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Chronic Exertional Compartment Syndrome (CECS): a literature review with focus on etiological, diagnostic and therapeutic framework

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Indice

Abstract

Chronic exertional compartment syndrome (CECS) of the lower leg is part of a group of overuse lower limb injuries that mainly affects young adults and active populations (sport athletes and military). It is characterized by painful symptoms occurring after a certain amount of exertion and cease immediately or shortly after cessation of activity. Due to the transient nature of symptoms, physical examination alone can mislead the correct diagnosis. The etiology and pathophysiology of this condition are poorly understood, and the criteria used to confirm the diagnosis are based on small sample sizes of symptomatic controls. Non-invasive diagnostic tools show promising screening capacity to help in the differential process. Effective treatment options are mainly of surgical nature, and a limited number of studies have been carried to investigate the efficacy of conservative management, especially for mid-to-long term outcomes. The objective of this thesis is to review the current available literature and to focus on etiological, pathophysiological, diagnostic and therapeutic findings to have a better understanding of the syndrome and its possible management perspectives. Literature search identified 34 articles across the four selected topics. Results show conflicting evidence concerning CECS etiology and pathophysiology, its diagnostic accuracy and its conservative treatment outcomes, proving that more robust and large studies are strongly needed to unsure a better clinical knowledge on this syndrome.

1 Introduction

Chronic Exertional Compartment Syndrome – CECS - is a painful syndrome generally related to sports activity, such as running or cross-country skiing (1–3) but also reported in specific populations, subject to repetitive and continuous physical efforts, like military personnel (4,5). The symptoms resulting from this condition, as well as their duration, are variable and include *widespread, cramp*-like *pain and/or burning sensation,* together with *weakness and paresthesia* of the compartment(s) involved. These symptoms generally cease with rest or with the suspension of provocative activity. Given variable and recurrent symptomatology, this is a condition that is generally diagnosed after the exclusion of other pathological stress conditions, such as the *medial tibial stress syndrome (MTSS), stress fractures, ilio-tibial bendellette syndrome, tendinopathies, anterior knee pain, popliteal artery entrapment syndrome, radiculopathy or peripheral nervous entrapment* and other more serious pathological conditions, such as *deep vein thrombosis, arteriopathies and neoplasy* (6).

Historically, the first description of symptoms related to Exertional Compartment Syndrome (ECS) refers to Dr. Edward Wilson, in 1912. He was a medical officer on Captain RR Scott's expedition, which left to reach the South Pole earlier than the Norwegian R. Amundsen. On their way of return, Dr. Wilson developed the typical symptoms of anterior compartment syndrome and, because of the freezing weather, he later perished along with the rest of the expedition (3).

Although other cases of anterior compartment syndrome have been reported in the literature since 1912, no reference will be made to a chronic form of compartment syndrome until 1956, the year in which Mavor first described a recurrent form of anterior leg pain during the exercise, associated with muscle hernia and numbness of the affected district, successfully treated with surgery (7).

Over the years the terminology used to describe this condition has been varied and potentially confusing. Terms such as "*shin splints", "march synovitis", "anterior tibial pain syndrome", "medial tibial syndrome"* and "*chronic compartment syndrome"* have been used in describing the symptoms of lower limb pain related to physical exertion. More recently the term Chronic Exertional Compartment Syndrome has been defined, as a good descriptor of the clinical-pathological elements of the condition, remaining appropriate for the various anatomical districts involved (3).

The incidence of this pathology in the general population is still unknown(8). In specific populations such as athletes, it ranges from 14% to 27% of all *exertional leg pain conditions*(1,9), with an average age of presentation between 26 and 28 years(10,11); despite the relative frequency of presentation, there is an average delay, between the moment of presentation and the moment of the correct diagnosis, of about 22-28 months. Prevalence studies have provided conflicting data, but more recent studies report males and females to equally susceptible of developing CECS (8,12). A study by Waterman et al. in 2013, conducted on 4100 subjects with a positive diagnosis of CECS within a population (military personnel) of 8,320,201 at risk individuals, reported an incidence rate of 0.49 cases/1000 people at risk per year(4).

The etiology of CECS is multifactorial and is still a topic of discussion. Several theories have been proposed in the literature, but the real cause and the underlying pathophysiological process have not yet been outlined (13).

The diagnostic process generally takes place by excluding other pathologies related to chronic stress conditions(6,14), then going to confirm the clinical picture by measuring (via catheter) the intra-compartment pressure of the structures involved, before and after the symptom-provoking exercise(13).

Various types of conservative treatment are reported, such as *massage* (15), *modification of the initial contact in running pattern*(16–18), *Chemodenervation with botulinum toxin A (BoNT-A)* (19) and *Percutaneous Fascial Fenestration US-guided* (9). Despite this availability of conservative approaches, the most effective treatment proposals reported in the literature are surgical, generally through Fascectomy of the myofascial compartments involved (20).

The development of this paper has the objective to illustrate the current etiological theories, the clinical evaluation and the diagnosis of subjects affected by CECS, to then examine the treatment proposals currently available in the literary panorama.

1.1 Anatomy

Understanding the anatomy of the lower limb is essential to understand the pathophysiology, diagnosis and treatment of CECS.

The leg district is divided into 4 compartments: *anterior, lateral, superficial posterior and deep posterior.* The existence of a 5th compartment has been reported, responsible for containing the m. tibialis posterior but its clinical relevance has not yet been defined (8).

The anterior compartment includes the m. tibialis anterior, the m. extensor digitorum longus, the m. extensor longus of the 1st finger and m. peroneus tertius. In the deep portion runs the deep *peroneal nerve*, together with the *anterior tibial* artery and vein. The limiting elements of this compartment are the Tibia, the Fibula, the interosseous membrane and the anterior intermuscular septum. This is generally the most frequently affected compartment in the case of CECS (3,21,22).

The lateral compartment includes the peroneus *longus* and *brevis muscles*. The deep part of the compartment is crossed by *the common peroneal nerve* and its *superficial* and *deep* branches. The compartment is delimited by the anterior intermuscular septum, the fibula, the posterior intermuscular septum and the deep fascia.

The *superficial posterior* compartment is surrounded by the deep fascia of the leg and contains the m. gastrocnemius (medial and lateral), the soleus and plantar muscles.

Finally, the deep posterior compartment develops between the tibia, the fibula, the deep transverse fascia and the interosseous membrane. The muscles contained within it are the m.

flexor digitorum longus, the m. flexor hallucis longus and popliteus muscle. This compartment lies posterior to the course of the tibial neuro-vascular structures.

The 5th compartment, the compartment of the m. tibialis posterior, is a further division of the deep posterior compartment; the existence of a fascial lining of this muscle has recently been demonstrated (8).

1.2 The Fascial System

The fascial system is defined as a three-dimensional continuum of fibrous, loose and dense connective tissue -containing Collagen- which permeates the human body. It incorporates elements such as adipose tissue, neuro-vascular and adventitious sheaths, aponeuroses, superficial and deep fscias, epinevrium, joint capsules, ligaments, meningeal membranes, myofascial expansions, periosteum, retinacles, septa, tendons, visceral fascias and all intra- and intermuscular connective tissues, including endo-/peri- and epimysium(23).

The Fascial System wraps and interpenetrates all organs, muscles, bones and nerve fibers, providing the body with a functional structure and ensuring an environment in which all systems and systems can function in an integrated way(23).

1.3 Myofascial compartments of the lower limb

The free part of the lower limb is covered, deeply to the subcutaneous tissue, by a superficial band that follows, dorsally, to the gluteal fascia that covers the posterior muscles of the hip and the inguinal ligament, anteriorly.

The thigh is superficially covered by *the femoral fascia* (also called *fascia lata*), laterally thickened in the iliotibial tract, and perforated anteriorly at the *femoral triangle* level. From the deep portion of the fascia originate two intermuscular septa, medial and lateral, which are fixed respectively to the medial and lateral lips of the femoral linea aspera. The intermuscular septa identify two muscle lodges, an anterior one containing the anterior musculature of the thigh, and one posterior containing the posterior and medial musculature of the thigh. The sartorius and tensor muscles of the fascia lata are placed superficially at these lodges, in a split of the fascia lata.

In the lower leg, the superficial fascia, following fascia lata and the popliteal fascia, transforms in the crural fascia. From the deep surface of the fascia originate the two crural intermuscular septa, anterior and posterior, which are inserted at the anterior and posterior margins of the fibula, identifying a lodge for the peroneal muscles. The bony part of the leg, together with the interosseous membrane and septa, separate the anterior muscles lodges from that of the posterior muscles; the superficial posterior musculature is separated from the deep one thanks to the deep crural band, dependent on the superficial one and which originates at the level of the tendon arch of the soleus muscle.

At the level of the instep the band has thickenings, the *retinacles*, which have the important function of keeping the numerous tendons of the leg muscles in the right position which will be inserted on the tarsal and metatarsal bones. Ventrally, there is the extensor muscles retinaculum (divided into upper and lower portion), the retinaculum of the flexor muscles medially and, laterally, the peroneal muscles retinaculum (also divided into upper and lower).

1.4 Epidemiology

Epidemiological knowledge is still limited, especially in relation to the general population. Most the available studies examine small groups of specific populations, such as military personnel (24) and young athletes (1)- from different sports- and, consequently, data relative to the incidence of this condition is not applicable to the general population, widely varying from 10% to 60% depending on the selected groups(5,10) (V. Tzortziou, N. Maffulli,

N. Padhiar, 2006; Styf JR, LM.Korner, 1986; P. Qvarfordt, JT. Christenson , B. Eklo, P. Ohlin, B. Saltin, 1983). More recently epidemiological studies have been conducted in the general population(8,12). Waterman et al. (2013) examined a large military population of 8,320,201 individuals, retrospectively included over a total period of 6 years (2006-2013), calculating an incidence rate of 0.49 cases per 1000 people-at-risk/year(4). A study conducted in Norway with a study sample of 3,000 individuals aged between 25 and 75 years, reports a prevalence rate of 7.6% in the general population (8).

1.5 Etiology and Risk Factors

The etiology of this condition is still debated and poorly understood. The hypothesis of an ischemic etiology, the symptomatology could manifest itself due to an ischemic damage to the tissues included in the affected muscle compartment, has long been put forward. Various mechanisms have been proposed as the cause of tissue ischemia, including arteriolar spasm, capillary obstruction, arteriovenous collapse and obstruction of venous outflow.(25)

Despite the variety of arguments provided, this hypothesis has been repeatedly questioned by imaging studies that have demonstrated the substantial absence of ischemic phenomena inside the compartment with high intra-compartment pressure (26–28).

It is now widely recognized that intra-compartment pressure has a role in the establishment of this condition, however there is still little evidence regarding the repercussions that the increase in intra-compartment pressure could have on the capillary muscle bed and on the composition of the fibers of the affected compartment. Among the risk factors most associated with the development of CECS we find:

-Young age: the average age of presentation for subjects with CECS is between 25 and 28 years (1,4,8). Despite the young average age, a plateau has been reported in the prevalence around 50 years (29), it has been hypothesized that this occurs for a greater availability of free time, suitable for sports practice;

- Caucasian Race: a higher incidence of affected caucasian subjects is reported in military populations(4);

-Sport activity: a higher incidence of the disease was found in *runners* and *skaters* (inline skaters are more subject to developing anterior CECS) (2,30,31);

Although different anatomical risk factors have been proposed such as *fascial thickening, poor tissue compliance* and *reduced capillary density*, the role they play in supporting symptomatology has not yet been clarified(32).

The mechanism responsible for the increase in intra-compartmental pressure has not yet been explained; the existence of ischemic phenomena in CECS has also been questioned (Amendola et al., 1990; Balduini et al., 1993; Trease et al., 2001). There is limited evidence regarding the repercussions that the increase in intra-compartment pressure can have on muscle capillary bed and on the composition of the fibers of the affected compartment. Information provided so far by the various studies on the relationship between sex and CECS is conflicting. Less recent literature reports a male prevalence, but two large studies report a female predominance.

Studies on large populations have recently been conducted with the aim to establishing more precisely which factors are most associated with this condition, two studies have recently examined more heterogeneous populations(4,12), identifying risk factors associated with the development of CECS such as age, sex, previous pathology of the lower limb, bilateral symptoms, sport practiced (*running and skating*) and tenderness / stiffness on palpation.

1.6 Pathophysiology

There is paucity of available data regarding the pathogenesis of chronic compartment syndrome and its effects on the muscles of the compartment involved(25).

The pathophysiology underlying CECS is unknown, but hypotheses have been formulated including increased muscle volume within the compartment, fascial thickening with consequent decrease in compartment compliance, stiffening of connective tissue (especially in diabetic patients(33)), reduced capillary flow and vascular congestion as a consequence of a reduced venous return(25,33). Moreover, if during the exercise the volume inside the compartment increases beyond the accommodation capacity of the compartment itself, a pathological increase in the intra-compartment pressure can occur and this is thought to lead to the development of CECS.

It is generally accepted that CECS occurs as a result of an abnormal pressure increase inside the muscle compartment during exercise (Barnes 1994). This increase in intra-muscular pressure seems to be enough to reduce capillary perfusion and endanger the survival of the tissue (Hargens & Mubarak, 1998). The pressure increase phenomenon must occur because of one in two possible processes: a limitation on the size of the compartment or an increase in its contents. The first could be due to a thickening of the fascial structures with a consequent decrease in compliance, while the increase in the volume contained in the compartment could be due to an increase in muscle volume during exercise, muscle hypertrophy, increased blood supply, an increase in capillary permeability or decrease in venous outflow (Barnes 1994).

It has been hypothesized that high intramuscular or sub-fascial pressure during exercise may cause tissue hypoxia and ischemic-type pain due to impaired blood flow. To date, however, there is no conclusive evidence regarding hypoxic cell damage or decrease in capillary perfusion. Other hypotheses have been formulated regarding muscle hypertrophy, the reduction of the compartment volume due to a lower fascial compliance or a decrease in periods of muscle relaxation(26).

Prolonged periods of ischemia are generaly associated with endothelial extravasation, increased vascular permeability, interstitial edema, nerve tissue damage and tissue necrosis (3,34).

Given the lack of histological studies related to this condition, there is data conflicting on the possible inflammatory, fibrotic or vascular nature of tis etiopathogenesis(35). Given that the pain of CECS is of a worsening nature, often described as *burning* (and generally resolves thanks to the cessation of activity), it is understandable that the studies conducted so far have focused on examining possible alterations in vascular function. Qvarfordt et al. reported a significant increase in lactate production in muscle biopsy findings of the anterior compartment, following exercise; this supporting the hypothesis of the ischemic origin of pain(10).

Other theories supporting vascular changes include:

-a pathological increase in muscle relaxation pressures;

-reduction of arteriovenous gradients;

-the hypothesis that in some patients the decrease in oxygen saturation in the muscle tissue and the pressures of muscle relaxation are higher than other subjects;

During exercise, muscle volume has been reported to increase by approximately 20% and this increases intra-compartment pressure, because the surrounding fascia does not expand proportionally, although these changes do not necessarily lead to tissue hypoperfusion and pain muscle(36). Based on s-PET (*single-Photon Emission Tomography*) and MRI imaging, no significant differences were found in the decrease of tissue perfusion between patients and controls(26,28).

1.7 Clinical Presentation and Differential Diagnosis

1.7.1 Patient's history

The starting point from which a series of useful information can be obtained for diagnostic framework is certainly the anamnestic interview. The classic presentation of a person suffering from this syndrome refers pain, generally described as pressure, burning or cramping, which occurs after a certain amount of effort (defined as time, distance or intensity), which ceases with rest or within 60min from the end of the effort itself(6). Secondary symptoms may be present, such as weakness of the muscles innervated by the peripheral nerve included in the affected compartment and *paresthesias* in peripheral nerve sensitive area(37). Symptoms may progress over time, increasing in intensity or appearing after less effort.

Given its insidious onset, the painful condition determined by CECS can initially lead affected subjects to independently change the degree or dynamics of sport activity to avoid worsening of symptoms and this generally leads to a delay in the diagnostic process(1).

The Clinical presentation of chronic compartment syndrome is somehow characteristic and should therefore alert the physician to consider its possible diagnosis, in a differential framework. Patients experience predictable painful symptoms in the lower limbs, which normally begin at the same time, the same distance or intensity of training and regress with rest. With untreated progression of this condition, pain can also arise during normal daily life activities or even at rest. In *anterior* CECS, a weakness in ankle dorsiflexion can result in a "slapping foot" on the ground during walking, with possible association of paresthesia with dermatomeric distribution(38,39).

As in acute compartment syndrome, edema of the limb is useful information to be found but, being the chronic picture linked to the activity, it may not be present during clinical evaluation, if carried out in a rest period. Pain in the compartment(s), pain during palpation and/or mobilization and palpable muscle herniations through fascial layers are commonly reported features.

Other symptoms may sum to those mentioned above, such as weakness of the muscles innervated by the nerve passing through the affected compartment, or paresthesias in the sensory afferent distribution of the nerve involved. Symptoms progress with time, as they can become more intense and require less activity to manifest themselves. Occasionally, affected patients report a decrease in athletic performance the day after an activity that triggered symptoms.

1.7.2 Clinical examination

A first physical examination conducted on athletes suspected of CECS can often be inconclusive if performed at rest in a clinical setting. However, what can result during the inspection and/or palpation is the presence of herniation of the muscular belly, made evident by a voluntary activation of the affected muscle. Pain and stiffness of the compartment on palpation and, in the event of long-lasting symptoms, atrophy of the muscles of the affected compartment may frequently be found.

1.7.3 Differential Diagnosis

The study of differential diagnosis is essential in order to be able to associate with good certainty, symptoms presented by patients with the right clinical frame, especially in case the same symptoms may be present in different pathological entities. In the case of CECS, different pathological conditions can manifest a similar symptomatology, creating confounding factors that can delay diagnosis and, consequently, treatment. The differential pictures that frequently create confusion in the diagnostic process of the syndrome are therefore (6,14):

-Medial Tibial Stress Syndrome -MTSS- (often reported in sports subject exposed to repetitive microtraumas, such as running, leading to painful symptoms)

- Stress fractures (also associated to a painful symptomatology that increases with the continuation of physical effort, until interruption; however, patient’s history often report an increase in the volume or intensity of training, prior to symptoms onset)

-Rhabdomyolysis

-Tendinopathies/Myositis

-Popliteal Artery Entrapment Syndrome -*PAES*-

-Sickle-cell Disease

-Radiculopathy/Peripheral Nerve Entrapment

-Deep Venous Thrombosis (DVT)

-Arterial Vascular Disease/Claudication

-Tumor

1.7.4 Imaging and Diagnosis

Imaging is not necessary for diagnosis confirmation but are often important for ruling-out other pathologies in the differential process(14).

The use of X-ray in a/p and oblique projections of the lower limbs can help exclude stress fracture cases; in addition, an X-ray examination of the lumbar spine can help identify any canal stenosis or disc degeneration, which could justify painful symptoms in lower limb region. The use of bone scan helps exclude periostitis cases or malignancy cases affecting the lower limb. Also, the use of Ultrasonography can be important to study the vascular components, for the exclusion of hematomas, DVT or vascular entrapments. Computed tomography (CT) and magnetic resonance imaging (MRi) can help rule out other significant causes of chronic lower limb pain(28,40).

1.7.5 ICP Testing

The current diagnostic *gold standard* for CECS, once other differential causes are excluded, is the intra-compartment pressure (ICP) measurement(21). This practice derives from the one implemented for the diagnosis of acute compartment syndrome, which is a direct result of tissue hypoxia, consequent extravasation of fluids and, therefore, the sudden increase in intra-compartment pressure which can lead to tissue necrosis, if left untreated.

The ICP measurement is commonly performed through a needle catheter which is inserted, after local anesthesia, into the muscle belly of the compartment to be tested. Different cutoffs points for ICP values have been proposed as diagnostic criteria for this condition; these includes measurements at *rest*, *mean*, *peak*, or *relaxation* (in the interval between two contractions), as well as ICP during exercise or post-exercise (Styf et al., 1987; Pedowitz et al., 1990). Critical values have been proposed for the diagnosis of CECS, such as: *pre-exercise* (eg≥15 mmHg; Pedowitz et al., 1990), *during exercise* (eg ≥50 mmHg; Puranen & Alavaikko, 1981), *relaxation* (eg ≥ 35-50 mmHg; Styf, 1988), and then at 1 '(eg ≥ 30 mmHg; Styf, 1988; Pedowitz et al., 1990) and / or 5' *post -exercise* (eg ≥ 20 mmHg; Pedowitz et al., 1990).

Although ICP measurement remains of fundamental importance for diagnostic purposes, the rationale behind the measurement techniques, as well as the application protocols, are matter of discussion.

1.8 Treatment Options

Being a condition in which the onset of symptoms is dependent to physical exertion, conservative treatment is reported as a first-line option, although its efficacy, especially in long term, is still limited(9); monodisciplinary approaches to treatment are generally described. In case of failure of conservative treatment, surgery can be performed through a fasciotomy of the involved compartment(s);

1.8.1 Conservative approach

There is a shortage of outcomes for conservative treatment in current literature; this is partly because most studies describe monodisciplinary approaches to treatment options for CECS(6,9);

These approaches include:

-limitation of activity;

-massage;

-cryotherapy;

-compression therapy;

- limb elevation;

- orthesis/splint application;

- *muscle strengthening* and *stretching interventions*;

- *shock-wave therapy*;

-chemodenervation (with BoNT-A);

-*gait retraining*;

-USG fascial fenestration;

1.8.2 Surgical approach

If conservative approach fails, surgical treatment is generally undertaken. This option is based on the assumption that intra-compartmental pressure must be reduced (in order to reduce symptoms) by making one or more longitudinal incisions on the skin and the underlying fascia.

1.8.3 Open Fasciotomy

The *Open* fasciotomy has been the *gold standard* for the treatment of CECS, thanks to its superior outcomes compared to non-surgical management(20).

The technique used for *anterior* and *lateral* compartments, with the patient liyng in supine decubitus and with the use of hemostasis, consists of a longitudinal incision of 6-10cm made at the intermediate-distal junction of the leg, halfway between the edge anterior tibia and anterior aspect of the fibula. The subcutaneous fat is separated from the underlying fascia and a transverse fold is made on the fascia of both compartments after having identified, inspected and protected the *superficial peroneal nerve.* All possible muscle adhesions are separated from the fascia, then the incision is expanded, both proximally and distally(3,20).

A medial incision of the same length made ca. 2cm posterior to the postero-medial margin of the tibia, is used in the decompression of the posterior compartments (*superficial* and *deep*). In this district care must be taken not to cause damage to *saphenous* vein and nerve , together with rigorous hemostasis to prevent post-operative hematomas. Hemostasis is suspended in the terminal stages of the surgery, before suturing; every possible source of bleeding is meticulously searched and will then be cauterized or tied(20).

1.8.4 Post-surgical rehabilitation

No specific guidelines have been proposed for post-operative management of patients with CECS. The author's recommendations on post-surgical management are the following(6):

1) initial use of P.R.I.C.E.-Protection, Rest, Ice, Compression, Elevation- during the first 10-14 days following surgery, to support the proliferation phase of tissue repair;

2) careful transition to reestablish range of motion and soft tissue mobility in the maturation and wound contraction phase;

Passive stretching, neurodynamic mobilization, strengthening and eventual sport-specific biomechanical analysis are also recommended to ensure successful return to previous level of fitness after surgery.

The patient is generally allowed to tolerate weightbearing immediately after surgery and surgical sites are monitored to prevent ant healing complication, such as infections or dehiscence (common complications following fasciotomy are listed below).

Athletes begin formal physical rehabilitation for knee and ankle mobility one week post-surgery, with expectation to return to activity within 6-8 weeks(6).

2 Materials and Methods

The electronic databases of PubMed, The Cochrane Library and PeDRO were searched and the articles published between 2000 and 2019 were selected.

Keywords used as search terms were as follows: *chronic, lower extremity, anterior compartment syndromes, compartment syndromes, * etiology, diagnosis, treatment and management*.

2.1 Inclusion Criteria

- publication in English, Italian or French
- studies concerning the anatomical district of the lower limb
- studies investigating the etiological profile, the diagnostic standard and the therapeutic options (with conservative or surgical approach)
- Case Control, Cross-Sectional studies, Cohort and RcT studies will be examined. Systematic reviews may be used, with/without Meta-analysis

- publication from 2000 until present day

2.2 Exclusion criteria

- publications in a different language from the included
- studies related to anatomical districts other than the lower limb
- studies examining Acute cases of compartment syndrome
- case series studies, case reports, expert opinions and non-randomized or uncontrolled clinical trials

2.3 Research Strings

Research strings for PubMed search were build using keywords and the Boolean operators AND and OR:

ETIOLOGY

((((((chronic exertional compartment syndrome OR anterior tibial compartment syndrome)) AND ((((etiology[MeSH Subheading]) AND causality[Title/Abstract]) OR causes[Title/Abstract]) OR pathogenesis[Title/Abstract])) AND ("2000/01/01"[PDat] : "2019/12/31"[PDat]) AND Humans[Mesh])) AND ("2000/01/01"[PDat] : "2019/12/31"[PDat]) AND Humans[Mesh])) AND full text[sb] AND ("2000/01/01"[PDat] : "2019/12/31"[PDat]) AND Humans[Mesh] AND English[lang])) AND full text[sb] AND ("2000/01/01"[PDat] : "2019/12/31"[PDat]) AND Humans[Mesh])

DIAGNOSIS

(((((((chronic exertional compartment syndrome OR anterior tibial compartment syndrome) AND ("2000/01/01"[PDat] : "2019/12/31"[PDat]) AND Humans[Mesh])) AND ((((diagnosis[MeSH Terms]) OR Diagnosis[MeSH Subheading]) OR (Diagnoses[Title/Abstract] AND Examinations[Title/Abstract])) OR (Examinations[Title/Abstract] AND Diagnoses[Title/Abstract]))) AND ("2000/01/01"[PDat] : "2019/12/31"[PDat]) AND Humans[Mesh])) AND ("2000/01/01"[PDat] : "2019/12/31"[PDat]) AND Humans[Mesh]))

TREATMENT

((((((((((((chronic exertional compartment syndrome OR anterior tibial compartment syndrome) AND ("2000/01/01"[PDat] : "2019/12/31"[PDat]) AND Humans[Mesh])) AND (((((((((Therapeutics[MeSH Terms]) OR Therapeutic[Title/Abstract]) OR Therapy[Title/Abstract]) OR Therapies[Title/Abstract]) OR Treatment[Title/Abstract]) OR Treatments[Title/Abstract]) OR therapy[MeSH Subheading]) OR treatment[Title/Abstract]) OR disease management[Title/Abstract])) AND ("2000/01/01"[PDat] : "2019/12/31"[PDat]) AND Humans[Mesh])) AND full text[sb] AND ("2000/01/01"[PDat] : "2019/12/31"[PDat]) AND Humans[Mesh]))

An advanced search has been performed on the PEDro database using the string “compartment AND syndrome”.

One last search has been done on The Cochrane Library database to seek for Randomized controlled Trials and Systematic Reviews.

3 Results

3.1 Included Articles

The first research conducted on PubMed through search strings, yielded a total of 517 results, then transferred to Mendeley, to facilitate the screening and selection process of the included studies. From the reading of the title and abstract it was possible to remove 441 articles for the following reasons:

-duplicate result

-topic not related to research

- anatomical district different from included

-studies conducted on cadaveric specimens

- publication language other than included

-articles examining cases of acute compartment syndrome

After the screening process, there were therefore 76 articles potentially usable for this review. After full-text reading, 43 articles were further discarded.

The second search launched on PeDRO through the advanced search function produced 4 results, which were then excluded for the following reasons:

-duplicate result

-topic not related to research

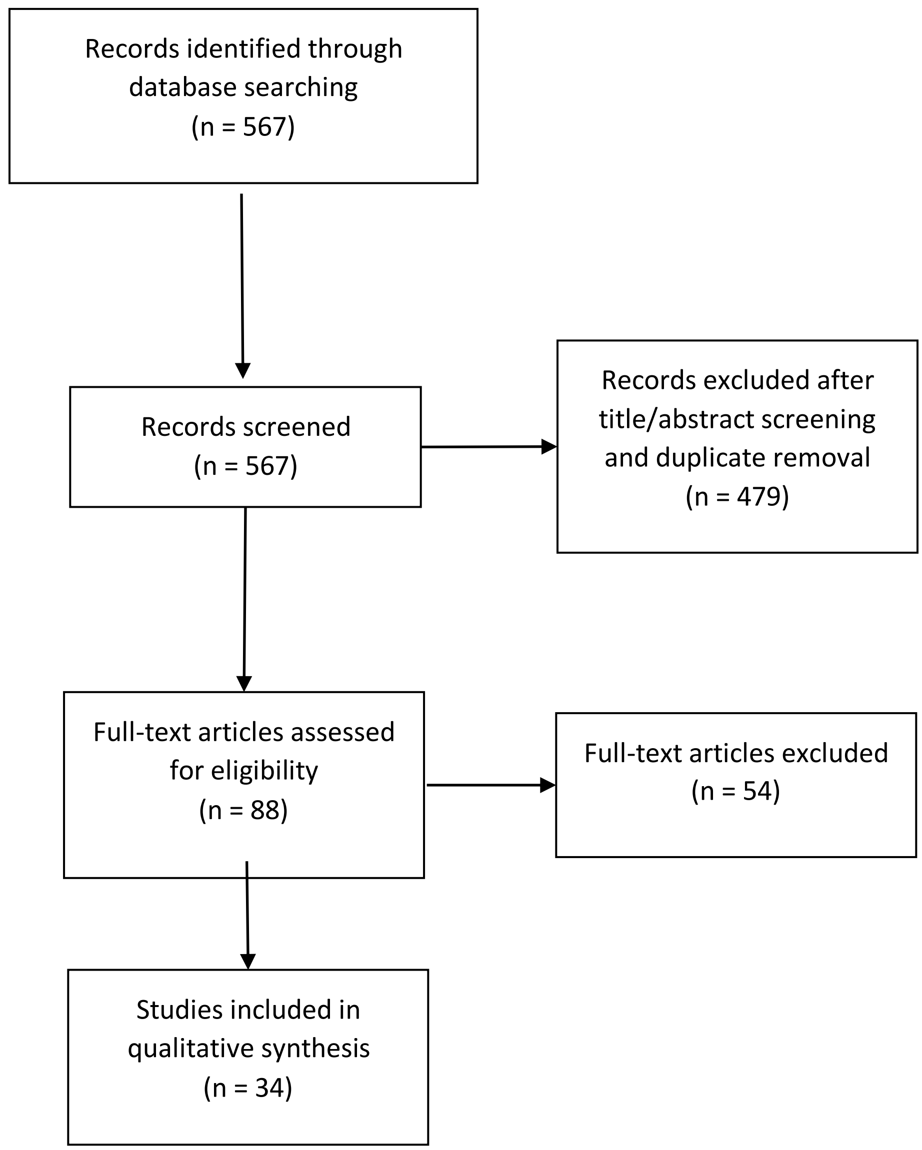
The last search launched on Cochrane Library yielded 46 results. After completing the screening process, a total of 34 articles were excluded for the following reasons:

-duplicate result

-topic not related to research

-different anatomical district

3.2 Flowchart diagram



3.3 Synoptic Tables-Etiology studies

Author/ publication year	***Study Design***	***Objective***	***Results***	***Outcomes***
D.B. Birtles et al., 2002	Case Control Study	To investigate the changes in AT muscle strength, fatigability, size, and pain in CECS patients during and after an isometric exercise protocol in a controlled study	The absolute MVC forces were similar, but MVC: body mass of the patients was lower ($P < 0.05$) as was the ratio of MVC to muscle cross-sectional area (P _<0.01). The extent of central and peripheral fatigue was similar in the two groups. The patients reported significantly higher levels of pain during exercise ($P < 0.05$ at 4 min) and after the first minute of recovery ($P < 0.001$). An 8% increase in muscle size after exercise was observed for both groups. There were no differences in the cardiovascular responses of the two groups.	Central fatigue was evaluated by comparing changes in electrically stimulated (2 s at 50 Hz) and voluntary contraction force before and during the exercise, and then throughout 10 min of recovery. Muscle size was measured by ultrasonography. Pain (with 10cm NPRS) and cardiovascular parameters (with a Finapres BP monitor) were also examined.
T.D.A. Barbour, C.A. Briggs, S.N. Bell, C.J. Bradshaw, D.J. Venter, P.D. Brukner, 2004	Case Control Study	To describe the histological features of the fascial-periosteal interface at the medial tibial border of patients surgically treated for chronic deep posterior compartment syndrome and to make statistical comparisons with control tissue	With regard to collagen arrangement, control tissue showed greater degrees of irregularity than subject tissue (p = 0.01). Subjects with a symptom duration of greater than 12 months (as opposed to less than 12 months) showed greater degrees of collagen irregularity (p = 0.043). Vascular changes approached significance (p = 0.077). With regard to the amount of fibrocyte activity, chronic inflammatory cell activity, mononuclear cells, or ground substance, there were no significant differences between controls and subjects. Good correlation was seen in scores measuring chronic inflammatory cell activity and mononuclear cells (r = 0.649), and moderate correlation was seen between fibrocyte activity and vascular changes (r = 0.574). Intra-observer reliability scores were good for chronic inflammatory cell activity and moderate for vascular changes but were poor for collagen and fibrocyte variables. Individual cases showed varying degrees of fibrocyte activity, chronic inflammatory cellular infiltration, vascular abnormalities, and collagen fibers disruption.	Tissue samples were analyzed with regard to six histological variables: *-fibroblastic activity* *-chronic inflammatory cells* *-vascularity* *-collagen regularity* *-mononuclear cells* *-ground substance* Collagen regularity was measured with respect to collagen density, fiber arrangement, orientation, and spacing. The observed changes were graded from 1 to 4 in terms of abnormality. Mann-Whitney U test, Spearman correlation coefficients, and intra-observer reliability scores were used.
D. Edmundsson, G. Toolanen, L-E. Thornell & P. Stal, 2009	Case Control (Bioptic) Study	To understand the pathophysiology of CECS, its consequences on muscles and the effect of treatment with fasciotomy, we have analyzed the capillary bed and muscle fiber composition at the time of fasciotomy and at follow-up 1 year later.	At baseline, CECS patients had lower capillary density (273 vs 378 capillaries/mm2, P<0.008), lower number of capillaries around muscle fibers (4.5 vs 5.7, P<0.004) and lower number of capillaries in relation to the muscle fiber area (1.1 vs 1.5, P<0.01) compared with normal controls. The fiber-type composition and fiber area did not differ, but focal signs of neuromuscular damage were observed in the CECS samples. At 1-year follow-up after fasciotomy, the fiber area and the number of fibers containing developmental myosin heavy chains were increased, but no enhancement of the capillary network was detected.	enzyme-, immunohistochemistry and morphometry analisys of: -Muscle Capillarity -fiber-type -composition fiber area

M. Dahl, P. Hansen, P. Stal, D. Edmundsson & S. P. Magnusson, 2011	Prognostic Study	We investigated whether the stiffness or thickness of the muscle fascia could help explain the raised intramuscular pressure and thus the associated symptoms in chronic compartment syndrome.	Mean fascial stiffness did not differ between healthy individuals (0.120 N/mg/mm; SD, 0.77 N/mg/mm), patients with chronic compartment syndrome (0.070 N/mg/mm; SD, 0.052 N/mg/mm), and patients with chronic compartment syndrome and diabetes (0.097 N/mg/mm; SD, 0.073 N/mg/ mm). Similarly, no differences in fascial thickness were present. There was a negative correlation between fascial stiffness and intramuscular pressure in the patients with chronic compartment syndrome and diabetes.	Mechanical analysis of Fascial Thickness and Fascial Stiffness
P. Federolf & E. Bakker, 2012	Case Control Study	The purpose of this study is to investigate whether differences existed in the activation characteristics of the tibialis anterior muscle between elite cross-country skiers with a history of anterior compartment pain (symptomatic group) and a pain-free control group.	The relative increase in EMG power per step when increasing the effort level of skating was larger in the symptomatic group than in the control group for tibialis anterior (143 ± 12% vs. 125 ± 23%; Cohen's d= 1.17), peroneus longus (123 ± 24% vs. 107 ± 6%; d= 0.91), and gastrocnemius lateralis (167 ± 51% vs. 117 ± 12%; d= 1.64). The symptomatic group showed more power in the lower frequency bands of the tibialis anterior's EMG spectra ($p < 0.001$), whereas no group differences were found in other muscles (all $p < 0.2$). Within the step cycle, these differences appeared in the swing phase and in the gliding phase during single leg support.	EMG signals were recorded on the muscles tibialis anterior, peroneus longus, soleus, gastrocnemius medialis, and gastrocnemius lateralis. The power ratio, the distribution of power among the frequency bands (power spectrum), and the normalized wavelet intensity patterns were compared between participant groups.
B. R. Waterman et al., 2013	Cohort study (prevalence)	To describe the role of age, sex, race, military rank, and branch of military service on the incidence rate of CECS in the US military, using the Defense Medical Epidemiology Database (DMED).	A total of 4100 diagnosed cases of CECS were identified within an at-risk population of 8,320,201, which correlates to an incidence rate of 0.49 cases per 1000 person-years. The annual adjusted incidence rate of CECS increased from 0.06 cases per 1000 person-years in 2006 to 0.33 cases per 1000 person-years in 2009. Age, race, and sex were considered primary risk factors with immediate translation to the general civilian population. Military rank and branch of service may be viewed as proxies for activity level and at-risk occupational exposure, with Army and Marine Corps branches of service and junior enlisted personnel expected to have elevated activity levels as compared with other subcategories within the cohorts of interest. Calendar year was also evaluated to determine temporal trends in the diagnosis of CECS of the lower extremity.	IR: Incidence Risk (with 95% CI) IRR: Incidence Risk Ratio (with 95% CI) **Population Characteristics** -Age (<20, 20-29, 30-39, 40+) -Sex -Race (Black, Other, White) -Military Rank (Junior Enlisted, J. Officer, Senior Enlisted, S. Officer) -Branch of Service (Army, Navy, Air Force, Marine Corps)
J. A. de Brujin et al., 2017	Retrospective Cohort Study	to describe a heterogeneous population of individuals suspected of lower leg CECS and to identify predictors of CECS	**Patient characteristics** A total of 1867 individuals have been evaluated for suspected CECS between 2001 and 2013; after 456 subjects have been excluded (atypical history and/or physical examination = 153; previous CECS analysis = 201; symptoms in lower arms/upper legs = 102), 1411 individuals suspected of lower leg CECS were included; -n = 698 patients diagnosed with CECS -n = 713 without CECS -earlier treatment modalities were comparable between groups; -CECS patients were 8 years younger (median 25 years, range 12-81 years) than non-CECS patients (33 years, range 14-90 years) and prevalence decreased with age; -Unilateral symptoms more often related to previous leg trauma than bilateral symptoms (14.4 % vs 3.9 %, $p < 0.01$); -Vascular pathology more often present in individuals with unilateral symptoms than bilateral symptoms (7.2 % vs 3.6 %, $p < 0.01$); -Deep-posterior CECS patients were 4 years younger than patients with anterior-CECS and 2 years younger than patients with lateral-CECS ($p<0.01$);	**Patient Selection** -Patient's history review; -Physical examination: tests for signs of vascular insufficiency, compartment tenderness and neurological examination were conducted; -ICP testing (In case history and p. examination were suggestive of CECS): measurements taken from *Anterior, Lateral and DeepPosterior Compartments*; the criteria used for positive thresholds was Pedowitz criteria (ICP ≥ 15 mm Hg at rest, ≥ 30 mmHg 1 min after provocative exercise or ≥ 20 mmHg 5 min later); **Statistical Analysis** -Univariable logistic regression (for associations of patient-related variables and the diagnosis CECS) -Multivariable logistic regression model (including significant variables as covariates)

			-Bilateral Symptoms: 72% anterior-CECS patients, 78% deep posterior-CECS patients and 53% of lateral-CECS patients (p<0.04); **Predictors of CECS** Univariable analysis found association (p<0.01) between CECS diagnosis and: -gender -age -clinical history -bilateral symptoms -sport type and competitive level -painful palpation (at examination) The multivariable regression model showed that *age, gender, history of lower leg pathology, type of sport (running or skating) and painful/tensed compartment during palpation* are independent predictors of CECS; the final AUC (Area Under the receiving operating characteristic Curve) was 0.66;	-Area Under the receiver operating characteristic curve (AUC) (to assess the discriminative ability of the final model) *All analysis was made using SPSS statistic version (v. 22.0.0.0) and R (v. 3.1.3)*
J. A. de Brujin et al., 2018	Retrospective Cohort Study	To determine the prevalence of CECS in older patients (≥50 years) and to assess whether older patients with CECS differ clinically from younger patients with CECS	**Patient selection** 1765 individuals evaluated for CECS; 354 were excluded (n=201 history and examination suggested different condition; n=153 previous analysis for CECS has been conducted); a total of 1411 subjects have been included; based on history, examination and elevated ICP, CECS has been diagnosed in 698 individuals (49%); Prevalence of CECS in older subjects (≥50years) was 38% (98/255); prevalence in patients younger than 50 years was 52% (600/1156); **Patient characteristics** -No differences found in *sex* or *duration of symptoms* between older and younger individuals (≤50y); -Previous conservative treatment: 57% (≥50y) vs. 80% (≤50y), p<0.01; -Previously used orthotics: 47% (≥50y) vs. 62% (≤50y), p<0.05; -Bilateral symptoms: 55% (≥50y) vs. 78% (≤50y), p< 0.01; **Sport activity** Available data for type of sport: 82/98 (≥50y), 552/600 (≤50y); No Sport participation: 62% (≥50y) vs. 7% (≤50y); Available data for level of sport participation: 66/98 (≥50y), 392/600 (≤50y); Competitive sports involvement: 5% (≥50y) vs. 69% (≤50y); **Symptoms** CECS symptoms were comparable between groups; Pain reported as main symptom: 94% (≥50y) vs 96% (≤50y), p<0.61; Tightness: 57% (≥50y) vs. 62% (≤50y), p<0.38; Cramps: 22% (≥50y) vs. 29% (≤50y), p<0.24; Altered sensation: 22% (≥50y) vs. 17% (≤50y), p< 0.29; Muscle weakness: 16% (≥50y) vs. 12%(≤50y), p<0.34; Tense/painful compartment (during examination): 66% in both groups, p<0.99; Painful medial tibial rim (during palpation): 11% (≥50y) vs. 36% (≤50y), p<0.01; **Affected compartments** AnteriorCECS diagnosis: 82% (≥50y) vs. 59% (≤50y); Deep-posteriorCECS diagnosis: 26% (≥50y) vs. 53% (≤50y); LateralCECS: 12% (≥50y) vs. 11% (≤50y); ICP data (anterior, lateral and deep flexor compartments) were comparable between groups;	**Patient Selection** -Patient's history review; -Physical examination: tests for signs of vascular insufficiency, compartment tenderness and neurological examination were conducted; -ICP testing (In case history and p. examination were suggestive of CECS): measurements taken from *Anterior, Lateral and DeepPosterior Compartments*; the criteria used for positive thresholds was Pedowitz criteria (ICP ≥ 15 mm Hg at rest, ≥ 30 mmHg 1 min after provocative exercise or ≥ 20 mmHg 5 min later); **Statistical Analysis** -Chi-square Test (to assess differences in categorical baseline characteristics) -Mann-Whitney test (to analyze continuous variables) *All analysis was made using SPSS statistic version (v. 22.0.0.0)*

3.4 Synoptic Tables-Diagnostic studies

Autore/anno	***Disegno di Studio***	***Obbiettivo***	***Risultati***	***Outcomes***
A. Fouasson-Chailloux, P. Menu, J. Allorent, & M. Dauty, 2018	Single-center Retrospective Cohort Study	To determine if the 12 classically reported clinical signs have predictive value for CECS	**Patient characteristics:** One hundred twenty-five patients were included in this study. 96 of these patients experienced intra-compartment pressure (ICP) ≥ 30 mmHg, considered to be affected by CECS, the remaining 29 patients recorded ICP <30 mmHg and were therefore considered to be unaffected by CECS. In the CECS group, the average age is 25.9 ± 10.5 years, a value comparable with the non-CECS group (p = .82). No differences were found concerning the distribution between the sexes (p = .27). Running is reported as most practiced activity, in both groups, followed by skating and football, in the absence of significant differences for the level of activity practiced. The evolution of the duration of symptoms was similar between the two groups (22 ± 7 months for the CECS group and 25 ± 6 months for non-CECS; p = .69). the Anterior and Lateral compartments were the most affected (83 in the CECS group and 23 in the non-CECS group; p = .34). 57 subjects in the CECS group reported bilateral symptoms, against 22 in the non-CECS group (p = .10). At rest, the mean ICP was 19.9mmHg ± 9 for the CECS group and 13.1mmHg ± 6 for the control group (p <.001). Post-exercise, the average ICP was 58.6 mmHg ± 20.5 for the CECS group and 19.9 mmHg ± 4 for the control group (p <.001). In the 29 patients with ICP <30 mmHg, the diagnoses were in 17 cases tendinopathies or muscular problems, in 4 cases nervous / vascular entrapment and in 2 cases stress fracture. No definitive diagnoses were made for 6 patients but, in 4 of these cases, CECS was considered clinically probable. Of the 96 patients with ICP ≥ 30 mmHg, 50 patients (52%) were effectively treated surgically and one patient was treated by botulinum toxin injection. 35 patients preferred to reduce sports (in 19 cases) or to cease / change sports (in 14 cases). **Study parameters:** 12 parameters that seem to be most relevant in the literature have been examined. Odd Ratios, Sensitivity and Specificity were then calculated for each of them. In our study population, the presence of bilateral pain, paraesthesia and stopping exercise due to pain were NOT recognized as predictors of CECS. In contrast, muscle stiffness and weakness, the presence of muscle hernias at rest or post-exercise have proven to be predictive of CECS. Pain at rest or on palpation and the absence of recurring pain during the same exercise were predictive of the absence of CECS. The association of two parameters (muscle stiffness and post-exercise muscle hernia)	-pre / post-exercise ICP 12 clinically relevant parameters have been studied: -no pain at rest -no pain on palpation (at rest) - bilateral pain - muscle stiffness - interruption of exercise due to pain - painful recurrence during same exercise -paresiaesia -radiated pain -muscle hernia at rest -muscle hernia post-exercise - post-exercise muscle weakness - post-exercise muscle hypertrophy (for each clinical parameter *Sensitivity, Specificity, Odds Ratio and Likelihood Ratios - P/ N-* have been calculated)

			contributed to the predictive model in the diagnosis of CECS. Elements such as the irradiation of symptoms and painful recurrence during the same exercise did not improve its predictive value. Initially, the classification of patients by risk was 76.8%. After the inclusion of the "muscle stiffness" parameter, 81.6% of the patients were correctly classified and, after the inclusion of the second parameter "post-exercise muscle hernia", 85.6% of the patients were correctly classified (88.6 % of subjects with CECS and 75.9% of subjects without CECS). In the predictive model, the Odd Ratio for "muscle stiffness" was 19.9 (95% CI [5.6–50.7]; p = .01) and 16.7 for the parameter "post-exercise muscle hernia" (95% CI [1.9– 141]; p = .04). these two parameters adapt well to the model, without differences between the predicted and observed values (Hosmer-Lemershow test: $\chi 2 = 0.33$; p = .848). The Cox-Snell and Nagelkerke R-squares reported are 0.328 and 0.496, respectively. The model predicted a variance of 36.7%, explained by the two predictors. The residual Student analysis showed six observations[fm1] (4.8%) not predicted by the model; an improvement of the same is reported to the exclusion of the above observations. The ROC curves presented an area of 0.808 [0.71–0.90], with a sensitivity of 82% and a specificity of 79% (LR +: 3.9).	
A. Roberts, A. Franklyn-Miller, 2011	Systematic Review	To conduct a systematic review of intramuscular pressure (IMP) assessed before, during and after exercise on the anterior tibial muscle in healthy subjects and then compare the results with the diagnostic criterion commonly used in CECS	38 articles were included in the review. In most cases the proposed exercises were *treadmill, walking / running or active dorsiflexion exercises.* IMP measurements were also reported for activities such as cycling, skiing and leg press exercise. On average, the duration of the exercise was less in dorsiflexion (from 10 '' to 20 '), when compared with running (from 1.5' to 120 '). The measurement techniques were carried out by means of a catheter filled with saline solution (fluid filled catheter - needle, wick, or slit-) or a transducer tipped catheter catheter. The solid-state transducer intracompartment catheter (STIC) was also used, which combines both of the techniques described above. The lowest IMPs were recorded pre-exercise, at rest; the decreasing IMPs instead represented the IMP peaks, although these varied according to the type of exercise. The IMPs calculated during the relaxation phase (range 0-30mmHg) were slightly greater than the IMPs at rest (range 0-20mmHg). Three studies reported IMP measurements 1 to 4 days post-exercise. These studies generally found a complete return to resting IMPs over the measured time frame. Hargens et al. (1989) noted, 2 days post-exercise, that major IMPs were recorded after eccentric dorsiflexion exercises, compared with concentric exercise. There was generally a greater variation in IMP peaks than in post-exercise IMPs. Standard deviations reported were approximately three times greater than those recorded at rest. Ten studies report IMP recordings during exercise, nine of these during running (duration -range- 5'-20 '). The average pressures recorded under stress varied from 23mmHg to 66mmHg. Nine studies reported the pressures in the relaxation phase but only in	-età dei soggetti -tecnica di misurazione -type and duration of exercise -n° of compartments measured -IMP reported at all time points

			one of these was the exercise running. The average of the relaxation pressures recorded during running was almost always higher than those recorded during the dorsiflexion exercise. Five studies (including a case study) of the 34 included, showed that the pre-exercise average recorded pressure was greater than that reported by the Pedowitz criterion of 15mmHg and two studies reported an average pressure, during the exercise, greater than the criterion Puranen threshold of 50mmHg. All studies report a relaxation pressure that is below the threshold reported by Styf (≥ 35-50mmHg). A study reports the mean pressures at 1 'and 5' post-exercise, both exceeding the thresholds for the Pedowitz criterion, respectively 30mmHg and 20mmHg (Potteiger et al., 2002).	
A. Whitney et al., 2014	Diagnostic study	Our hypothesis was that a diagnosis of compartment syndrome based solely on single pressure measurements has a high false-positive rate.	No clinical evidence of compartment syndrome was observed postoperatively or during follow-up until 6 months after injury. Using the accepted criteria of delta P of 30 mm Hg from preoperative diastolic blood pressure, 35% of cases (n = 16; 95% confidence interval, 21.5Y48.5%) met criteria for compartment syndrome. Raising the threshold to delta P of 20 mm Hg reduced the false-positive rate to 24% (n = 11; 95% confidence interval, 11.1Y34.9%). Twenty-two percent (n = 10; 95% confidence interval, 9.5Y32.5%) exceeded absolute pressure of 45 mm Hg.	-Physical examination (*pre/post-operatively, 6months FU)* -Pressure measurements
B. D. Steinberg, 2005	Correlational Diagnostic Study	To study a noninvasive method of evaluating limbs at risk of compartment syndrome	18 Volunteers were enrolled (9 men, 9 women) -Height (range):165–193 cm; -Weight (range): 52.6–131.9 kg; -Forearm fat thickness (range): 0.3–1.8 cm; -Medial leg fat thickness (range): 0.5–3.4 cm. Two variables significantly impacted both interstitial pressure measurements and quantitative hardness measurements: 1) Gender of the volunteer; 2) Arm fat thickness. In order to determine if a strong correlation exists between hardness and interstitial pressure, and whether these two measures moved in a systematic and regular way together, we looked at the Pearson's correlation coefficients. The correlation coefficients for the 4 compartments demonstrate a strong statistically significant (Po:0001), linear relationship (range 0.78–0.9; average 0.84) between pressure and hardness. Pearson's correlation coefficients were also obtained for the interstitial intra-compartmental pressure and the quantitative hardness ratio. These were positive and statistically significant (Po:001), (range from 0.71–0.84; average 0.77). Results suggest that both the hardness ratio and the hardness measurement are strongly correlated with interstitial pressure. Mean quantitative hardness for the group with interstitial pressures greater than 50mmHg (considered compartment syndrome), was statistically different (T test: Po:0001) from the mean hardness for the group with interstitial pressures less than 30mmHg (no compartment syndrome) .For each compartment, the mean hardness was close to two times greater for those	- Comparison of interstitial pressure to quantitative hardness measurements (using *noninvasive compartment syndrome evaluator - NCSE-*) - all values reported with relative *Standard Deviations* and *Mean* values

			who had compartment syndrome compared to those that did not. Finally, in order to evaluate whether the quantitative hardness and hardness ratio measures were significant predictors of compartment syndrome, we performed a z-test probit regression analysis. The hardness measures are the explanatory variables and explain variation in the likelihood of compartment syndrome occurring. The results show that both quantitative hardness and the hardness ratio are highly significant predictors of compartment syndrome (Po:001).	
D. Roscoe et al., 2014	Cohort study (diagnosis)	(1) To compare dynamic ICP measurement and anthropometric factors between patients with CECS and asymptomatic controls (2) To establish the diagnostic utility of dynamic IMCP measurement	Pain experienced by study subjects increased incrementally as the study progressed ($P < 0.001$). Pain levels experienced by the case group during each phase of the exercise were significantly different ($P = 0.021$). Subjects had higher ICP immediately upon standing at rest compared with controls (23.8 mm Hg [controls] vs 35.5 mm Hg [subjects]; $P = 0.006$). This relationship persisted throughout the exercise protocol, with the greatest difference corresponding to the period of maximal tolerable pain (68.7 mm Hg [controls] vs 114 mm Hg [subjects]; $P < 0.001$). Sensitivity and specificity were consistently higher than the existing criteria with improved diagnostic value (sensitivity = 63%, specificity = 95%; likelihood ratio = 12.5 [95% CI, 3.2-49]).	ICP measurements, tanken: -pre-exercise (while *supine* or *standing*) -during exercise (in *phase I-II-III)* -Post-exercise -*supine*- at 1' and 5' -Pain levels *Sensitivity, Specificity* and *Likelihood Ratio* were calculated for these variables
D. Roscoe et al., 2018	Case Control Study	To investigate the differences in barefoot plantar pressure (BFPP) characteristics between ICP-proven CECS cases and asymptomatic controls prior to the onset of painful symptoms.	Cases were aged between 21-40 (mean=27.5, sd=4.9); controls between 19-40 (mean=28.3, sd=7.4). Controls (1.81m ±0.06) were significantly taller (p=0.002) than cases (1.71m ±0.13); although there were no differences in weight or height-to-leg length ratio. One control subject's data could not be processed correctly by the RSScan software due to large feet (UK size 13) and was excluded from analysis. LL was not significantly correlated with any BFPP variables. WS correlated with FPA and ST for all four conditions; ANCOVA was carried out on these variables with speed as the covariate. IFFC-time was not correlated with WS. HMHL variables showed varying degrees and directions of association with WS; in each case only one side at one speed was significant. HMHL variables were therefore tested using the t-test. The ANCOVA assumption of the homogeneity of regression slopes was not met by the FPA (all conditions) and the ST variable in the marching condition, however when the difference is small and group sizes are equal, this type of heterogeneity was shown early on in the literature to be an insignificant problem with the ANCOVA remaining robust and valid. ANCOVA results agree with t-tests using the same variables. Cases had significantly	1. Stance time (ST, ms) 2. FPA: Foot Progression Angle; 3. COFx: The mean of the medial-lateral displacement of centre of force (COF) curves. 4. IFFC-time (plantarflexion rate): Time(ms) from IFC to initial full forefoot contact when all metatarsal heads, M1-5 (IFFC), are in contact with the ground. 5. HM/HL: The medial-lateral distribution of pressure under the heel was measured as HM/[HM+HL] at IFC, 5% of ST and at IFFC. Higher measures indicate medial distribution of the total pressure under the heel which has been inferred as a marker of pronation, but no validation studies have previously been

			shorter ST and IFFC-times than controls however there were no differences in stride-length when normalized to leg length, as per the recommendations of Hof28, for this study group. The differences in ST and IFFC-time were consistent between left and right feet and at both speeds. While there were some significant differences present in the other variables, these were not consistent between walking and marching. The area under the ROC curve ranged from 0.746 (95%CI: 0.636-0.87) to 0.773 (95%CI: 0.671-0.875) representing 'fair predictive validity' for IFFC-time.	performed to prove an association with movement. 6. FORE: The ratio, between inner and outer metatarsal loading: 100((M1-M5)/Zone average).
D.B. Birtles Et Al., 2002	Case control Study	It has been hypothesized that patients with anterior CECS are more susceptible to pain, fatigue and edema after performing eccentric exercises.	**Subject characteristics:** Patients and controls were matched by age [Average: 30.3 (Standard Deviation: 8.0) years and 32.3 (9.0) years, respectively], body mass [78.5 (16.2) kg and 70.1 (10.0) kg] and Body mass index [26.2 (4.4) kg m^2 and 23.7 (2.8) kg m^2) without significant differences between the two groups **Muscle strength:** No differences were found between the initial isometric strength between the two groups. On average, the eccentric force detected was greater in patients (P <0.05) but theforce ratio *eccentric: isometric* was similar in both groups. The stimulation intensity employed for the two groups was similar (approximately 50mA) and generated similar forces. Voluntary isometric strength dropped to 90.2 (2.5%) [(geometric mean (SEM)] and 86.5 (2.4%) compared to pre-exercise values, respectively in patients and controls (P <0.0005). 5% of the voluntary force was recovered by both groups after 10 'from the end of the exercise but remained slightly lower than the pre-exercise measurements (P <0.005). The force generated by the 50Hz stimulation increased slightly at the end of the exercise (P <0.01), remaining fairly constant during recovery, 87-90% of the pre-exercise values. In contrast, the low frequency force decreased significantly (P <0.005 and P <0.05 respectively, for patients and controls) in the immediate post-exercise period, remaining at 80% of the initial value. During the 10 'recovery this decreased further up to 58% for patients and 56% for controls. The 10: 50Hz ratio was reduced to 80% immediately after exercise in both groups (P <0.01) and decreased further throughout the recovery period. There were no significant differences in low frequency fatigue levels between the two groups. **Muscle thickness:**The mean pre-exercise muscle thickness was similar in patients [29.8 (1.1) mm] and controls [28.9 (0.7) mm]. There were no significant changes in post-exercise muscle volumes in either group. None of the post-exercise measurements were significantly different from the pre-exercise ones and there was no difference between patients and controls in any of the measurement / evaluation phases. **Pain scores:** None of the subjects reported pain or discomfort / discomfort in the anterior tibial before exercise and there were no significant differences	- Maximum voluntary contraction (MVC) - Force generated by electro-stimulation at 10 Hz and 50 Hz - Muscle density (Measured in real time by ultrasound) -Pain or discomfort (reported on NPRS scale, 0-10) -Tenderness (reported on NPRS scale, 0-10) (Before physical exercise, then at 24 and 48 hours post-exercise)

			between the two groups during the exercise phase or the recovery phase. The perceived pain values at 24h and 48h post-exercise were very variable in the patient group, in some cases reporting high values of 5-7 / 10, while in the control group very low intensities were reported. NPRS values during walking, active dorsiflexion, plantar flexion and palpation were significantly higher (P <0.05) than in controls, 24 hours post-exercise. After 48h the patient group experienced greater pain during dorsiflexion, plantiflexion and palpation (P <0.05).	
D.V. Litwiller, 2007	Cohort study	Define and evaluate a MR screening protocol for CECS of the lower limb, using an in-scanner exercise protocol and a new "dual birdcage" design coil for optimization of acquired images.	The ROC analysis showed a threshold relative to the T2-weighted T2 signal strength, having a sensitivity of 96%, a specificity of 90% and an accuracy of 96% for CECS. Patients with CECS achieved their peak ratio of signal intensity, compared to baseline, during the first recovery period from isometric dorsiflexion exercise, while unaffected subjects or patients suffering from stress pain in the lower limb (for other causes) reached peak values during the course of the year (P <0.001).	-Signal-to-noise ratio (SNR) -Peak deviation uniformity (PDU) - Analysis of Receiver operating characteristic (ROC) (Per il quale sono state calcolate sensibilità e specificità)
E. E. Sigmund et al., 2013	Health Insurance Portability and Accountability Act (HIPPA)-compliant study	To evaluate the performance of diffusion tensor imaging (DTI) in the evaluation of chronic exertional compartment syndrome as compared to T2-weighted (T2w) imaging.	All diffusivities significantly increased (P < 0.0001) and FA decreased (P < 0.0014) with exercise. Longitudinal diffusion responses were significantly smaller than transversal diffusion responses (P < 0.0001). Nineteen of 98 patient Compartments were classified as CECS on T2w. MD increased by 3.8 6 3.4% (volunteer), 7.4 6 4.2% (normal), and 9.1 6 7.0% (CECS) with exercise.	-Longitudinal and transverse diffusion Eigenvalues -mean diffusivity (MD) -fractional anisotropy (FA) patients were classified by their response on T2w: normal (<20% change), and CECS (>20% change). -Mixed model analysis of variance compared subject groups and compartments in terms of response factors (post/pre-exercise ratios) of DTI parameters.
E. E. Sigmund et al., 2014	HIPAA-compliant study	The purpose is to carry out diffusion tensor imaging (DTI) at multiple diffusion times (DT) in skeletal muscle in normal subjects and chronic exertional compartment syndrome patients and analyze the data with the random permeable barrier model (RPBM) for biophysical specificity	-15 subjects (6 F, age -range- 15/30y; 9 M, age -range- 18-36y); All subjects and muscle compartments showed nearly time-independent diffusion along and strongly time dependent diffusion transverse to the muscle fibers. RPBM estimates of fiber diameter correlated well with corresponding autopsy reference. D0 showed significant (p<0.05) increases with exercise for volunteers. At the group level, response factors of all three parameters showed trends differentiating controls from CECS patients, with patients showing smaller diameter changes (p = 0.07), and larger permeability increases (p = 0.07) than controls.	**DTI data collection** - Diffusion times (Td): 30ms, 170ms, 500ms and 1020ms; -Signal to Noise Ratio (SNR) and Normalized Standard Deviation (NSD), taken pre-/post-exercise, for all compartments, at two different Td values;
G. Andreisek Et Al., 2009	Prospective Case Control Study	Rilevare cambiamenti temporali durante l'esercizio, nei segnali di RM in T2* e *Arterial Spin Labelling* (*ASL*) in pazienti con CECS del compartimento anteriore e soggetti di controllo.	Study population: 19 subjects (11M, 8F) CECS group (CG): 9 (6M, 3F; mean age 33.7y, range 20-47y); Healthy group (HG): 10 (5M, 5F; mean age 29y, range 23-36y); Both groups showed a peak in ΔT2* and ΔASL at 3' post-exercise, followed by a decrease of seguito da una diminuzuine del segnale in funzione del tempo trascorso. La massima ΔT2* nel CG è del 26%, 29% nel HG; la massima ΔASL registrata è stata 183% nel CG e 224% nel HG. Dopo 15' il segnale ASL è ritorrnato ai valori di baseline; ciò nonostante, il	Patient reported outcomes (baseline, immediate post-exercise, 3', 6', 9', 12' e 15' post-exercise): -pain -muscle weakness -tenderness -ΔT2* and ΔASL normalized values

			segnale in T2* è rimasto elevato (8% nel CG; 10% nel HG). Non è stata rilevata nessuna differenza statisticamente significativa tra soggetti affetti e controlli nel ΔT2* e ΔASL post-esercizio (p = 0.21–0.98).	
J. G. H. van den Brand et al., 2005	Cohort Study	To investigate the diagnostic value of Intra-compartment pressure testing, Magnetic resonance imaging and near-infrared spectroscopy in the diagnosis of chronic exertional compartment syndrome.	Fifty patients (100 legs) participated in the pre-fasciotomy visit; 3 refused fasciotomy; 2 were lost to follow-up. Of 45 patients who completed the post-fasciotomy visit, the diagnosis of chronic exertional compartment syndrome was retrospectively confirmed in 42 patients and discarded in 3 patients. The sensitivity for intra-compartmental pressure (cutoff point, 35 mmHg) found in this study was 77% (67%-86%, exact 95% confidence interval), lower than estimates from the literature (93%). The sensitivity (previously defined cutoff) for near-infrared spectroscopy was 85% (76%-92%, exact 95% confidence interval), validating the estimate found in the literature (85%). Sensitivity of magnetic resonance imaging was comparable to that of intra-compartmental pressure and near-infrared spectroscopy; associated specificity at a given sensitivity appeared to be lower with magnetic resonance imaging.	*(Before Fasciotomy)* -intracompartmental pressure -near-infrared spectroscopy - magnetic resonance imaging data (taken during and after a treadmill exercise) *(After Fasciotomy)* - intracompartmental pressure -near-infrared spectroscopy
L. Trease et Al., 2001	Prospective blinded comparison study	To correlate the results of a series of 201Tl SPET scans with the compartment pressure test, to determine its ability to diagnose compartment syndrome and to establish the association between ischemia and pain.	**Compartment pressure testing:** 34 participants, 25 (74%) showed positive CPT, and nine (26%) showed negative CPT. **201Tl SPET imaging comparison:** *Quantitative Analysis*- No significant difference in the pixel ratio at any slice comparing the positive and negative CPT groups in either ROI; *Intra-observer reliability for quantitative analysis*- slight but statistically significant difference between the mean pixel count of readings 1 and 2 for both compartments have been demonstrated; *Inter-observer reliability for quantitative analysis*- Correlation co-efficients demonstrated very high *r* values indicating excellent reproducibility, with 11 of 12 compartments slices analysed having an *r* value >0.90, and five of 12 slices having an *r* value of >0.97; *Qualitative analysis*- Chi-square analysis revealed that there was no significant difference between CPT groups for qualitative scores less than or equal to and scores greater than 5 in the anterolateral compartment. No statistical analysis was possible for posterior compartment; *Qualitative analysis in patients with symptoms in more than one compartment*- no significant difference in the anterior or posterior qualitative scoring in the stress images between those patients who had an isolated compartment with CECS and those with more than one compartment involved. *Quantitative comparison*- no difference in perfusion between the patients (+ve CPT) and controls (–ve CPT); *Qualitative comparison*- no significant difference in perfusion between those patients with positive and those with negative CPT results, when exercise type was removed as a confounding factor;	-ICP measurements (indwelling slit catheter) -sPET imaging acquisitions at 5’ and 180’ (2’ after 201Tl chloride injection) -statistical analysis

L. Trease et al., 2001	Comparative Study	To clarify the etiology of chronic exertional compartment syndrome (CECS), and to investigate the diagnostic applications of 201Tl SPET in CECS	**Patient Characteristics** -Study population: 34 subjects (20 M, 14 F) -Age: mean 29y (range 18-55y) -Anterior CECS: 12 subjects -Posterior CECS: 12 subjects -Combination (ant+postCECS): 10 subjects **Compartment pressure testing** Of the 34 participants, 25 (74%) had a positive CPT, and nine (26%) had a negative CPT. **Quantitative analysis** Performed on the anterolateral and deep posterior ROIs in all 11 slices within the CPT leg. No significant difference in the pixel ratio at any slice comparing the positive and negative CPT groups in either ROI (interaction term not significant, group main effect [anterolateral: F (1,30) = 1.35, P=0.25] [deep posterior: F (1,30)= 1.30, P=0.67]). **Intra-observer reliability for quantitative analysis** A correlation co-efficient was calculated for each slice. High r values indicated excellent reproducibility for slices in both the anterior (r range 0.93–0.98) and the deep posterior compartments (r range 0.85–0.97) across the six slices examined. A slight but statistically significant difference between the mean pixel count of readings 1 and 2 for both compartments were demonstrated. **Inter-observer reliability for quantitative analysis** Correlation coefficients demonstrated high r values indicating excellent reproducibility, with 11 of 12 compartments slices analyzed having an r value > 0.90, and five of 12 slices having an r value of > 0.97. **Qualitative analysis.** One patient was deemed to have a perfusion deficit consistent with CECS (score of ≤5). The remaining 33 patient stress and redistribution images were considered normal. Chi square analysis: no significant difference between CPT groups for qualitative scores less than or equal to and scores greater than 5 in the anterolateral compartment. In the deep posterior compartment, statistical analysis could not be performed, as there were no patients with scores of less than 5 to suggest an ischemic compartment.	-*Compartment Pressure Testing (CPT)* - 201Tl SPET imaging and comparison (with *Qualitative* and *Quantitative analysis)*
O. Aweid Et Al., 2012	Systematic Review and Recommendations	(1) Is a diagnostic standard available? (2) Which ICP threshold criterion should be used to diagnose CECS? (3) What are the criteria and options for surgical management?	32 studies were included in the review. The studies differ in ICP measurement techniques; the most frequently measured compartment is the anterior compartment, the exercise protocols used varied from running to walking, up to plantar and dorsal ankle flexion exercises. In pre-exercise measurements, the average range ranged from 7.4 to 50.8 mmHg in subjects with CECS, and between 5.7 and 12 mmHg in control subjects; measurements during exercise showed pressures between 42 and 150 mmHg in subjects with CECS and between 28 and 141mmHg in control subjects. There is no overlap between affected subjects and controls in 1 'post-exercise measurements, showing values between 34 and 55.4mmHg (in affected subjects) and between 9 and 19mmHg (in controls). The general quality of the studies is not high; The evidence on the criteria commonly used for ICP measurement in the diagnosis of CECS is weak.	The data extrapolated from the studies include: study design, number of subjects, number of control subjects, instrument for ICP measurement used, compartments evaluated, position of the limb during measurement, position of the catheter, exercise protocol used, timing of measurements , resting pressures (average), maximum compartment pressure (average), post-operating pressure (average), diagnostic criterion used and if a

				reference standard was used. The improvement of post-fasciotomy symptoms was taken as the diagnostic reference standard for CECS.
P. S. Oturai, T. Lorenzen, J. Nørregaard, L. Simonsen, 2006	Prospective Diagnostic study	To evaluate SPECT imaging as a potential tool for the diagnosis and characterization of CECS	Seven of the 16 subjects experienced an increase in post-exercise intra-compartment pressure (ICP). Two data sets (one subject with increased ICP in the deep right posterior compartment and one subject with normal ICP) were not processed because they were lost. Six of these subjects showed, on SPECT with contrast medium (Tetrofosmina), a stress-induced hypoperfusion in the muscle compartments studied. Only three (50%) of the six evaluable subjects showed scintigraphic hypoperfusion and an increased ICP; the other three subjects, however, showed hypoperfusion in the absence of a high ICP. Variables such as age, the distance traveled on the treadmill (necessary to reproduce the typical symptom of the lower limb), sex and distribution of the muscle compartments clinically involved, were not significantly different between the groups, with normal or high ICP (P> 0.2). In four subjects, scintigraphic hypoperfusion was detected in compartments without clinical signs of CECS. According to the clinical presentation, the pressures of these compartments were not detected.	- Intra-compartment pressure (ICP); measured *at rest, at 1 ', at 5' and eventually 15 'post-exercise.* -Perfusion scintigraphy with 99mTc-tetrofosmine
S. Rajasekaran, C. Beavis, A-R. Aly, D. Leswick, 2013	Prospective comparison study	Verify the hypothesis that in patients with CECS of the anterior compartment they experience an increase in the thickness of the anterior compartment (ACT) post-exercise, compared to control subjects (verified by ultrasound)	Pressures detected in the anterior compartment were used to diagnose CECS in affected patients, in accordance with the modified Pedowitz criteria. The mean percentage change in anterior compartment thickness in affected patients compared to control subjects at 0.5 'was 21.3% versus 6.32% [95% CI, 6.92-35.6 and 0.094-12.5, respectively; P = 0.011]; at 2.5 ', it was 24.6% against 4.22% (95% CI, 10.7-38.5 and 21.85-10.3, respectively; P = 0.003); finally, at 4.5 'the values were 24.9% against 5.08% (95% CI, 14.3-35.5 and 20.813-11.0, respectively; P = 0.003). The mean thickness of the anterior compartment in CECS patients compared to control subjects increased significantly after exercise (P = 0.003), both at 0.5 ', 2.5' and 4.5'.	-Thickness anterior compartment (ACT) -Percentage variation in ACT relative to the rest condition -Pressure compartmental

3.5 Synoptic Tables-Treatment studies

Autore/Anno	***Disegno di Studio***	***Obbiettivo***	***Risultati***	***Outcomes***
R. Thein et al., 2019	Comparative Study	To compare the functional results between conservative treatment and surgical management in patients presenting with CECS of the anterior compartment diagnosed by the medical history and compartment pressure measurements in accordance with the previously reported Pedowitz diagnostic criteria	Study population: 43 patients (mean age 23.8 + 7.6 years) Surgery: 31 (72.1%) Conservative Treatment: 12 (27.9%) mean Follow-up time (surgery - postsurgical examination): 28.15 mean (SD:±17.50) months. Mean time from the beginning of exercise to the beginning of pain in the total group was 6.29 (SD: ±5.10) mi with an overall pain score at diagnosis of 7.38 (SD:±1.98). Pain improved (DP) on follow-up examination by 1.59 (SD:±2.10) points and by 4.27 (SD:±3.05) points in conservatively treated and surgically managed patients, respectively, representing a statistically significant difference ($p< 0.014$). The mean Tegner scores at diagnosis for conservatively treated and surgically managed patients, respectively, were 4.50 (SD:±1.93) and 2.48 (SD:±1.78; $p < 0.004$), with a mean change in the Tegner score (DT) after treatment of 0.09 (SD:±3.14) and 3.22 (SD:±3.19), respectively ($p < 0.009$). Three patients in the conservatively managed group (25% of 12) and 24 patients in the operated group (77.4% of 31) reported full resumption of their pre-diagnosis activity level ($p < 0.001$). Mean SF-36 scores at follow-up for conservatively treated and surgically managed patients were 79.15 (SD: ±17.50) and 89.2 (SD: ±10.86), respectively ($p < 0.004$). In the operative group, short-term complications included hematoma in three patients and superficial peroneal nerve sensory impermanent in one patient, all resolved in 4 weeks and 3-month postoperatively, respectively.	-ICP measurements (*before/after exertion*) -Pain rating with 0-10 VAS (*before/after treatment)* -Tegner Score (*before/after treatment)* *-SF-36 (at the time of follow-up)* *-return to pre-diagnosis activity level*
D. Campano, J. A. Robaina, N. Kusnezov, J. C. Dunn, and B. R. Waterman, 2016	Systematic Review	To review published literature to characterize the at-risk demographic, operative indications, surgical techniques, functional outcomes, and reoperation and complication rates after operative management of chronic exertional compartment syndrome (CECS) of the lower leg.	Among the 204 original articles, 24 primary studies with 1,596 patients met the inclusion criteria. The mean age was 26.6 years (SD: ±8.9 years), and the majority of patients were male patients (70%). The total study population mostly comprised military service members (54%) and athletes (29%). Of the athletes, 83% were recreational; 9% were college level; and 8% were either national, international, or professional. The most commonly involved compartment was the anterior compartment (51%; 95% confidence interval [CI], 48.6% to 52.3%), followed by lateral (33%; 95% CI, 31.4% to 34.9%), deep posterior (13%), and superficial posterior (3%). The cumulative posterior involvement rate was 16% (95% CI, 15.1% to 17.8%). Mean follow-up was 48.8 months (SD: ±22.1 months; 95% CI, 47.1 to 50.5 months). Six	Classification of clinical and functional outcomes was made using the Likert Scale in 11 of the included studies (24) -Satisfaction (after surgery) rates were recorded in 9 of the included studies -return to *previous* (or *full*) *activity was reported in 11 studies* -Success rates for specific compartment release was calculated

			percent underwent revision surgery. The overall complication rate was 13% (due to postoperative neurologic dysfunction, infection, and other reasons).	
S. Cook and G. Bruce, 2002	Retrospective Cohort Study	To determine the success of fasciotomy of lower limb compartments with elevated intercompartmental pressure.	Fourteen patients met the inclusion criteria. Eleven reported success with complete resolution of symptoms and return to military fitness levels. Two reported no change and significant residual symptoms. One reported worsening symptoms and one required re-operation with a successful result.	-relief of symptoms -clinical result of surgery (*no residual symptoms/improvement but relapse re-operation/no improvement/symptoms worsening)* -Complications (*no complications/altered sensations*) -return to full-duty by completing the *Physical Fitness Test* (PFT) (*fail/pass* with reported changes)
D. S. Edmundsson, G. L. Toolanen and P. S. Stal, 2017	Observational Study	Considering the well-known vascular complications related to diabetes, we hypothesize that CECS complications (unusual low capillarization and focal signs of injury in the muscles) may be involved in the pathogenesis of CECS in diabetic patients.	Before treatment, walking distance until occurrence of pain was limited (<0.2 km). Intramuscular pressure was significantly higher than in reference subjects. Muscle analysis showed changes pathognomonic for neuropathy and myopathy and a restricted capillary network, with significantly more severe changes in the muscles of diabetic than non-diabetes patients. Treatment with fasciotomy improved clinical signs, increased walking ability and reduced muscle abnormalities, but muscle capillarization remained low.	-Intra-Muscular Pressure (IMP) monitoring (*at rest* and *1', 5', 10' and 15' post-exercise*) -Pain Ratings were made using the *Borg Scale* -Biopsy of muscle tissue samples (at *time of surgery* and *1 year follow-up*)
J. L. Howard, N. G. H. Mohtadi and J. P. Wiley, 2000	Retrospective Descriptive Cohort Study	To evaluate outcomes in patients who had a fasciotomy performed on their leg(s) for chronic exertional compartment syndrome (CECS).	Fifty patients had anterior/lateral compartment involvement, 8 patients had deep posterior compartment involvement, and 4 patients had anterior /lateral/ deep posterior compartment involvement. The demographics of the 39 respondents and 23 non-respondents were similar. The mean percent pain relief of respondents was 68% (95% CI [confidence interval] - 54% to 82%). There was no relationship between percent pain relief and the documented immediate post exercise compartment pressures. A clinically significant improvement was reported by 26 of 32 (81%) anterior/lateral compartment patients and 3 of 6 (50%) patients with deep posterior compartment involvement. Patient level of activity after fasciotomy was classified as equal to or higher than before the operation with a lower degree of pain by 28 of 36 (78%) patients, while 8 of 36 (22%) patients reported lower activity levels than before the operation. Of the patients reporting lower activity, seven were due to exercise related pain in the post-operative leg(s) and one was due to lifestyle changes. Thirty of 38 patients (79%) were satisfied with the outcome of the operation. Four of 62 patients (6%) failed the initial surgical procedure and required revision surgery for	A questionnaire was designed and developed to assess: - pain (using a 100 mm visual analogue scale) -level of improvement -level of maximum activity -satisfaction level -occurrence of reoperations

			exercise-induced pain. In addition, one of these individuals also had a sympathectomy and another had a neurolysis performed at the time of revision surgery. Three of the 62 (5%) patients had subsequent operations for exercise-induced pain on different compartments than the initial surgical procedure. One individual had an unsuccessful operative repair of a posttraumatic neuroma. Postoperative complications were reported by 5 of 39 (13%) patients in the additional comments section of the questionnaire.	
M. Z. Meulekamp, W. Sauter, M. Buitenhuis, A. Mert and P. van der Wurff, 2016	Retrospective Observational Study	Evaluation of patient characteristics and short-term results of the rehabilitation program for service members used in the Military Rehabilitation Centre Aardenburg.	The results showed a significant improvement in all groups (MTSS, CECSc - conservative, CECSo - operative) regarding the Patient-Specific Functional Scale (PSFS). Only the CECSo group showed significant improvement on the Numeric Pain Rating Score (NPRS). None of the patient characteristics like gender, age, military service, duration of symptoms, and treatment setting were identified to correlate with outcome results.	-Numeric Pain Rating Score (*NPRS*) -Patient Specific Functional Scale (*PSFS*), divided in 4 sub-categories: 1) *Hobbies* 2) *ADL* 3) *Military Activities* 4) *Sport Activities* (both administered at the beginning -*week 1*- and the end -*week 6*- of rehabilitation)
J. D. Packer et al., 2013	Cohort study	To verify if higher preoperative post-exertion compartment pressures are correlated with higher success and patient satisfaction rates after treatment with fasciotomy	The mean follow-up period for the nonoperative treatment group (n = 27) was 5.6 years (range, 2.1-10.6) and for the operative group (n = 73) was 5.2 years (range, 2.0-11.3). The operative group had a higher success rate (81%) compared with the nonoperative group (41%) (P.001), and the operative group had a higher patient satisfaction rate (81%) compared with the nonoperative group (56%) (P = .011). There was no significant correlation between compartment pressures and patient outcomes. Patients with combined anterior and lateral compartment releases had an increased failure rate compared with isolated anterior release (31% vs 0%, respectively; P = .035). Surgical patients who were post-college had a lower satisfaction rate (66%) compared with high school (89%) and college patients (94%) (P = .017).	-ICP testing (pre-/post-exertion) - Post-treatment Outcome: -*Success (Excellent/Good)*; -*Failure (Fair/Poor)* -Satisfaction with Result of treatment: *Yes/No* -Complications in Operative Group -Return to Sport
S. Rajasekaran, MD and M. M. Hall, 2016	Systematic Review	Systematically review the literature for nonsurgical treatment options for CECS of the lower leg.	Four treatment options were identified (from least to most invasive): *massage, gait changes, chemodenervation, and ultrasound-guided (USG) fascial fenestration;* *A treatment algorithm* has been proposed in the discussion. Currently, limited evidence in the form of Case Series or Case Reports is only available for these treatment options.	Each study was subsequently reviewed, and the level of evidence of each article was ranked according to the scale published by the *Journal of Bone and Joint Surgery*. *Strength* and *Weaknesses Points were reported.*
D. Slimmon, K. Bennell, P. Brukner, K. Crossley and S. N. Bell, 2002	Retrospective cohort study	To establish long-term surgical success rates for the technique of fasciotomy combined with partial fasciectomy and to compare the results in different lower leg compartments.	Study Population: 62 (27M, 35F; Unilateral Surgery: 7 (4M, 3F) Bilateral Surgery: 55 (23M, 32F) Ant-compartment only: 21 (7M, 14F) Post-compartment only: 26 (13M, 13F) Combined (ant-post) surgery: 25 (7M, 8F) Of the 50 patients who underwent a single operation, 60% (30) reported an excellent or good outcome. Average pain and pain-on-running were significantly reduced, although	Questionnaire (modified from Coleman et al., 2000) given in 3 separate times: 1)before surgery; 2)at their optimum response after operation; 3)at follow up time; **Questionnaire Items** -Description and duration of symptoms

			some subjects still reported considerable levels of pain. Fifty-eight percent (36 of 62) were exercising at a lower level than before injury and, of these, 36% (13) cited the return of their compartment syndrome or the development of a different lower leg compartment syndrome as the reason for a reduction in exercise levels. Some subjects indicated early initial improvement followed by subsequent deterioration.	-Presence and duration of post-operative complications -Operation Outcome (in terms of *pian, return to pre-injury sport, competitive sport level, weekly exercise)* -Overall perception on operation outcome (rated as *Excellent, Good, Fair, Poor*);
J. P. H. Tam, A. G. F. Gibson, J. R. D. Murray, M Hassaballa, 2018	Retrospective Cohort Study	1)To assess patient-reported outcomes pre-/ post-fasciotomy (mini-open approach) and at 6 moths follow up 2)To identify potential relationships between ICP and patient-reported pain.	A total of 138 patients were eligible for inclusion in this study (mean age 29.7 ± 9.7 years, 110 M, 28 F) of which 109 patients (VRS n = 61, VAS n = 48) reported pain level at pre- and post-operative stages. Mean pre-operative VAS score was 8.52 ± 0.71 and decreased to 0.77 ± 0.69 post-operatively. An insignificant positive correlation (r = 0.046, two-tailed p = 0.76) was found between VAS pain and ICP. A significant moderate positive correlation (r = 0.497, two-tailed p = 0.01) was found between VRS pain and ICP.	**Patient Reported Outcomes** -Pain (using a 3-item Verbal Rating Scale -VRS- or a 0-10 Visual Analog Scale -VAS-) -Activity Level -Associated Symptoms **Statistical Analysis** - Spearman's rank correlation (to assess the strength of correlation between pain -VRS or VAS- and ICP -mmHg-)
W. J. F. van Zoest, A. R. Hoogeveen, M. R. M. Scheltinga, H. A. Sala, J. B. A. van Mourik and P. R. G. Brink, 2008	Retrospective Cohort Study	To evaluate the efficacy of a surgical treatment of deep posterior CECS of the leg using predefined cut-off points of compartment pressure (more than 20mmHg at rest and 5 minutes after exercise, and 25mmHg immediately after and one minute after exercise)	The mean follow-up in both the "high-pressure group" and the "low-pressure group" was 36 ± 4 months (range 19–44). Patients were followed in the outpatient department at 2, 6 and 12 weeks after surgery. Further follow-up was performed by means of the questionnaire. Eighty-five out of 110 patients that were eligible for study returned their questionnaire. Thirty-five individuals of this group were not suitable for follow-up since more than one leg compartment was involved, and an additional four patients chose not to participate in further follow-up. Therefore, forty-six individuals were available for analysis (19 males, 27 females). The activities, which had caused the complaints, were running (n = 17, 37%), field hockey and soccer (n = 13, 28%), walking (n = 11, 24%), speed skating (n = 3, 7%), and cycling (n = 2, 4%). Eight individuals participated in sports at the international level (17%), 10 at the national level (22%) and 20 at the recreational level (48%). In line with the measurement regime, 27 patients were surgically treated (mean age 35 ± 16 years for the high-pressure Group; mean age for low-pressure group was 43 ± 12 years). Pain is the foremost clinical symptom, but paresthesia and loss of muscle strength also occurred in almost 20% of patients. Some patients presented with more than one symptom. Results of surgery were considered good to excellent by 33% of patients, and fair by 19% of patients. The remaining 48% considered their surgical procedure unsuccessful. Surgical results showed no correlation with pre-surgery compartmental pressure levels. In contrast, 84% of the low-pressure group judged their current situation improved compared to 3 years earlier. A portion of this group improved following inlays and physical	-Dynamic ICP testing (-Symptoms reported by patients pre-operatively - Questionnaire (21 items, adjusted for both "high" and "low" pressure groups)

			therapy (n = 6,32%). Interestingly, various other diagnoses were established in the course of their conservative treatment for CECS (n = 10, 53%). Four patients were surgically treated for a herniated disc with good results. Three additional patients received successful treatment for intermittent claudication. Corrective venous surgery with marked improvement in previous symptomatology was performed in two patients. One patient was diagnosed with a popliteal entrapment syndrome and received a successful vascular procedure.	
M. B. Winkes, A. R. Hoogeveen and M. R. Scheltinga, 2013	Systematic Review	To provide a critical analysis of the existing literature on the surgical management of deep posterior-CECS aimed at identifying parameters determining surgical results.	7 studies of level III evidence reporting on a total of 131 patients met inclusion criteria (>5 patients, reporting intra-compartmental pressures (ICP), clearly stating postoperative outcome). Only four studies strictly adhered to predefined ICP criteria. Cutoff ICP levels varied widely among the 7 studies. Surgical procedures ranged from a superficial crural fasciotomy to multiple fasciotomies of various deep posterior compartments. No single surgical procedure proved superior. Prolonged high ICP levels following provocation were associated with postoperative success. Success rates after fasciotomy were modest, ranging from 30% to 65%. Risk factors for failure of surgery were not identified.	

4 Discussion

4.1 Etiology and Risk Factors

Current knowledge of CECS etiology is limited and still highly debated. Of the various elements suspected of being involved in the syndrome buildup, tissue ischemia during exertion, has been indicated by authors as one of the starters of the pathological mechanism. Transient ischemia seem to be due to increased intra-compartment pressure, which can generally depend on two factors: the lack of fascial compliance, which does not allow to support the increase in muscle volumes during activity and an increase in internal pressures, due to the increased blood supply and to muscle edema phenomena(32). Edmundsson et al. have stated, through a pre/post-fasciotomy biopsy study on the anterior compartment, that subjects affected by CECS show, when compared to controls, a lower capillary density, a lower number of capillaries around the muscle fibers and a lower number of capillaries relative to the muscle fiber area; however, this phenomenon is described as a probable constitutional and not acquired characteristic, since during follow up (at 1 year), an increase in muscle fibers size was found, but there was no increase in the density of the surrounding capillary bed(25).

Among the proposed etiological hypotheses, fascial compartment rigidity and/or thickness as predisposing factors for the increase in intra-compartmental pressures; however, this is not supported by results obtained by Dahl et al., which shows lack of correlation between fascial stiffness and intra-compartmental pressure in CECS patients(32).

Barbour et al., in a histological study of fascial and periosteal tissue samples from affected subjects and controls, noted that in relation to collagen organization, control samples showed a greater degree of disorganization than patients. On the other hand, by dividing the group of affected subjects by overall duration of symptoms, the subjects with symptoms lasting longer than 12 months showed a greater collagen irregularity (intended as orientation) compared to shorter onsets(35).

A study by Birtles et al. found that comparison between affected subjects and controls, during the execution of an isometric work protocol, no differences were found in the expression of the maximum force (maximal voluntary contraction - MVC), although the MVC/body mass ratio showed a lower relative strength in the patient group, as well as the ratio between MVC/transverse section (an increase of about 8% was noted in both groups of the muscle cross section area, at the same time no differences were found between groups for the central and peripheral fatigue values; instead, a significant difference in the intensity of perceived pain during work ($p < 0.05$ at 4 ') and at 1' of recovery ($p < 0.001$) was highlighted(41).

In an EMG study conducted on cross-country skiers, Federolf and Bakker showed a higher level of EMG effort in the symptomatic group (Ant-CECS) for the anterior tibial muscle, concentrated in the gliding phase (monopodial stance); this suggests that neuromuscular balance control could play an important role in supporting the pain of anterior compartment and possibly the development of Ant-CECS(2);

The knowledge developed about incidence and risk factors for the development of this condition is similarly limited and discussed. This is due, partly at least, to the fact that specific populations generally studied for CECS are subject to an intensive physical/sports activity regime (athletes of different sports and military disciplines). In a study conducted on a large military population (4,100 subjects recruited from a population at risk of 8,320,201 individuals), Waterman et al. reported an annual incidence rate of 0.49 / 1000 people-year, while noting an increase in the annual incidence over the study period (from 0.06 / 1000 people-year in 2006 to 0.33 / 1000 people-year in 2009). This, as reported by the study group, is due to the fact that the ICD-9 (International Classification of Diseases Clinical Modification, 9th revision) code for CECS was created only in the year 2005(4).

More recently de Bruijn et al. conducted two studies on a heterogeneous population of 1411 individuals with CECS, in an attempt to identify predictive factors for the development of the syndrome, determine the prevalence of the syndrome in a population of individuals over 50 years of age and to compare clinically, younger patients with older ones;

The predictive factors identified were as follows: age, gender, previous pathologies of the lower limb, type of sport practiced (running or skating on the track) and the presence of a painful / tensed compartment(12,42);

Younger subjects show a higher prevalence than subjects ≥50 years (52% vs. 38%); this could be attributable to a greater participation in sports (93% vs. 38%) and competitive (69% vs. 5%) by younger subjects, even if not directly reported by the authors.

The clinical differences between the two age groups were: -

-greater frequency of diagnosis of anterior-CECS in subjects ≥50 years (82% vs. 59%);

- greater frequency of diagnosis of deep posterior-CECS in subjects ≤50 years (53% vs. 26%);

No differences were found between the groups for the reported symptomatology and for the values of the ICP detected(12).

4.2 Diagnosis

The only proven gold standard to diagnose CECS is the ICP testing; yet, it is an invasive technique.

Some critique arises when considering the studies carried to determine the diagnostic criteria and its relative pressure thresholds; At least three different criteria can be found in current literature: Puranen & Alavaikko (1981), Styf (1987-1988) and Pedowitz (1990). The majority of studies used to form the basis of the criteria for diagnosis did not include healthy controls for comparison, exposing results to significant flaws if compared with the quality assessment of diagnostic accuracy study methodology checklist for this kind of studies (Whiting et al., 2003). According to Roberts and Franklyn-Miller, conflicting evidence regarding the validity of ICP as a mean of making diagnosis of CECS. With the exception of relaxation pressures, many of the confidence intervals at all time points overlap the commonly used criteria set by Puranen and Pedowitz. If a measured ICP is above the cutoff point, the clinician cannot have confidence as to

whether the subject belong to the upper end of distribution curve of healthy subjects or to the lower end of the curve of CECS subjects(13).
In a systematic review, Aweid et al. states that the only ICP values that seem not to overlap between patients and control subjects are the ones taken at 1' post-exercise, although there's the need to develop an agreed ICP test protocol for diagnosing CECS because the variability here contributes to the large differences in ICP measurements and hence diagnostic thresholds between studies(43).
Roscoe et al. proposed a dynamic ICP testing procedure to improve the diagnostic value for this method; they found that performing a 5' (and beyond) dynamic ICP test while completing the exercise protocol to maximal tolerable pain adds significant diagnostic value over existing techniques (reaching a *sensitivity* of 63% and a *specificity* of 95%; LR= 12.5 [95% CI, 3.2-49])(44).

Non-invasive means like MRi scanning(45), DTI imaging(46,47), SPECT imaging(48), barefoot plantar pressure(39) and non-invasive compartment syndrome evaluator – NCSE(49)- have been studied in search of a diagnostic adjoint.
In an MRi study carried by Andreisek et al., the group investigated temporal changes and differences between T2* and ASL signals during and after (up to 15 minutes) calf muscle exercise; T2* measurements showed an immediate response to muscle activity both in affected subjects and control group, indicating immediate muscle reoxygenation and overcompensation with oxyhemoglobin(45). No significant changes have been observed between patients and study time, in the observation period of 15'. A relative change of (ASL) arterial inflow was determined and an immediate increase of 183% and 224% has been found in patients and control subjects, respectively, with an almost complete normalization of ΔASL 15 minutes after muscle exercise. This implies that overall muscle perfusion has normalized after 15 minutes, reflecting a normal demand for fresh oxygenated blood by the muscles and suggesting normalization of vasodilatation and blood oxygenation level. The authors couldn't find any no statistically significant differences in T2* relaxation times or arterial spin labeling signal,

indicative of differences in muscle oxygenation and perfusion status, were found between patients with chronic exertional compartment syndrome and control subjects(45).
In a small cohort study Litwiller defined the first “in-scanner” exercise protocol using an original “dual birdcage” coil; results suggest that this could be a useful triage tool for suspected CECS patients to avoid undergo invasive ICP testing if unnecessary. The ROC analysis showed a relative weighted T2 intensity threshold of 1.54, having a *sensibility* of 96%, a *specificity* of 90% and an *accuracy* of 96%(50).

SPET technique showed no significant differences between the studied groups(26,48), arising doubt on the ipoperfusion occurring during activity in CECS patients (Trease, 2001-all but one CECS patient showed normal stress and redistribution images; Oturai, 2006-four subjects manifested scinticrafic ipoperfusion in compartments not affected by CECS).

Studies have been carried to assess the utility of Diffusion Tensor Imaging as an ancillary procedure that would help identify those suspected of having CECS; Sigmund et al. investigated, in two different studies, the changes occurring in DTI scans compared with T2 MRi scans among healthy volunteers and suspected CECS subjects; the first study found a clear relationship between exercise and diffusivity increase ($p< 0.0001$) as well as a decrease in fraction anisotropy ($p< 0.0014$), defining CECS affected compartments(47);
Findings in the second study (2014) suggest that some difference exists, especially regarding fiber diameter change ($p=0.07$) and permeability increase ($p=0.07$) after exercise; Free diffusivity and apparent permeability metrics show significantly different exercise response between the control and patient groups; increased inter-fiber fluid accumulation (muscular edema) may be a driving component of these observations(46).

A number of studies went to further investigate muscular response to exercise and the role of barefoot plantar pressure in linking specific activities (such as marching) to an increased rate of plantar flexion after initial foot contact (IFC); The differences between CECS cases and controls were only significant during marching suggesting this activity is an ingrained adaption differing from the subject’s normal gait pattern(39);

In a small prospective comparison study by Rajasekaran, Beavis and Leswick, the thickness of the anterior compartment (ACT) has been studied both pre- and post-exercise in CECS patients and Controls; compartment thickness has been assessed using ultrasound scanning, showing a significant increase in patients ACT at all time points, compared to controls(51).

Among non-invasive diagnostic means, a *non-invasive compartment syndrome evaluator* has been used to test volunteers to prove a correlation between interstitial pressure and hardness measurement; this correlation proven to be true (in simulated conditions; a tourniquet was used to artificially raise ICP within the compartments), giving hope for future non-invasive means to diagnose CECS(49).

4.3 Treatment

Although nonoperative treatment options are frequently described in clinical review articles as a first-choice treatment option for CECS of the lower leg, the evidence for them as a whole has been unclear. The systematic review carried by Rajsekaran and Hall proved that current literature on non/operative management of CECS is limited and weak, whereas only case series or case reports are available. Describing the different forms of nonoperative management, four different treatment options could be identified: massage, gait changes, chemo-denervation and USG fascial fenestration(9);

Just one case series reported in the review investigated the effect of massage on anterior-CECS (Blackman, Simmons and Crossley, 1998), concluding it was effective in reducing symptoms and increasing the amount of tolerated exertion; on the other hand, many weaknesses (apart the inherent weakness of the case series study itself) are shown in the review:

-Patients were not allowed to participate to any exacerbating activity during treatment period (5 weeks); this alone could have lowered the post-exertional pain and increased the amount of work completed.

-Repeated dorsiflexion exercise regimen could not be clinically applicable because it may not exacerbate symptoms as the specific activity would do;
Nevertheless, massage shown no apparent adverse effects and therefore it may be suggested as an adjunct treatment, if the patient wants to pursue a nonoperative treatment option.

Gait modifications were first described by Kirby and McDermott (1983), their result suggested a decrease in compartment pressure in those who changed IFC (during running) from rearfoot to forefoot, even if mean pressures recorded were not significantly different. Diebal et al. published two case series studies to address whether this kind of approach could be a viable and cost-effective strategy to reduce symptoms in long-term, asserting that running modification provides pain relief in patients with anterior or antero-lateral CECS(18,52).

The chemo denervation option (carried out with Botulinum Toxin A) reported by Isner-Horobeti et al. provided a novel option for those patients presenting with CECS; this option may be considered as a first line alternative to surgery in patients with superficial or deep-posterior CECS, although the present study only investigated anterior and lateral compartments(19). More concern is raised because this treatment is reported to decrease strength, in case this option is proposed to a competitive athlete. The identification of myofascial structures has been made by electrical stimulation, but the use of ultrasound should be considered because it may provide higher accuracy and further soft tissue protection.

Finnoff and Rajasekaran described a novel alternative to surgery, the USG fascial fenestration(53); however, this technique is described in a case report and for that reason further studies are needed, at least in a form of case series, to better understand its effectiveness and complication rates. Moreover, the authors suggest that this procedure should only be performed by an experienced interventional sonologist(9).

Tam et al. in a large retrospective cohort (138 subjects) assessed pre/post-fasciotomy outcomes at a 6-months follow-up, showing significant improvements in perceived pain (pre-op VAS=8.52

vs. post/op VAS=0.77). Very weak correlation was found VAS pain scores and ICP but, a significant positive correlation (Spearman's Rank Correlation) was found between VRS pain and ICP (r=0.497)(54).

Packer et al. compared the follow-up of two groups (operative group=73subjects; non-operative group=27subjects) in a cohort study. the mean follow-up time was 5 years; a significant difference was found between success rates (operative group=81%, non-operative group= 41%). No significant correlation was found between compartment pressures and patien outcomes(55).

Long term success rates have been studied in a retrospective cohort of 62 patients by Slimmon et al., combining traditional fasciotomy with a partial fasciectomy. Of those who underwent unilateral surgery (50), 60% reported an excellent or good outcome. 58% of the total population was forced to exercise at a lower level than before injury and 36% reported syndrome recurrence or affecting other compartment and lowered sport activity level. Some subject indicated early initial improvement follewd by a deterioration(36).

Cook and Bruce reported that 11 out of the 14 surgically treated repored complete resolution of symptoms and return to professional activity; 2 subjects reported no change in pain and one reported worsening symptoms and one other required reoperation(56).

An observational study carried by Meulekap et al. evaluated short-term results of a 6-weeks rehabilitation program developed for military service members in Aardenburg (Netherlands), showing significant improvements for all groups on the PSFS (patient specific functional scale); the CECS operative group showed to benefit most by the rehabilitation program, suggesting that a multidisciplinary approach to treatment is vital for ensuring good outcomes(57).

In a recent comparative study Thein et al. compared functional results between conservative treatment and surgical management of the anterior compartment over a 28-months follow-up, resulting in a statistically significant improvement for the surgical treatment group over the conservative group in terms of: Pain, Tegner Score (before/after treatment), SF-36 (during follow-up) and full resumption of pre-diagnosis activity level(58). Surgery group faced more short-term complications, such as hematoma (3 subjects) and peroneal nerve sensory impairment (1 subject), all resolved within 4 weeks to 3 month post-operatively(58).

Surgical option is still recognized as the gold standard for CECS treatment; two systematic reviews (20,59) provided critical analysis for unity of diagnostic criteria, surgical techniques, functional outcomes and to identify success, failure and reoperation rates.
Campano et al. found no unity in the application of diagnostic criteria, as only 9 of the 24 included studies used the Pedowitz criteria for diagnosis confirmation(20);
The traditional technique is the one described by Rorabeck et al. (1983), consisting in a 2-incision technique trough which all 4 compartments could be released; since then many variations of this approach have been proposed, aiming to reduce the invasiveness of the procedure, such as partial fasciectomy and endoscopic fasciotomy, thought to reduce post-operative fibrosis; yet no technique showed to be better than the traditional open fasciotomy(20).
After operative management the overall clinical success rate was 66% (although each study's metrics varied) with rates ranging from 48% to 100%(20); Early studies reported greater improvement after surgery, although this is most likely a function of the varied outcome metrics. In a long-term study by Winkes et al., only a 48% success rate was found among athletes, and Roberts et al. found 48% of the patients showed no improvement or worsening conditions(20).
Compartment involvement has been the chief determinant of outcome among the subgroups and has a strong backing of evidence across many studies in which the deep posterior compartment has resulted in inferior outcomes compared with the anterior compartment(20,59).
Despite variability among metrics by which successful outcomes were measured, rates of complications and, ultimately, revision surgery remained minimal(20); most complications were classified as neurologic dysfunction, primarily of the peroneal nerve with subjective numbness, altered sensation, regional hypersensitivity, entrapment, and/or neuroma formation(20).
Iatrogenic peripheral nerve injury may occur intraoperatively, marking it as a major source of

discussion vis-à-vis differing surgical techniques. There may be extensive postoperative fibrosis, which requires revision because of pain and/or nerve entrapment. In the setting of revision surgery, the surgeon should be mindful of the many possible causes of recalcitrant symptoms, including incomplete fasciotomy, fascial hernia, nerve entrapment with the fascial or fibrotic tissue, or incorrect diagnosis masquerading as CECS.

Endoscopic assisted release and minimally invasive techniques were recently reviewed by Lohrer et al., showing that there is no statistically relevant difference between the results of endoscopic (unweighted mean success rate=86.3%) and minimally invasive (unweighted mean success rate=80.0%) CECS release. In the reviewed literature, endoscopic fascial release was performed in 30 patients; Contrary to this, 268 patients were treated with minimally invasive procedures(20). The authors states that endoscopic release is proven to be feasible and the results seems to be equal or better than the traditional open technique or the minimally invasive technique (with the specific advantage of improved visibility during performed surgery).

4.4 Conclusion

Chronic Exertional Compartment Syndrome is a condition that is still widely debated. It is predominant in athletic or military population, particularly at young age. Although its etiology and pathophysiology are still poorly understood, many elements (such as low capillary bed density, altered fascial thickness or volumetric compliance, and so on) suggests that its onset is multifactorial. Several the assumptions that have initially been made on CECS are derived from Acute Compartment Syndrome, a life-threatening condition that generally may occur after hi-energy traumas, hence the assumptions made for CECS could be partially inappropriate. Nonetheless accurate diagnosis is possible by retrieving the patient’s relevant history, conducting physical examination and addressing reported symptoms in differential diagnosis (to rule out other possible specific causes) and then by measuring dynamic intra-compartment pressure to confirm diagnosis.

The diagnostic pressure testing criteria are not universally accepted, the studies carried to determine the different criteria have shown methodological flaws, and there is no specific procedure for catheter insertion angle and depth; also, there is lack of standardized sport/activity-specific exercise protocols to elicit symptoms while testing.

The first treatment option to consider is conservative management, although very little and low-quality literature can be found on this subject, generally reported in case series or few case control design and RCTs are completely missing on this topic. Post-operative rehabilitation is poorly addressed and yet no guidelines have been published help orient post-operative path. Surgical treatment is proven to be the therapeutic gold standard and open fasciotomy is the most common procedure involved, yet minimally invasive techniques and endoscopically assisted release are gaining momentum, mostly because limited skin incisions has proven to lower post-operative fibrosis incidence; however, its comparative efficacy relative to traditional technique is not currently known. Failure and revision rates seem to be minimal, but incomplete fasciotomy, fascial defects, nerve entrapments and extensive post-operative fibrosis are among the main causes of surgery failure/revision.

5 Key Points

I. CECS is a stress-related condition whose clinical diagnosis is oftentimes made by ruling out other differential causes and therefore detailed history and in-depth physical exam are crucial to orient the diagnostic process;

II. The actual understanding of this condition derives by the knowledge of acute compartment syndromes, which are completely different

III. There is yet no wide agreement on the ICP criteria and cut-off points to diagnose CECS, although dynamic pressure testing has proven to be more accurate than the classic technique to confirm diagnosis;

IV. Non-invasive diagnostic techniques are a promising screening tool to avoid unnecessary invasive tests

V. There is a variety of conservative options, but large and robust studies (ie. RcT) are yet to be published, leaving a veil of uncertainty on intervention's efficacy and long-term effects;

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