- ressonância magnética

Introduction

Compartment syndrome can occur in any body segment that has little or no capacity to expand, due to an imbalance in the content/container relationship, which can lead to hypoperfusion and consequent suffering of the structures of a particular compartment.[1] The condition can be acute or chronic, and both types occur in very different clinical contexts. The former is mostly related to trauma, and it needs an immediate and clinical diagnosis followed by emergency fasciotomy to save the affected body segment; the latter is exercise-induced, and is diagnosed by the clinical picture, the exclusion of differential diagnoses, and subsidiary exams,[2] and the correct diagnosis is made, on average, from 22 to 28 months after the initial presentation of symptoms.[3] We should highlight that, according to some series, the diagnostic delay can reach 7 years.[4]

Chronic compartment syndrome is an exercise-induced condition characterized by pain and a feeling of increased pressure, which improves with repose. About 95% of the cases occur in the legs, although other sites can also be affected, such as the feet, the hands, the forearms, and the paravertebral muscles, as well as other less frequent sites.[5] Initially, it was thought that the condition was more prevalent in men; however, there was a strong selection bias, because the studies were performed in the military population. It is currently believed that there is no gender tendency.[3,5,6]

Chronic exertional compartment syndrome (CECS) is a common and often underdiagnosed entity, which accounts for about 10% to 60% (mean of 1/4) of exercise-related leg pain,[7] and is responsible for about 14% to 27% of cases with no definite diagnosis of leg pain,[8] second only to spectrum fracture/tibial stress syndrome.[2] It is traditionally strongly associated with high-performance physical activity, especially running among young athletes in the 3rd or 4th decades of life,[9] with bilateral involvement in most cases, although more recent studies[4,10,11] have shown a considerable prevalence in low-performance practitioners, even when walking or trotting, including middle-aged or even elderly patients. De Bruijn et al.[11] evaluated 698 CECS patients, 98 (14%) of whom were 50 years of age or older. These patients most often had unilateral complaints, and the deep posterior compartment was more rarely affected when compared to the younger athletic population. In addition, there are also cases in the pediatric population, especially in girls who engage in high-performance sports that involve running.[12]

Pathophysiology

The pathophysiology of CECS is complex, controversial and not yet fully elucidated, and there are several theories about its genesis. The initial studies were based on the knowledge of acute compartment syndrome, in which intracompartmental pressures rise to extreme levels, leading to hypoperfusion and tissue necrosis. However, in CECS, tissue pressures do not rise the same way as in acute conditions, so there are no irreversible ischemic changes.[5] Although the increased tissue pressure is responsible for the symptoms, the ultimate cause of pain is questioned. Some studies[13] have refuted the ischemic theory because it was not possible to demonstrate a significant difference in tissue perfusion through nuclear medicine studies,[13,14] while other authors,[15] through spectroscopy studies, have shown that ischemic changes are detectable only when the blood pressure values are extremely high (≥ 160 mm Hg). However, tissue hypoxia is believed to be relative, that is, oxygen demand is greater than the supply only during exercise, returning to normal at rest,[16] and maybe that is why some of these studies have not been able to detect such changes. Similarly, when post-exercise contrast MRI sequences were performed a few years ago, what was evidenced was muscle enhancement (related to tissue inflammation), not hypoperfusion, as evidenced in cases of acute compartment syndrome. Other theories attribute the pain to the stimulation of fascial, periosteal, and intramuscular nerves due to excessive compartmental distention[5,6,14,17] or the release of inflammatory mediators.[15]

Therefore, briefly and objectively, it is postulated that the reduction in the complacency of the affected compartment, associated with the increase in muscular volume during exercise, would lead to supraphysiological elevation of tissue pressure and reduction of venous return, which would be responsible for triggering the pain through at least two main mechanisms: 1) stimulation of the muscular, fascial and periosteal nerves; and 2) momentary reduction in tissue perfusion pressure, with consequent relative and transient cellular hypoxia, resulting in the release of cytokines and other inflammatory mediators that would stimulate nociceptors.

Clinical Picture

The syndrome is characterized by bilateral pain in 80% to 95% of the patients, related to and reproduced by exercises, which ceases immediately or after a few minutes of rest. The athletes report burning, fullness, feeling of swelling and cramps. In addition, in an attempt to increase the exercise, there is worsening of the picture with the appearance of neurological symptoms such as paresthesia and weakness in the territory of innervation of the fibularis muscles, in the case of the anterior and/or lateral compartments, and in the territory of the tibial nerve, in the case of the deep posterior compartment. Weakness and feeling of skin retraction are also reported. The condition can be insidious, and usually occurs at a given moment of intensity or duration of the physical activity, with a tendency to recur ever earlier, forcing the athlete to stop, and thus reducing the physical performance. The symptoms are usually worse on the second day of strenuous physical training and, in extreme cases, they may occur at rest. Although possible, progression of CECS to acute compartment syndrome is extremely rare.[2,7–9,18]

Diagnosis

The diagnosis of CECS is traditionally made by a tripod of procedures: 1) clinical picture; 2) exclusion of differential diagnoses; and 3) needle manometry.[9,18,19] The initial imaging investigation of exercise-related leg pain should be performed with plain x-rays, although in most cases the result of the examination is normal. Magnetic resonance imaging (MRI) of the leg following the conventional protocol, that is, without sequences after the exercise, is a consensus in the literature as the best method to exclude differential diagnoses.[3,7,20]

Needle manometry is still considered the best diagnostic method for CECS, but it is not universally accepted.[21,22] Other authors consider a good response to fasciotomy as the gold standard, although, not infrequently, there are cases of postoperative relapse,[23] especially in the military population.[24,25] Relapse is greater when the anterior and lateral compartments are affected concurrently, or in case of involvement of the deep posterior compartment, when compared to the previous compartment only.[9] In addition, other methods such as post-stress MRI and near-infrared spectroscopy are also diagnostic alternatives.[26]

Some studies[21,22,27] have questioned the use of manometry, as it is a method with several intrinsic limitations, such as: the need to perform several invasive measurements, possibly in several compartments; variability of the accuracy of the equipment used; the degree of flexion of the ankle and the depth of the catheter alter blood pressure values, and different protocols use different depths or do not even indicate a specific standardization regarding the depth of needle positioning; and correct placement inside deep posterior compartment is problematic.[28] In addition to these limitations, it is noteworthy that there is an overlap of postexercise pressure values in controls and symptomatic patients.[21,22] In addition, the most commonly used protocol, by Pedowitz et al.,[29] has important limitations, such as: absence of a valid comparison group, since symptomatic patients who did not reach the cutoff pressure values were compared to symptomatic patients above the arbitrarily established limit, that is, the groups had already been preselected to have differences; the cutoff points were changed during the study; and finally, this was a study with a low level of evidence considering the parameters used by the American Academy of Orthopedic Surgery.[21,22] Another limitation of manometry is the limited availability of the equipment in Brazil.[30]

In order to overcome these limitations, new needle manometry protocols have been suggested,[7] and they even recommend the systematic use of conventional MRI for the exclusion of differential diagnoses.

Magnetic Resonance

Magnetic resonance imaging is the best imaging method to assess exercise-related leg pain because it detects entities such as tibial stress syndrome, tibial stress fracture, neural entrapments, muscle and tendon injuries, exercise-related thrombosis, and fascial hernias. To diagnose popliteal artery entrapment syndrome (PAES), it is necessary to cranially extend the axial sections to assess any anatomical variations in the origin of the sural triceps that may be related to the condition (remembering that in the functional type there are no variations). In addition, a directed angiographic study, which can be performed by MRI (MR angiography) in suspected cases, is also necessary.

The conventional leg MRI protocol, that is, without post-exercise sequences, is normal in cases of CECS. Signal changes with diffuse muscle edema pattern without tears or strains in preexercise sequences may correspond to late-onset muscle pain (delayed onset muscle soreness, DOMS) and radiological differential diagnosis, since the clinical presentation is different. Delayed onset muscle soreness may result in acute compartment syndrome.

The use of liquid-sensitive sequences (T2-weighted with fat suppression or short-tau inversion recovery [STIR]) after physical exertion has been shown to be sensitive in the diagnosis of CECS;[31–34] therefore, it is an excellent noninvasive alternative to needle manometry. It is important to remember that the use of a paramagnetic contrast medium is not necessary for this diagnosis. Our institution's MRI protocol for CECS research is illustrated in ►**Figure 1**.

In the medical literature, the use of postexercise MRI in the diagnosis of CECS is not recent. In 1990, Amendola et al.,[13] demonstrated that postexercise MRI was able to diagnose CECS in 4 of 5 patients with diagnoses confirmed by manometry, although there was no statistically significant results in this small sample. In 1998, Eskelin et al.,[31] compared postexercise sequences (treadmill running) on low field magnets (0.1 T) with needle manometric pressure values in symptomatic and asymptomatic patients, demonstrating that the increase in signal intensity was statistically significant ($p < 0.01$) in patients with high blood pressure when compared to asymptomatic and symptomatic patients with normal or borderline values.

Verleisdonk et al.,[32] evaluated 12 controls (24 compartments) and 21 cases (41 compartments) of manometry-confirmed anterior CECS with improvement after fasciotomy, enabling the return of the patients to their physical activity. The patients were evaluated by high-field MRI (1.5 T) before and after the exercise, confirming that the increase in signal intensity is statistically significant in CECS patients when compared to controls ($p < 0.05$). In addition, it has been shown that, after fasciotomy, the intensity of the postexercise signal returns to normal values ($p < 0.05$), suggesting that the method can also be used for posttreatment control, if necessary.

Other studies[33,34] also confirmed the validity of postexertion MRI in the diagnosis of CECS, using a 1.54-fold increase in signal intensity as the diagnostic cutoff value, with sensitivity of 96% and specificity between 87% and 90%. These studies, however, used a protocol of dorsiflexion and plantar flexion exercises inside the apparatus, which makes the method difficult to reproduce, as it would require different reels and specific exercise platforms, with very restricted access. In addition, we believe that individuals should be subjected to the activity that causes their pain and not to resistance plantar flexion and dorsiflexion exercise protocols, which do not necessarily reproduce training or competition conditions.

In the clinical practice, firstly, conventional MRI sequences are performed to exclude differential diagnoses. Subsequently, the patients are submitted to running (or even walking) on a treadmill, according to their physical abilities, until they can no longer tolerate the activity due to pain. Shortly after stopping activity, they immediately return to the MRI for the acquisition of fat-suppressing liquid-sensitive axial sequences (T2/STIR). It is important not to extend the intervals between physical activity and image acquisition in the second phase of the exam, as this may lead to false-negative results. Furthermore, it is believed that the acquisition of a late additional sequence could increase the diagnostic specificity in the case of persistent muscular edema.[35]

Imaging findings in CECS are relatively simple, and correspond to increased compartmental volume, increased muscle signal intensity, and bulging of the interosseous membrane in postexercise MRI sequences (►**Figure 2**). It is worth remembering that, to be valued, the high T2/STIR

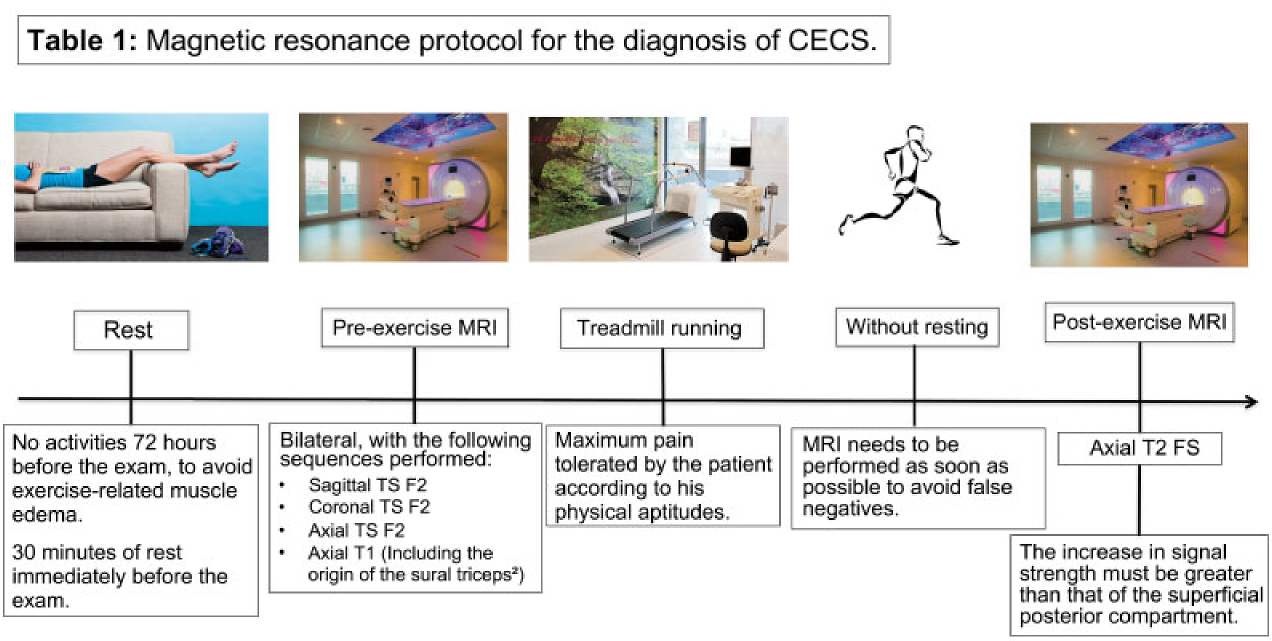

Fig. 1 Magnetic resonance protocol for the diagnosis of chronic exertional compartment syndrome (CECS).

signal must be higher than the signal of the superficial posterior compartment, since this compartment is very rarely affected;[8] therefore, it can be used as a reference for comparison. Quantitative measurements can also be performed, and some authors[35,36] suggest that an increase in signal strength of more than 20% of the preexercise versus postexercise sequences should be considered significant for the diagnosis.

In our clinical practice, and in agreement with part of the literature,[2,3,6] the descending order of involvement is: 1) anterior compartment; 2) lateral compartment; and 3) deep posterior compartment. However, other articles[8,35] mention the deep posterior as the second most affected compartment. According to De Bruijn et al.,[11] the deep posterior compartment would be the second most affected in young athletes, while the lateral compartment would be the second most affected in middle-age or older physical activity practitioners. Another very common form of presentation is the association of the involvement of the anterior and lateral compartments (►**Figure 2**); although less frequent, the association between the anterior and posterior compartments is not rare either (►**Figure 3**). It is important to remember that the posterior tibial muscle belly may behave like a fifth compartment isolated from the other posterior muscles (►**Figure 3**); therefore, the ideal positioning of the manometry catheter should be inside it. Winkes et al.[28] evaluated the accuracy of the positioning of the manometry catheter by palpation in the deep posterior compartment with MRI, and demonstrated that in 42% of the cases the position was accurate (inside the posterior tibialis); in 38%, the position was suboptimal (inside the deep posterior compartment, but outside the posterior tibial compartment); and, in 21% of the cases, the position was inaccurate (outside the deep posterior compartment or in its transition with superficial posterior compartment).

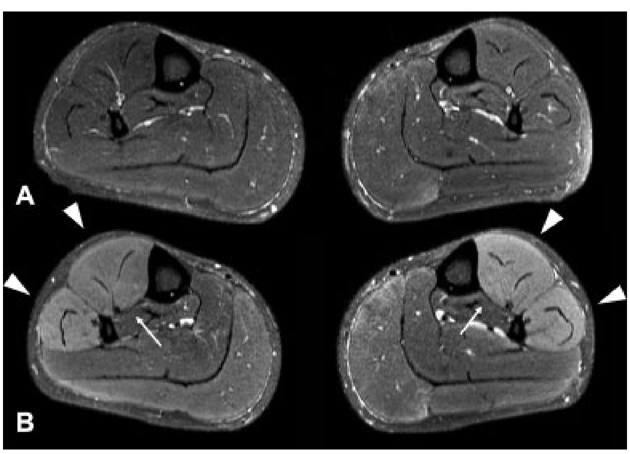

Fig. 2 A 38-year-old man who had recently started to perform physical activities (alternating running with walking) reported burning pain and cramps that kept him from running. (**A**) Axial T2-weighted sequences with fat suppression without significant changes. (**B**) Posteffort sequences demonstrating increased signal intensity and increased muscle volume of the anterior and lateral compartments on both sides (arrowheads), in addition to bulging of the interosseous membranes (thin arrows). Anterolateral CECS is also a very common form of presentation.

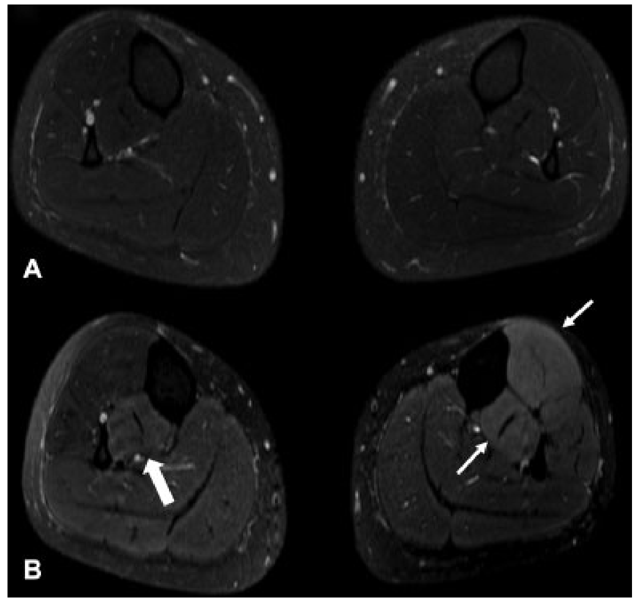

Fig. 3 A 38-year-old woman with complaints of anterior leg pain during treadmill exercise (brisk walking/running). (**A**) Preexercise FS (Fat-saturated) axial T2-weighted sequences unchanged. (**B**) The postexercise sequences show higher signal strength in the posterior tibial muscle on the image of the right leg (thick arrow), as well as impairment of the anterior and posterior tibial compartments in the left leg (thin arrows). The posterior tibialis muscle may behave as a separate compartment from the other deep posterior muscles.

In short, magnetic resonance imaging is a non-invasive method, easily accepted by patients, with good availability in large centers in Brazil, it is the best exam for the exclusion of differential diagnoses, and a scientifically-validated option for the diagnosis of CECS.[31–34] Its disadvantages correspond to the different protocols proposed, and to the few studies published with a small number of patients when compared to manometry studies. More studies with a larger number of patients and comparing the MRI with the new manometry protocols are still needed.

Differential Diagnostics

The differential diagnoses of CECS are the main causes of exercise-related leg pain: stress fracture/tibial stress syndrome, chronic muscle and tendon injuries, muscle hernias, popliteal artery entrapment, external iliac artery endofibrosis, exercise-related venous thrombosis and neural entrapments. It is important to remember that these conditions can coexist, especially in athletes.[9] Our protocol to approach exercise-related leg pain by MRI is illustrated in ►**Figure 4**.

Since the list of differential diagnoses is extensive, the detailed discussion of each entity is beyond the main scope of the present paper. However, vascular causes, especially PAES, deserve attention because they are the most problematic differentials,[37] since the clinical symptoms are often indistinguishable, which may lead to inadequate diagnosis and treatment.[38] Popliteal artery entrapment syndrome is a rare condition that affects young adults, and in which the popliteal artery is compressed by hypertrophy or anatomical

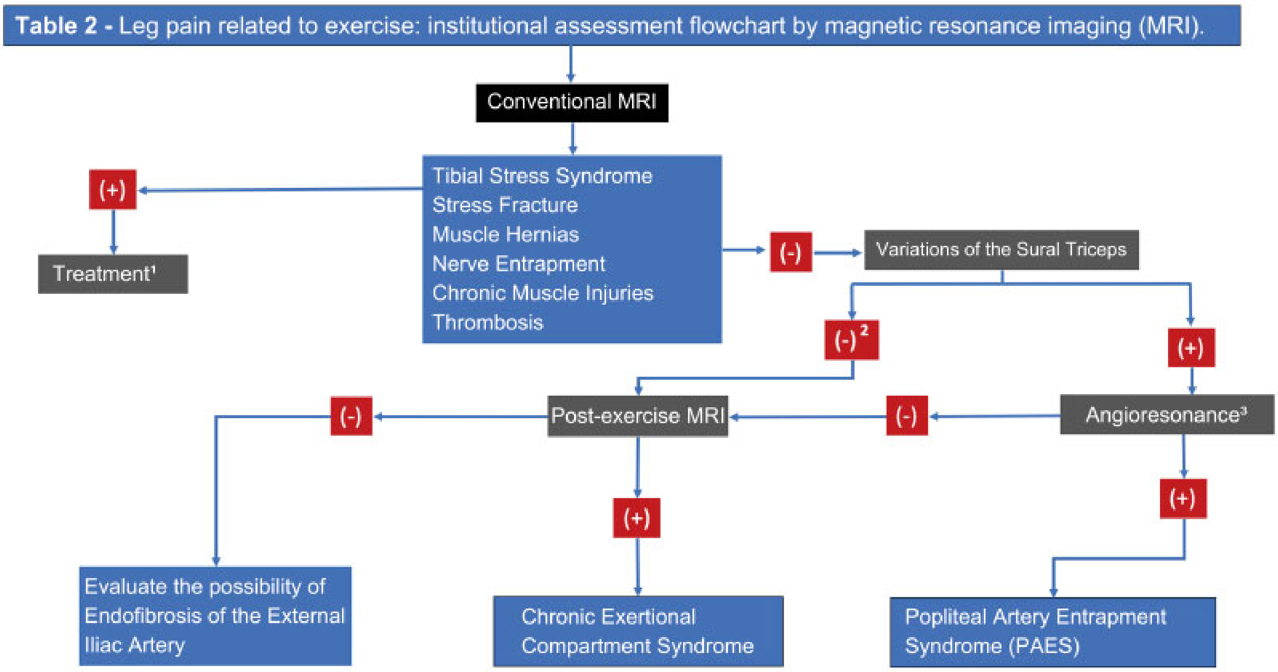

Fig. 4 Leg pain related to exercise: flowchart of the institutional assessment by magnetic resonance imaging (MRI).

variations of the sural triceps, resulting in exercise-related leg pain symptomatology, with cramps and paresthesia, which are quickly relieved by rest. The symptoms may be more related to the intensity than to the duration of the exercise. Although nonspecific, reducing the ankle-brachial index to provocative maneuvers (plantar flexion and dorsiflexion) may favor the diagnosis of vascular pathologies. The Doppler ultrasound with provocative maneuvers consists of a screening test with good sensitivity and bad specificity, since the changes in the spectral patterns of flow, and in the peak systolic velocity, may occur in healthy patients. Angiographic examinations conducted by computed tomography or MRI (CT angiography or MR angiography) have been very useful in detecting stenosis and its length, occlusion and collateral circulation, with the advantage of better characterization of anatomical variations (►**Fig. 5**), fibrotic bands, embryological remnants and differential MRI diagnoses. Although invasive, digital angiography is traditionally the gold standard method.[38,39] In addition, normal manometric values favor the diagnosis of PAES,[40] although some studies[39–41] report that the association between CECS and PAES is not uncommon.

External iliac-artery endofibrosis is a rare condition that should be remembered especially in the case of endurance athletes (cyclists, triathletes and long-distance runners) with exercise-related leg pain, with no definite diagnosis, even after extensive etiological investigation with subsidiary examinations.[37,41]

Treatment

The treatment may be surgical or non-surgical. Non-operative options may be attempted before surgery, and they include ice, anti-inflammatory drugs, stretching, physical therapy, changing sneakers, and, more recently, changing the gait in runners who land with the hind foot in the case of anterior CECS. In non-athletes, changing the activity, and reducing the intensity and the duration of it are also options. The use of botulinum-toxin injections into the compartments was able to reduce compartmental pressure by 50% for up to 9 months;[42] however, the most common side effect was reduced muscle strength. Most conservative treatments are not effective, as the recurrence of symptoms is frequent.[3]

Surgical treatment with fasciotomy followed by rehabilitation is the option with the best results in the general population, with approximately 80% of patients returning to the baseline performance they had before the symptoms.[9] Surgical release of the compartments can be performed by traditional, minimally-invasive or endoscopic fasciotomy. Care should be taken with the superficial fibular nerve, as it punctures the muscular fascia and is externalized from the lateral compartment, about 10 cm cranially to the lateral malleolus. Recurrences are related to incomplete release, misdiagnosis, excessive fibrocicatricial changes, or inadequate rehabilitation.[3]

New surgical techniques include ultrasound-guided fasciotomy, thermal fasciotomy, and surgical release with transillumination or endoluminal guidance.[3,9]

Final considerations

The diagnosis of CECS is by common exclusion, and it is underdiagnosed in the context of exercise-related leg pain. Although needle manometry is still the gold-standard method in the medical literature, the needle equipment is rarely available in Brazil, the method has several limitations, and it

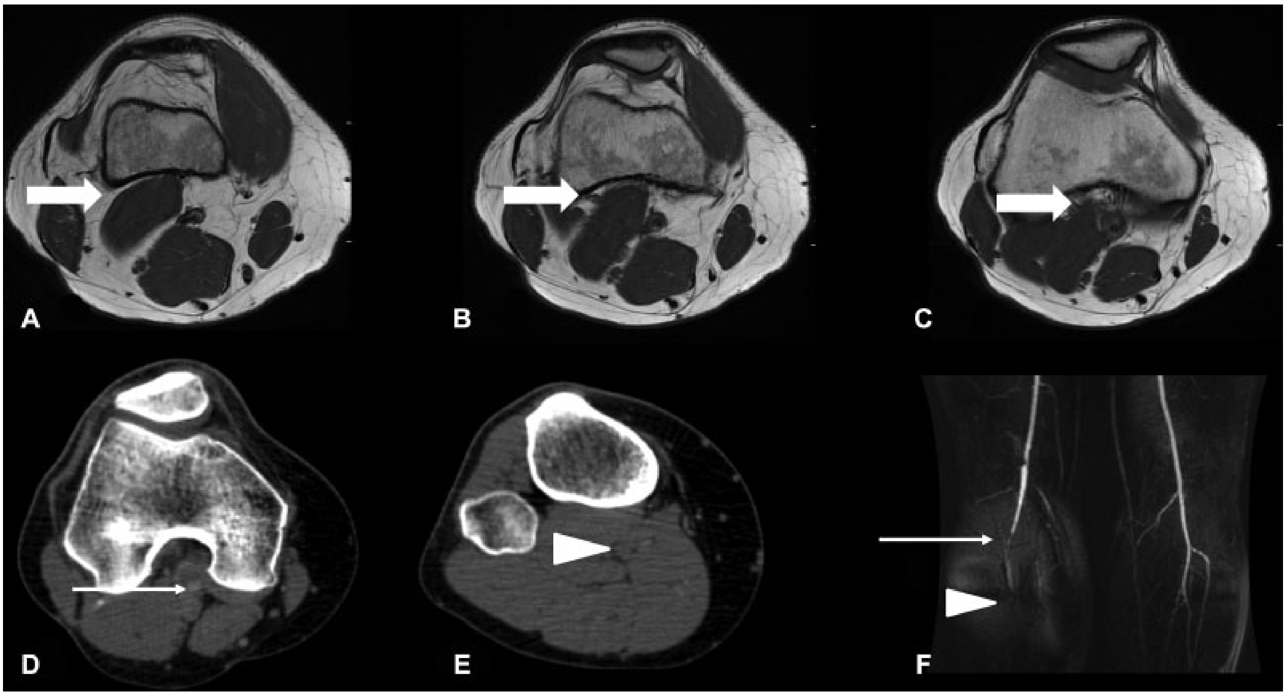

Fig. 5 Popliteal artery entrapment syndrome in a 23-year-old non-athlete man complaining of leg pain and cramps during running. T1-weighted axial magnetic resonance imaging (**A**, **B** and **C**), axial computed tomography angiography (**D** and **E**) and three-dimensional magnetic resonance angiography (**F**). Vascular compression in this case occurred due to the superior origin of the lateral head of the gastrocnemius (thick arrow in **A**, **B** and **C**), causing stenosis (thin arrow in **D** and **F**) and distal flow occlusion (arrowhead in **E** and **F**). In contrast to this case, variants of the medial gastrocnemius are more common.

is, thus, questioned by some authors.[21,22] Protocol-specific MRI, including postexercise sequences, is an excellent noninvasive option for needle manometry in the diagnosis of chronic exertional compartment syndrome, as well as the best option to rule out differential diagnoses.

Conflict of Interests
The authors have none conflict of interests to declare.

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