1) Review

2) Title:

A SYSTEMATIC REVIEW OF CURRENT SURGICAL AND CONSERVATIVE TREATMENT IN LOWER LIMB CHRONIC EXERTIONAL COMPARTMENT SYNDROME

EINE SYSTEMATISCHE ÜBERSICHT ÜBER DIE AKTUELLE CHIRURGISCHE UND KONSERVATIVE BEHANDLUNG DES CHRONISCHEN BELASTUNGSBEDINGTEN KOMPARTMENTSYNDROMS DER UNTEREN EXTREMITÄTEN

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5) Summary/Abstract

Background: Chronic exertional compartment syndrome (CECS) is a muscular overuse injury, usually affecting runners, athletes, or military personnel. The present study aims to provide a systematic overview of the surgical and conservative treatment options and their effectiveness in lower limb CECS. **Method:** A systematic literature search of PubMed, Embase and Scopus from 1990 to 2019 was conducted, following the PRISMA guidelines. After application of the inclusion criteria, 44 studies dealing with different treatment options for CECS were included. The quality of the evidence was measured using an adapted version of the Critical Appraisal Skills Programme (CASP). **Results:** A total of 1036 original articles were identified. Within the 44 selected articles, 37 deal with surgical fasciotomy or fasciectomy, six use conservative management in form of gait-retraining and physical therapy and one study evaluated the effect of botulinum toxin injections (BoNT-injections) in the affected compartments. Fifteen studies reported satisfaction rates above 70% in patients treated with fasciotomy. Conservative management showed good, but slightly lower results than surgical treatment. Comparative studies between surgical and conservative treatment demonstrated high risk of selection bias. Overall, literature on treatment of CECS is very heterogenous in terms of both outcomes and population. **Conclusion:** Fasciotomy is an effective treatment in most patients suffering from CECS of the lower leg. Results of conservative treatment by gait-retraining and of treatment with BoNT-injections are promising. Specifically, gait-retraining may be considered as treatment of choice in military personnel, as in this population fasciotomy appears to be less effective than in athletes. Meanwhile, in an athlete population,

where fasciotomy remains the standard treatment for CECS, conservative management in form of gait-retraining should at least be envisioned in patients with post-surgical symptom recurrence. However, further evidence in form of high-quality studies with larger populations is needed regarding this topic.

Zusammenfassung:

Hintergrund: Das chronische belastungsbedingte Kompartmentsyndrom („chronic exertional compartment syndrome“, CECS) ist eine muskuläre Überlastungsverletzung, die in der Regel Läufer, Sportler oder Militärangehörige betrifft. Die vorliegende Studie soll einen systematischen Überblick über die chirurgischen und konservativen Behandlungsmöglichkeiten und deren Wirksamkeit bei CECS der unteren Extremitäten geben. **Methode**: Es wurde eine systematische Literaturrecherche in PubMed, Embase und Scopus von 1990 bis 2019 unter Beachtung der PRISMA-Richtlinien durchgeführt. Nach Anwendung der Einschlusskriterien wurden 44 Studien berücksichtigt, die sich mit verschiedenen Behandlungsoptionen für CECS befassen. Die Qualität der Studien wurde anhand einer angepassten Version des Critical Appraisal Skills Programme (CASP) gemessen. **Resultate**: Insgesamt wurden 1036 Originalartikel identifiziert. Von den 44 ausgewählten Artikeln befassen sich 37 mit einer chirurgischen Fasziotomie oder Fasziektomie, sechs mit einer konservativen Behandlung in Form von Gangschulung und Physiotherapie und eine Studie evaluierte die Wirkung von Botulinumtoxin-Injektionen in die betroffenen Kompartimente. Fünfzehn Studien zeigten Zufriedenheitsraten von über 70% bei Patienten, die mit Fasziotomie behandelt wurden. Die konservative Behandlung zeigte gute, aber etwas schlechtere Ergebnisse als die chirurgische Behandlung. Vergleichende Studien zwischen chirurgischer und konservativer Behandlung zeigten ein hohes Risiko für Selektionsverzerrungen. Insgesamt ist die Literatur zur Behandlung von CECS sehr heterogen, sowohl was die Ergebnisse als auch die Population betrifft. **Schlussfolgerungen**: Die Fasziotomie ist bei den meisten Patienten mit CECS am Unterschenkel eine effektive Behandlung. Die Ergebnisse der konservativen Therapie durch Gangschulung und der Behandlung mit BoNT-Injektionen sind vielversprechend. Insbesondere die Gangschulung kann als Behandlung erster Wahl bei Militärangehörigen in Betracht gezogen werden, da in dieser Population die Fasziotomie weniger effektiv zu sein scheint als bei Sportlern. Bei Sportlern, bei denen die Fasziotomie nach wie vor die Standardbehandlung für CECS ist, sollte eine konservative Behandlung in Form einer Gangschulung zumindest bei Patienten mit einem postoperativen Symptomrückfall ins Auge gefasst werden. Allerdings sind zu diesem Thema weitere Erkenntnisse in Form von qualitativ hochwertigen Studien mit größeren Populationen erforderlich.

6) Keywords: Chronic exertional compartment syndrome, exercise-induced leg pain, surgical and conservative treatment, fasciotomy, gait retraining

List of abbreviations:

BoNT-A: Botulinum Neurotoxin – A (7)

CASP: Critical Appraisal Skills Programme (7)

CECS: chronic exertional compartment syndrome (52)

ICP: intracompartmental pressures (4)

INTRODUCTION

The Chronic Exertional Compartment Syndrome (CECS) has an incidence rate of 33% in running athletes and military personnel. [1] It is described as an exercise-induced increase of intramuscular pressure, leading to decreased tissue perfusion and muscular impairment, i.e., ischemic pain, muscle weakness, cramps, numbness and paresthesia. [2] Most of the time, symptoms due to CECS disappear at rest. [3]
The exact physiopathology of CECS is not well established and still debated in the literature. [4] Some authors suggest that increased tissue pressures are caused by a noncompliant thicker fascia. [5, 6] Another hypothesis is, that the origin of CECS consists in a venous abnormality, which leads to a blood stasis. [7] The CECS can affect all four muscular compartments of the leg, amongst which, the anterior one is most frequently involved. [8]
There are different treatment options from conservative to surgical modalities. [9] Conservative treatments are often used in first place and followed by surgical interventions if symptoms persist. [10] Conservative management includes cessation of provoking activity, stretching, strengthening, massage, shoes modification, gait retraining and forefoot running. [10] Different surgical techniques for decompressive fasciotomy or fasciectomy are reported in the literature. Currently, limited incision fasciotomy represents the standard treatment for patients suffering from CECS, especially for athletes having the intention to return to sports at their previous level. [8]
To our knowledge, there are no available guidelines for the management of CECS and we observe a lack of clear evidence comparing different treatment options. More specifically, the existing systematic reviews about the management of CECS in the lower leg mostly focus on either only surgical treatment options or only conservative management. [11-13] The aim of this systematic review was to provide a larger overview of all treatment options for CECS of the lower leg, including recent evidence and new treatment options.

METHODS

Protocol

This systematic review followed the preferred reporting items for systematic reviews and meta-analysis (PRISMA) guidelines. [14] Therefore, structured search, studies selection, risk-of-bias assessment of individual studies and result synthesis were performed. A formal protocol was developed and submitted to PROSPERO (CRD42020175994).

Sources and search strategy

Keywords were identified using the PICO(s) methods. By combining the keywords regarding the population (runners or military or patient with CECS) and the intervention (surgical or conservation management), two investigators (H.R, A.N) performed a systematic research of the literature in three databases: Embase, PubMed and Scopus. For all three databases, the systematic search included published articles up to October 2019.

Inclusion criteria

To be included, studies must be either randomised clinical trials, cohort studies or case series studies with minimum ten subjects, written in English or French and published in 1990 or later. The cut-off of 1990s was chosen to eliminate a big amount of similar low-quality studies on surgical treatments published in the 1970s and 1980s and to focus instead on more recent and up-to-date evidence. Case reports, descriptions of surgical techniques, literature reviews, systematic reviews, and meta-analysis were excluded. All types of treatment for CECS were included. The participants were both male and female adults or adolescents suffering from

CECS in the leg, and either were participating in sports or serving as militaries. If pre- and post-intervention values were given, all types of outcome were accepted, with exception of studies focussing only on the diagnosis of CECS.

Eligibility criteria and study selection

After duplicates' removal, a first selection based on information revealed in the titles and abstracts was performed by two independent reviewers (H.R. and A.N.) using the inclusion criteria. (Table 1) Then, a second procedure, following the same protocol, was performed using the full text. A consensus between the two reviewers was reached at each step. In case of disagreement, a third reviewer (A.R.) was consulted.

Data extraction

The data extraction was performed independently by two reviewers (A.N. and H.R.). A standardised form was used to collect the following data for each study: design, outcome measures, details about participants, groups and timing, a description of the intervention, the main results and conclusion of the study.

Study quality appraisal and risk of bias assessment

To assess the quality of the included studies, a modified version of the Critical Appraisal Skills Programme (CASP) was used. One of the reviewers (H.R.) answered a set of twelve questions about the methodology of the study with yes (Y), no (N) or not applicable (NA) in order to evaluate the quality of each study. The question set was based on the 'CASP-Cohort-Study-Checklist 2018'. [15] Questions 7 and 8 relative to detailed results ("What are the results of the study?" and "How precise are the results of the study?") were excluded, because they could not be answered with 'yes' or 'no'. However, answers to these questions were considered to answer question 9 ("Do you believe the results?"). Concerning the length of follow up (question 6b), we decided to sort the studies into short term and long term follow ups instead of answering the question by 'yes' or 'no'.

Data synthesis

Two reviewers (A.N. and H.R.) considered the results of the studies and included reports with comparable outcome into the qualitative analysis. Moreover, a subgroup-analysis regarding the type of intervention and the length of follow up was performed.

RESULTS

Study selection

Throughout the three searched databases, 1668 articles were found (346 from Pubmed, 817 from Embase, 505 from Scopus). After removal of duplicates, 1036 articles were screened. At the end of the selection process, 44 articles were in included. (Figure 1)

Characteristics of the studies

The studies included, 24 case series studies, 20 cohort studies and no randomised controlled trial. The characteristics of the studies are described in Table 22. The population ranged from 10 to 611 patients, with a total of 3129 treated patients across all articles. 41 studies included both male and female subjects with the exception of one study who included only females [16], another only males [17] and one did not specify gender of participants. [18] The age of

the participants ranged from 13 to 71-years-old. The mean age of patients was always between 16 and 31.8 years. Moreover, three studies focused on adolescents. [16, 19, 20]. There were 13 studies on a military population [17, 18, 21-31] and 19 studies assessing runners or athletes on different levels, from amateur athletes to national and international athlete. [1, 2, 4, 16, 19, 32-45] Irion et al. [46] only included elite-level athletes. For the other 11 studies, the type of activity was either mixed or not detailed [20, 47-56].

Fourteen studies included patients with CECS of one specific compartment. Four studies [32, 43-45] focused on deep posterior CECS, while eight studies focused on CECS of the anterior compartment of the leg [4, 17, 18, 27, 34, 40, 47, 53]. One study [55] included only patients with lateral CECS [55] and another one compared outcome between both anterior and posterior. [2]

Out of the 44 retrieved studies, one evaluated the treatment of CECS by botulinum toxin injection (BoNT-A injection) [34], six focused on conservative management by gait-retraining [1, 22, 24, 26, 30, 31] and 37 on surgical decompression techniques such as fasciotomy or fasciectomy. [2, 4, 16-21, 23, 25, 27-29, 32, 33, 35-56] Four out of these 37 studies compared surgical and conservative treatment [28, 45, 50, 53].

All studies were sorted into two groups, depending on the length of follow-up. There were 15 studies with short-term (ST; <2 years) and 27 studies with long-term (LT; >2years) follow up. The study of Roscoe et al. [17] can be attributed to both groups, because their length of follow-up lies between 6 and 60 months and one study did not detailed the length of the follow-up. [29]

Reported Outcomes

Commonly reported outcomes were pain through Visual Analogue Scale, Verbal Rating Scale or Numerical Analogue Scale (n=21), other symptoms such as feeling of tightness, numbness of the affected leg (n=15) and subjective outcome and patient satisfaction (n=17). Functional outcome measures included return to sport rate and time to return to sport (n=14), post-intervention activity level (n=13), return to military service (n=7), functional questionnaires such as *Foot and Ankle Ability Measure*, *Single Assessment Numeric Evaluation*, *Lower Extremity Functional Scale*, *Lower Leg Outcome Survey*, *Exercise-Induced Limb Pain questionnaire*, *Global Rating of Change score* and *Tegner score* (n=15). Pre- and post-intervention intra-compartmental pressure measurements were reported in eight studies. Quality of life was assessed with *European Quality of Life - 5 Dimensions*, *Short-Form-12,* or *Short-Form-36* (n=5).

Risk of bias

A modified CASP Checklist for Cohort Studies was used to evaluate the quality of the included studies. The details of the CASP results for each study can be found in table 3. Each report was assessed following the CASP scale criteria and was then classified as a study with high risk of bias or low risk of bias. Some questions were non-applicable for a few studies. For instance, Question 10 “Can the results be applied to the local population?” is sometimes answered with the specific population of the study, e.g.., anterior CECS only. Ten of the included studies [18-20, 24, 26, 28, 30, 31, 34, 46] demonstrated a low risk of bias, while 26 studies [1, 2, 4, 16, 17, 22, 25, 27, 29, 32, 33, 35, 36, 38, 40, 41, 43-45, 48-54] showed a moderate risk of bias. Eight studies [21, 23, 37, 39, 42, 47, 55, 56] had a high risk of bias. (Table3)

Results of the studies

Surgical modalities

Different surgical techniques were used for the fasciotomies. Of the 33 studies using surgical treatments for CECS, 21 studies used a minimally invasive surgical technique, where the fascia is cut subcutaneously after a small skin incision was made [2, 4, 16, 19-21, 28, 36-40, 45, 46, 48, 49, 51-53, 55, 57]. Five of the studies used an open fasciotomy technique [32, 33, 43, 44, 54]. An endoscopic/percutaneous approach was used in three of the included studies [23, 35, 47]. A fasciectomy consists in removing a piece of the fascia instead of only cutting it. Three studies worked with this technique [18, 27, 41]. Another five studies did not detail the type of fasciotomy [17, 25, 29, 42, 50].

Of the 33 studies using surgical treatments for CECS, 14 reported, a significant decrease of pain and symptoms. Five studies reported complete relief of pain in at least 75% of patients (405/451) [20, 21, 33, 39, 54], while in three studies less than 65% of patients (28/ 53) were completely pain free. [4, 35, 42] Patient satisfaction rate was assessed in 20 of the 37 studies. In 11 of these reports, at least 75% of the patients (425/488) were satisfied with their outcome [2, 16, 20, 36, 38, 40, 47-49, 52, 57]. In 6 studies, satisfaction rate was between 50% and 75% (260/387) [23, 25, 35, 41, 42, 51] and in three studies, it was below 50% (55/124 operated) [43, 44, 55]. Moreover, three studies reported normalization of ICP after surgery. [17, 20, 32] Four studies observed the return-to-sport rate without precising the level of post-operative sports activity. In all these studies, at least 75% of patients (182/222) returned to sport post-operatively [16, 19, 20, 37]. In another four studies, more than 80% of patients (59/66) returned to their previous activity level post-surgery [4, 36, 39, 46]. In another three studies, this rate was between 60 and 80% of patients (487/673) [29, 38, 42] In two studies, less than 50% of patients (35/92) were able to return to their pre-injury activity level [41, 55]. Complication rate was assessed in 16 studies. Five of them reported some sort of complications in more than 15% of the operated legs [4, 25, 29, 42, 47]. In seven studies, complication rate was between 5 and 15% [19, 23, 33, 44, 49, 51, 54] and in four studies, it was below 5% [20, 21, 36, 48]. Complications are defined differently in each study. Some of the studies only mentioned severe complications [20, 36] whereas others also listed minor ones [41, 42]. The most frequently observed complications were hematoma, cellulitis, wound infection, and transitory numbness of the leg due to an injury of the superficial peroneal nerve [4, 18, 19, 25, 29, 33, 37, 39, 41, 42, 44, 47, 48, 50, 51, 54]. Symptom recurrence was lower than 10% in two of the reports [48, 54] and between 30% and 50% in the other two papers assessing this outcome [29, 46]. Revision surgery rate was assessed in three studies, showing reoperation rates of 5.9%, 6% and 18.8% [19, 29, 57]. Four studies showed better results for fasciotomy in isolated anterior CECS [2, 16, 42, 57]. In opposition to this, one cohort study showed better results for fasciotomy in patients with posterior CECS [41].

Conservative modalities

All the included articles on conservative management options focused on gait-retraining. Only the study of Meulekamp et al. used a physiotherapy and rehabilitation program, which also included gait-retraining [26].

Of the six studies dealing with conservative treatment options for CECS, mainly gait-retraining, four presented results on pain and symptoms. They demonstrated a significant decrease in mean pain on visual analogue scale (VAS) [22] or on verbal rating scale (VRS) in 25/45 patients (55.5%) [26], while the other studies reported full relief of symptoms in 22/40 patients (52%) and in 7/10 patients (70%) [1, 31]. Two studies showed that ICP of the affected compartments decreased significantly with gait-retraining [22, 24].Concerning the effects on function and return to sport, different outcomes were assessed. Three studies report Global-rating-of-change scores (GROC) between 4.9 and 7 (quite a bit better – a very great deal better) [1, 22, 24]. Single assessment numeric evaluation score (SANE) also was significantly improved in

three studies [22, 24, 30]. Two of the studies reported a significant increase in pain-free running distance [22, 24]. The study using BoNT-injections showed a significant decrease in mean ICP of the affected compartments, complete pain relief in 15/16 patients (94%) and reduced muscle strength in 11/16 patients (69%) post-intervention. [34]

Comparative studies

Four studies compared surgical treatment and conservative management. All these reports observed some sort of improvement in each group of patients, with the surgical treatment option giving superior results in all these studies. In the first study, patient satisfaction rate was 81% (59/73) for surgically treated patients and 56% (15/27) for conservatively treated patients [50]. In the second study, pain and Tegner-score improved in both groups, but greater change was observed in the fasciotomy-group. Full return to sport at pre-injury level was observed in 24/31 patients treated surgically (77.4%) and in 3/12 patients treated conservatively (25%) [53]. In the third study, 16/19 (84%) of conservatively treated patients improved, while patient satisfaction rate for surgical treatment was 52% (14 out of 27 patients) [45]. In the fourth study, complaints had strongly decreased in 44/56 surgically treated patients (83%) and conservative treatment was effective in 21/32 patients (70%) [28].

DISCUSSION

The purpose of this systematic review was to study the different treatment options for CECS of the lower leg and to evaluate their effectiveness according to the literature. ~~To our knowledge, this is the first systematic review that included both surgical and conservative treatments. [11, 12]~~ There were no randomised controlled trials among the 44 included studies, in which 37 described surgical treatment and seven focused on conservative modalities.

Due to the small number and the heterogeneity of studies dealing with conservative treatments and treatment by botulinum toxin, it is impossible to clearly conclude about the effectiveness of these treatment options. There are remarkable differences between the trials in terms of intervention, outcome measures and study design, which could explain the great disparity of the results. Generally, conservative management shows slightly lower satisfaction rates compared to fasciotomy. Nevertheless, conservative management, especially gait retraining and forefoot running seem to be an effective long term treatment option in case of symptom recurrence and more specifically for a military population.

Concerning the differences between a military and a civilian population, fasciotomy appears to have less favourable outcomes in soldiers than in civilians. [26, 58] Similarly, in the systematic review of Vogels et al., surgical complication rates, recurrence and reoperation rates were higher in a military population than in civilians. [10] This can be attributed to the special physical demands of military service, but also to the effect of military boots on the lower limb function. [26] However, Zimmermann et al. found that changes in running kinematics are similar in military boots compared to those in running shoes. [30] Further research is needed to better understand the differences in treatment outcomes between civilians and militaries treated for CECS.

As mentioned previously, the results of our literature search concerning surgical treatment options such as decompressive fasciotomy or fasciectomy for patients with CECS are in line with those of other reviews. For instance, Campano et al. described an overall 66% success rate (range 48-100%) for surgical fasciotomy. [12] Likewise, in the systematic review of Ding et al., satisfaction rates ranged from 48-94%. Return to full military duty was achieved in 30-63% of patients. [13] Vogels et al. reported an overall satisfaction rate of 85±13% and return

to full activity in 65±25% of patients. These results are similar, but less disparate than our findings with satisfaction rates ranging from 33% to 96% and return to full activity in 30% to 100% of patients. In our review, there was no clear effect of the different surgical techniques. However, all three studies using fasciectomy showed only moderate results. This could either be linked to the surgical technique or to the military study population.

The four comparative studies included in this review observed some sort of improvement in each group of patients, with the surgical treatment option giving superior results in all these reports. However, we believe that the methodology of these reports should be questioned and therefore caution should be taken interpreting the results. None of the studies used randomization for group allocation. In the study of Thein et al., patients could choose whether they prefer to undergo surgery or be treated conservatively [53]. In the other comparative studies [28, 45, 50], the non-operative treatment was only applied in patients with ICP below cut-off values for CECS-diagnosis. These methods of group allocation are very likely to induce selection bias. In addition, the conservative or non-operative treatments were not standardized and not detailed in the studies. We conclude that there is an important lack of high-quality comparative studies analysing different treatment options for CECS of the leg.

Prior to 2012, conservative management of CECS included mainly resting periods, decreasing the patients' level of physical activity, massage and stretching of the affected muscles and use of anti-inflammatory drugs. The efficacy of these techniques was very poor. [59]

In our systematic review, six studies on conservative management of CECS were included, five of whom are focusing on gait retraining and forefoot running to alleviate the symptoms of CECS. To understand the utility of gait retraining in patients with CECS, Breen et al. proposes to consider CECS as a mechanical muscular overload. This can be treated by a change in running kinematics in order to reduce the overload pattern. [1] Most runners spontaneously adopt a rearfoot strike pattern, which is often associated with a marked dorsiflexion of the foot at landing. This causes an important increase in the eccentric activity of the tibialis anterior muscle. [24] Shifting the eccentric load towards the posterior structures of the lower leg may help to reduce symptoms of CECS. These structures, such as the Achilles tendon, seem better suited to absorb impact force at ground contact.

Results of the included studies on gait retraining are promising. Breen et al. report that 70% of their patients were running pain-free at one year follow-up, which is a similar satisfaction rate as observed in standard fasciotomy treatment. [1] Helmhout et al. proved increases in running distance and self-reported outcome scores at short term, also for a home-based program. This is advantageous because of its reduced time and resource investments. [24] In the case series of Diebal et al., all patients were able to return to sports without limitations and surgery was avoided in all cases. [22] Zimmermann et al. report a 57% treatment success rate at two-year follow-up and recommend surgery only after failure of optimal conservative management. [31]

In the systematic review of Vogels et al., satisfaction rate for conservative treatments was 47±42% and return to activity rate was 50±45%. Like in our SR, there were huge differences between the outcomes of different types of conservative treatments. Outcomes were best for structured gait-retraining interventions and for BoNT-A injections. [10] Overall, the results of these studies on conservative treatment seem favourable. Nonetheless, these were non-controlled studies with a small number of participants. Controlled studies with a larger population will be needed to provide further evidence on this subject.

There was a remarkable degree of heterogeneity in the literature concerning CECS of the lower leg. Study populations differed in the type and level of their physical activity provoking symptoms of CECS. These activities varied from marching in military servicemen [31] over recreational running [38] to professional athletes [46]. Furthermore, as already mentioned in

other reviews, [13] we observed a lack of uniformity in the outcome measurements, which makes comparisons between the studies difficult. A quantitative synthesis was not possible. Most of the included studies used subjective, non-validated questionnaires as primary outcome measure. [2, 4, 37] Only in few studies outcomes were assessed using validated standardized questionnaires or objective measurements. [24] Another factor leading to heterogeneity amongst the studies, is the absence of treatment guidelines. There are great differences concerning the decision whether to apply conservative or surgical treatment and concerning the post-operative rehabilitation and length of follow-up. In some of the studies, surgical treatment is applied 'after failure of conservative management'[35, 39], but there is neither a precise definition of this 'failure' nor of the type of conservative management used. The post-surgical rehabilitation also varies from one study to another and often isn't detailed. For example, time before patients are allowed to start jogging post-surgery varies between two weeks and two months. [51, 55] Further research investigating the role of post-surgical treatment is necessary in order to elaborate rehabilitation guidelines in this condition.

One of the strengths of this review is that more articles and patients were included than in the previous reviews [11, 12, 60, 61]. Furthermore, we bring together both surgical and conservative treatment in one review. Several limitations need to be considered when interpreting the results of this systematic review. Firstly, there is a risk of selection bias. As only articles published in English or French from 1990 to 2019 were reviewed, it is likely that there are studies relevant to the discussion, published before 1990, in other languages, or on other databases, which were not analysed. Secondly, due to the heterogeneity of the studies, it was difficult to clearly summarize all the results.

There is a need for further evidence concerning the treatment of CECS by controlled comparative studies with standardized outcome measures. As conservative treatment in form of gait retraining seems to be an effective treatment option [24, 31], especially in a military population, this should be investigated in future research. Another point which is currently only rarely treated in the literature is the efficacy of a post-fasciotomy rehabilitation program. It is not well explored if such a physical therapy rehab could possibly improve the outcomes of fasciotomy by accelerating and guiding return to sport. Further evidence is needed to answer this question.

CONCLUSION

Based on the results of this systematic review, we can conclude that fasciotomy is an effective treatment in most patients suffering from CECS of the lower leg. Results of conservative treatment by gait-retraining and of treatment with BoNT-A injections are promising. Specifically, gait-retraining may be considered as treatment of choice in military personnel, as in this population fasciotomy appears to be less effective than in athletes. In this case, fasciotomy should be applied after failure of optimal conservative management. Meanwhile, in an athlete's population, where fasciotomy remains the standard treatment for CECS, conservative management in form of gait-retraining should at least be envisioned in patients with post-surgical symptom recurrence. However, further evidence in form of high-quality studies with larger populations is needed in this subject.

8) REFERENCES

[1] D. T. Breen, J. Foster, E. Falvey, and A. Franklyn-Miller, "Gait re-training to alleviate the symptoms of anterior exertional lower leg pain: a case series," (in eng), *Int J Sports Phys Ther*, vol. 10, no. 1, pp. 85-94, Feb 2015.

[2] A. A. Schepsis, D. Martini, M. Corbett, and J. T. Andrish, "Surgical management of exertional compartment syndrome of the lower leg. Long-term followup," (in English), *American Journal of Sports Medicine,* Article vol. 21, no. 6, pp. 811-817, 1993, doi: 10.1177/036354659302100609.

[3] B. Liu, G. Barrazueta, and D. E. Ruchelsman, "Chronic Exertional Compartment Syndrome in Athletes," (in English), *Journal of Hand Surgery,* Review vol. 42, no. 11, pp. 917-923, 2017, doi: 10.1016/j.jhsa.2017.09.009.

[4] G. Gatenby, S. Haysom, B. Twaddle, and S. Walsh, "Functional Outcomes After the Surgical Management of Isolated Anterolateral Leg Chronic Exertional Compartment Syndrome," (in English), *Orthopaedic Journal of Sports Medicine,* Article vol. 5, no. 11, 2017, doi: 10.1177/2325967117737020.

[5] J. Styf, L. Körner, and M. Suurkula, "Intramuscular pressure and muscle blood flow during exercise in chronic compartment syndrome," (in eng), *J Bone Joint Surg Br*, vol. 69, no. 2, pp. 301-5, Mar 1987.

[6] W. D. Turnipseed, C. Hurschler, and R. Vanderby, Jr., "The effects of elevated compartment pressure on tibial arteriovenous flow and relationship of mechanical and biochemical characteristics of fascia to genesis of chronic anterior compartment syndrome," (in eng), *J Vasc Surg*, vol. 21, no. 5, pp. 810-6; discussion 816-7, May 1995, doi: 10.1016/s0741-5214(05)80012-6.

[7] J. Lecocq, M. E. Isner-Horobeti, A. Dupeyron, J. L. Helmlinger, and P. Vautravers, "[Exertional compartment syndrome]," (in fre), *Ann Readapt Med Phys*, vol. 47, no. 6, pp. 334-45, Aug 2004, doi: 10.1016/j.annrmp.2004.05.009. Le syndrome de loge d'effort.

[8] S. Vajapey and T. L. Miller, "Evaluation, diagnosis, and treatment of chronic exertional compartment syndrome: a review of current literature," (in English), *Physician and Sportsmedicine,* Review vol. 45, no. 4, pp. 391-398, 2017, doi: 10.1080/00913847.2017.1384289.

[9] W. A. Van der Wal, P. J. Heesterbeek, J. G. Van den Brand, and E. J. Verleisdonk, "The natural course of chronic exertional compartment syndrome of the lower leg," (in English), *Knee surgery, sports traumatology, arthroscopy : official journal of the ESSKA,* Article vol. 23, no. 7, pp. 2136-2141, 2015, doi: 10.1007/s00167-014-2847-2.

[10] S. Vogels, E. D. Ritchie, T. T. C. F. van Dongen, M. R. M. Scheltinga, W. O. Zimmermann, and R. Hoencamp, "Systematic Review of Outcome Parameters Following Treatment of Chronic Exertional Compartment Syndrome in the Lower Leg," (in English), *Scandinavian journal of medicine & science in sports,* Article in Press 2020, doi: 10.1111/sms.13747.

[11] S. Rajasekaran and M. M. Hall, "Nonoperative management of chronic exertional compartment syndrome: A systematic review," (in English), *Current Sports Medicine Reports,* Review vol. 15, no. 3, pp. 191-198, 2016, doi: 10.1249/JSR.0000000000000261.

[12] D. Campano, J. A. Robaina, N. Kusnezov, J. C. Dunn, and B. R. Waterman, "Surgical Management for Chronic Exertional Compartment Syndrome of the Leg: A Systematic Review of the Literature," (in English), *Arthroscopy - Journal of Arthroscopic and Related Surgery,* Review vol. 32, no. 7, pp. 1478-1486, 2016, doi: 10.1016/j.arthro.2016.01.069.

[13] A. Ding, M. Machin, S. Onida, and A. H. Davies, "A systematic review of fasciotomy in chronic exertional compartment syndrome," (in English), *Journal of vascular surgery*, Article in Press 2020, doi: 10.1016/j.jvs.2020.05.030.

[14] A. Liberati *et al.*, "The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration," (in English), *BMJ (Clinical research ed.)*, Article vol. 339, p. b2700, 2009, doi: 10.1136/bmj.b2700.

[15] C. A. S. Programme, "CASP Cohort Study Checklist," 2018.

[16] L. J. Micheli, R. Solomon, J. Solomon, V. F. P. Plasschaert, and R. Mitchell, "Surgical treatment for chronic lower-leg compartment syndrome in young female athletes," (in English), *American Journal of Sports Medicine*, Article vol. 27, no. 2, pp. 197-201, 1999, doi: 10.1177/03635465990270021401.

[17] D. Roscoe, A. J. Roberts, D. Hulse, A. F. Shaheen, M. P. Hughes, and A. N. Bennet, "Effects of anterior compartment fasciotomy on intramuscular compartment pressure in patients with chronic exertional compartment syndrome," (in English), *Journal of the Royal Army Medical Corps*, Article vol. 164, no. 5, pp. 338-342, 2018, doi: 10.1136/jramc-2017-000895.

[18] C. Simpson, D. Roscoe, S. Hughes, D. Hulse, and H. Guthrie, "Surgical outcomes for chronic exertional compartment syndrome following improved diagnostic criteria," (in English), *Journal of the Royal Army Medical Corps*, Article in Press 2019, doi: 10.1136/jramc-2019-001171.

[19] J. J. Beck, F. A. Tepolt, P. E. Miller, L. J. Micheli, and M. S. Kocher, "Surgical Treatment of Chronic Exertional Compartment Syndrome in Pediatric Patients," (in English), *The American journal of sports medicine*, Article vol. 44, no. 10, pp. 2644-2650, 2016.

[20] S. García-Mata, A. Hidalgo-Ovejero, and M. Martinez-Grande, "Chronic exertional compartment syndrome of the legs in adolescents," (in English), *Journal of Pediatric Orthopaedics*, Article vol. 21, no. 3, pp. 328-334, 2001, doi: 10.1097/00004694-200105000-00013.

[21] S. Cook and G. Bruce, "Fasciotomy for chronic compartment syndrome in the lower limb," (in English), *ANZ Journal of Surgery*, Article vol. 72, no. 10, pp. 720-723, 2002, doi: 10.1046/j.1445-2197.2002.02526.x.

[22] A. R. Diebal, R. Gregory, C. Alitz, and J. P. Gerber, "Forefoot running improves pain and disability associated with chronic exertional compartment syndrome," (in English), *The American journal of sports medicine*, Article vol. 40, no. 5, pp. 1060-1067, 2012.

[23] A. S. Finestone, M. Noff, Y. Nassar, S. Moshe, G. Agar, and E. Tamir, "Management of chronic exertional compartment syndrome and fascial hernias in the anterior lower leg with the forefoot rise test and limited fasciotomy," (in English), *Foot and Ankle International*, Article vol. 35, no. 3, pp. 285-292, 2014, doi: 10.1177/1071100713514390.

[24] P. H. Helmhout, A. R. Diebal, L. van der Kaaden, C. C. Harts, A. Beutler, and W. O. Zimmermann, "The effectiveness of a 6-week intervention program aimed at modifying running style in patients with chronic exertional compartment syndrome: Results from a series of case studies," (in English), *Orthopaedic Journal of Sports Medicine*, Article vol. 3, no. 3, 2015, doi: 10.1177/2325967115575691.

[25] J. R. McCallum, J. B. Cook, A. C. Hines, J. S. Shaha, J. W. Jex, and J. R. Orchowski, "Return to duty after elective fasciotomy for chronic exertional compartment syndrome," (in English), *Foot & ankle international*, Article vol. 35, no. 9, pp. 871-875, 2014, doi: 10.1177/1071100714539661.

[26] M. Z. Meulekamp, P. van der Wurff, A. van der Meer, and C. Lucas, "Identifying prognostic factors for conservative treatment outcomes in servicemen with chronic exertional compartment syndrome treated at a rehabilitation center," (in English),

Military Medical Research, Article vol. 4, no. 1, 2017, doi: 10.1186/s40779-017-0145-2.

[27] A. J. Roberts, P. Krishnasamy, J. M. Quayle, and J. M. Houghton, "Outcomes of surgery for chronic exertional compartment syndrome in a military population," (in English), *Journal of the Royal Army Medical Corps,* Article vol. 161, no. 1, pp. 42-45, 2015, doi: 10.1136/jramc-2013-000191.

[28] E. J. M. M. Verleisdonk, R. F. Schmitz, and C. Van Der Werken, "Long-term results of fasciotomy of the anterior compartment in patients with exercise-induced pain in the lower leg," (in English), *International Journal of Sports Medicine,* Article vol. 25, no. 3, pp. 224-229, 2004, doi: 10.1055/s-2003-45255.

[29] B. R. Waterman, M. Laughlin, K. Kilcoyne, K. L. Cameron, and B. D. Owens, "Surgical treatment of chronic exertional compartment syndrome of the leg: Failure rates and postoperative disability in an active patient population," (in English), *Journal of Bone and Joint Surgery - Series A,* Article vol. 95, no. 7, pp. 592-596, 2013, doi: 10.2106/JBJS.L.00481.

[30] W. O. Zimmermann, N. R. I. Van Valderen, C. W. Linschoten, A. Beutler, R. Hoencamp, and E. W. P. Bakker, "Gait retraining reduces vertical ground reaction forces in running shoes and military boots," (in English), *Translational Sports Medicine,* Article vol. 2, no. 2, pp. 90-97, 2019, doi: 10.1002/tsm2.62.

[31] W. O. Zimmermann, M. R. Hutchinson, R. Van den Berg, R. Hoencamp, F. J. G. Backx, and E. W. P. Bakker, "Conservative treatment of anterior chronic exertional compartment syndrome in the military, with a mid-term follow-up," (in eng), *BMJ Open Sport Exerc Med,* vol. 5, no. 1, p. e000532, 2019, doi: 10.1136/bmjsem-2019-000532.

[32] R. M. Biedert and B. Marti, "Intracompartmental pressure before and after fasciotomy in runners with chronic deep posterior compartment syndrome," (in English), *International Journal of Sports Medicine,* Article vol. 18, no. 5, pp. 381-386, 1997, doi: 10.1055/s-2007-972650.

[33] J. Islam and J. V. Robbs, "Management of chronic exertional compartment syndrome," (in English), *S. AFR. J. SURG.,* Article vol. 53, no. 2, pp. 59-61, 2015, doi: 10.7196/sajsnew.7855.

[34] M. E. Isner-Horobeti, S. P. Dufour, C. Blaes, and J. Lecocq, "Intramuscular pressure before and after botulinum toxin in chronic exertional compartment syndrome of the leg: a preliminary study," (in English), *The American journal of sports medicine,* Article vol. 41, no. 11, pp. 2558-2566, 2013.

[35] H. Lohrer and T. Nauck, "Endoscopically assisted release for exertional compartment syndromes of the lower leg," (in English), *Archives of Orthopaedic and Trauma Surgery,* Article vol. 127, no. 9, pp. 827-834, 2007, doi: 10.1007/s00402-006-0269-4.

[36] N. Maffulli, M. Loppini, F. Spiezia, A. D'Addona, and G. D. Maffulli, "Single minimal incision fasciotomy for chronic exertional compartment syndrome of the lower leg," (in English), *Journal of orthopaedic surgery and research,* Article vol. 11, no. 1, p. 61, 2016, doi: 10.1186/s13018-016-0395-9.

[37] E. Mouhsine, R. Garofalo, B. Moretti, G. Gremion, and A. Akiki, "Two minimal incision fasciotomy for chronic exertional compartment syndrome of the lower leg," (in English), *Knee Surgery, Sports Traumatology, Arthroscopy,* Article vol. 14, no. 2, pp. 193-197, 2006, doi: 10.1007/s00167-004-0613-6.

[38] N. Pasic, D. Bryant, K. Willits, and D. Whitehead, "Assessing outcomes in individuals undergoing fasciotomy for chronic exertional compartment syndrome of the leg," (in English), *Arthroscopy - Journal of Arthroscopic and Related Surgery,* Article vol. 31, no. 4, pp. 707-713, 2015, doi: 10.1016/j.arthro.2014.10.018.

[39] S. M. Raikin, V. R. Rapuri, and P. Vitanzo, "Bilateral simultaneous fasciotomy for chronic exertional compartment syndrome," (in English), *Foot and Ankle International,* Article vol. 26, no. 12, pp. 1007-1011, 2005, doi: 10.1177/107110070502601201.

[40] A. A. Schepsis, S. S. Gill, and T. A. Foster, "Fasciotomy for exertional anterior compartment syndrome: Is lateral compartment release necessary?," (in English), *American Journal of Sports Medicine,* Article vol. 27, no. 4, pp. 430-435, 1999, doi: 10.1177/03635465990270040501.

[41] D. Slimmon, K. Bennell, P. Brukner, K. Crossley, and S. N. Bell, "Long-term outcome of fasciotomy with partial fasciectomy for chronic exertional compartment syndrome of the lower leg," (in English), *American Journal of Sports Medicine,* Article vol. 30, no. 4, pp. 581-588, 2002, doi: 10.1177/03635465020300041901.

[42] V. Wieczorek, J. F. Luciani, E. Brunet-Guedj, P. Feugier, and A. Thevenon, "Short and mid-term outcomes of surgery treatment of chronic compartment syndrome in the lower leg," (in French), *Science and Sports,* Article vol. 27, no. 1, pp. 39-45, 2012, doi: 10.1016/j.scispo.2011.03.005.

[43] M. B. Winkes, A. R. Hoogeveen, S. Houterman, A. Giesberts, P. F. Wijn, and M. R. Scheltinga, "Compartment pressure curves predict surgical outcome in chronic deep posterior compartment syndrome," (in English), *The American journal of sports medicine,* Article vol. 40, no. 8, pp. 1899-1905, 2012.

[44] M. B. Winkes *et al.*, "Fasciotomy for Deep Posterior Compartment Syndrome in the Lower Leg: A Prospective Study," (in English), *The American journal of sports medicine,* Article vol. 44, no. 5, pp. 1309-1316, 2016, doi: 10.1177/0363546515626540.

[45] 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, "Chronic deep posterior compartment syndrome of the leg in athletes: Postoperative results of fasciotomy," (in English), *International Journal of Sports Medicine,* Article vol. 29, no. 5, pp. 419-423, 2008, doi: 10.1055/s-2007-965365.

[46] V. Irion, R. A. Magnussen, T. L. Miller, and C. C. Kaeding, "Return to activity following fasciotomy for chronic exertional compartment syndrome," (in English), *European Journal of Orthopaedic Surgery and Traumatology,* Article vol. 24, no. 7, pp. 1223-1228, 2014, doi: 10.1007/s00590-014-1433-0.

[47] W. M. De Fijter, M. R. Scheltinga, and M. G. Luiting, "Minimally invasive fasciotomy in chronic exertional compartment syndrome and fascial hernias of the anterior lower leg: Short- and long-term results," (in English), *Military Medicine,* Article vol. 171, no. 5, pp. 399-403, 2006, doi: 10.7205/MILMED.171.5.399.

[48] M. Drexler *et al.*, "Single minimal incision fasciotomy for the treatment of chronic exertional compartment syndrome: outcomes and complications," (in English), *Archives of Orthopaedic and Trauma Surgery,* Article vol. 137, no. 1, pp. 73-79, 2017, doi: 10.1007/s00402-016-2569-7.

[49] J. M. Maher, E. M. Brook, C. Chiodo, J. Smith, E. M. Bluman, and E. G. Matzkin, "Patient-Reported Outcomes Following Fasciotomy for Chronic Exertional Compartment Syndrome," (in English), *Foot & ankle specialist,* Article vol. 11, no. 5, pp. 471-477, 2018, doi: 10.1177/1938640018783496.

[50] J. D. Packer, M. S. Day, J. T. Nguyen, S. J. Hobart, J. A. Hannafin, and J. D. Metzl, "Functional outcomes and patient satisfaction after fasciotomy for chronic exertional compartment syndrome," (in English), *The American journal of sports medicine,* Article vol. 41, no. 2, pp. 430-436, 2013.

[51] C. Pierret, J. P. Tourtier, E. Blin, L.Bonnevie, J. M. Garcin, and V. Duverger, "Chronic compartmental syndrome. A review of 234 patients," (in French), *Journal des Maladies Vasculaires,* Article vol. 36, no. 4, pp. 254-260, 2011, doi: 10.1016/j.jmv.2011.06.005.

[52] J. P. H. Tam, A. G. F. Gibson, J. R. D. Murray, and M. Hassaballa, "Fasciotomy for chronic exertional compartment syndrome of the leg: clinical outcome in a large retrospective cohort," (in English), *European Journal of Orthopaedic Surgery and Traumatology,* Article vol. 29, no. 2, pp. 479-485, 2019, doi: 10.1007/s00590-018-2299-3.

[53] R. Thein, I. Tilbor, A. Herman, G. Burstein, and S. Tenenbaum, "Return to sports after chronic anterior exertional compartment syndrome of the leg: Conservative treatment versus surgery," (in English), *Arthroscopy - Journal of Arthroscopic and Related Surgery*, Conference Abstract vol. 33, no. 10, pp. e103-e104, 2017.
[54] W. D. Turnipseed, "Diagnosis and management of chronic compartment syndrome," (in English), *Surgery*, Article vol. 132, no. 4, pp. 613-619, 2002, doi: 10.1067/msy.2002.128608.
[55] A. P. M. van Zantvoort, J. A. de Bruijn, H. P. H. Hundscheid, M. van der Cruijsen-Raaijmakers, J. A. W. Teijink, and M. R. Scheltinga, "Fasciotomy for Lateral Lower-leg Chronic Exertional Compartment Syndrome," (in English), *International journal of sports medicine*, Article vol. 39, no. 14, pp. 1081-1087, 2018, doi: 10.1055/a-0640-9104.
[56] J. L. Howard, N. G. H. Mohtadi, and J. P. Wiley, "Evaluation of outcomes in patients following surgical treatment of chronic exertional compartment syndrome in the leg," (in English), *Clinical Journal of Sport Medicine*, Review vol. 10, no. 3, pp. 176-184, 2000, doi: 10.1097/00042752-200007000-00005.
[57] J. L. Howard, N. G. Mohtadi, and J. P. Wiley, "Evaluation of outcomes in patients following surgical treatment of chronic exertional compartment syndrome in the leg," (in English), *Clinical journal of sport medicine : official journal of the Canadian Academy of Sport Medicine*, Article vol. 10, no. 3, pp. 176-184, 2000.
[58] J. C. Dunn and B. R. Waterman, "Chronic Exertional Compartment Syndrome of the Leg in the Military," (in English), *Clinics in Sports Medicine*, Article in Press 2014, doi: 10.1016/j.csm.2014.06.010.
[59] D. Farr and H. Selesnick, "Chronic exertional compartment syndrome in a collegiate soccer player: a case report and literature review," (in English), *American journal of orthopedics (Belle Mead, N.J.)*, Article vol. 37, no. 7, pp. 374-377, 2008.
[60] M. B. Winkes, A. R. Hoogeveen, and M. R. Scheltinga, "Is surgery effective for deep posterior compartment syndrome of the leg? A systematic review," (in English), *British journal of sports medicine*, Review vol. 48, no. 22, pp. 1592-1598, 2014, doi: 10.1136/bjsports-2013-092518.
[61] K. Anuar and P. Gurumoorthy, "Systematic review of the management of chronic compartment syndrome in the lower leg," (in English), *Physiotherapy Singapore*, Review vol. 9, no. 1, pp. 2-15, 2006.

9) TABLES

Table 1. Selection criteria

Table 1. Selection criteria

Selection criteria	**Inclusion criteria**	**Exclusion criteria**
Design	RCT, observational studies including 10 or more participants.	observational studies with less than 10 participants, systematic reviews, meta-analysis, technique description, abstract conference, book chapter.
Language	English, French	Others
Date	published in 1990 or later on	Published before 1990

Population	athletes, military, CECS in the leg, chronic, exercise induced. The participants could be either adults or adolescents.	acute, traumatic cause, upper limb
Intervention	surgical or non-surgical treatments	no treatment
Control	with and without control group	None
Outcome	all outcomes	None

Selection criteria are presented by order of application during the selection process. Abbreviations: RCT= Randomized clinical trial, CECS= chronic exertional compartment syndrome.

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Table 2. Data extraction

Author	Design	surg/ cons/ mixed	Intervention	n	Mean age	Affected compart-ment	Results	Conclusion
Beck	Retrospective case series	surg	fasciotomy	155	16.4±1.38	ant/lat/ post	RTS 79.5%; CR 11.2%; RR 18.8%	Fasciotomy in pediatric patients: good results; RR higher if ant&lat release or shorter previous conservative management.
Biedert	Controlled case series	surg	fasciotomy	15	29.1±10.3	dp	mean ICP returned to normal values	Fasciotomy restored normal ICP in dp CECS & complete relief of EILP.
Breen	Case series	cons	gait-retraining	10	30.5±8.8	ant	CRS 70%; mean GROC 4.9; mean EILP improvement 49.2%	Gait-retraining: sign. Reduction of pain & increase in function -> treatment of choice for ant. CECS
Cook	Retrospective cohort study	surg	fasciotomy	14	27 (22-28)	ant/lat/ post	RTFD 85.7%; CRS 78.5%; CR 0%	fasciotomy = effective treatment after failure of cons. treatment
De Fijter	Retrospective cohort study	surg	minimally invasive percutaneous fasciotomy	72	21 (18-37)	ant	PSR 93.6%; CR 18%	minimally invasive fasciotomy = effective in ST&LT, complications are mild
Diebal	Prospective consecutive case series	cons	forefoot running	10	20.2±1.5	ant/lat	sign. changes: ICP, running distance, Borg RPE, SANE, LLOS; GROC 5-7	forefoot running ↘ ICP, pain, disability, surgery avoided in all cases
Drexler	Retrospective case series	surg	minimal incision fasciotomy	54	23.6 (16-43)	ant/lat	PSR 75.5%; CR 4.2%; RS 8.4%; sign. changes: SF-12, Tegner	minimal incision fasciotomy: high PSR, acceptable CR
Finestone	Retrospective case series	surg	percutaneous fasciotomy	36	24 (16-54)	ant	PSR 71%; CR 8.6%; sign. changes: pain, activity level, running distance	percutaneous fasciotomy of ant. compartment only is adequate

Garcia-Mata	Case series	surg	subcutaneous fasciotomy	23	16 (14-18)	ant/lat/ post	PSR 100%; RTS 100%; CRS 100%; CR 4.5%; ICP returned to normal values	fasciotomy ↘ ICP and reliefs symptoms if diagnosis is correct
Gatenby	Retrospective case series	surg	fasciotomy	31	27.5 (16-50)	ant/lat	RTS 90%; CR 19.4%; sign. decrease in pain	Isolated ant&lat release recommended for patients without symptoms of post. CECS
Helmhout	Prospective cohort study	cons	forefoot running center-based vs. home-based	22	26.1±8.6 (CB); 21.2±1.7 (HB)	ant/lat	sign. changes: ICP, running distance, SANE, LLOS, PSC; GROC 6	forefoot running ↘ ICP, pain, disability, ↗ running distance, self-reported outcome scores; HB-program: reduced investment (time & resources)
Howard	Retrospective descriptive cohort study	surg	fasciotomy	62	31.8±12	ant/lat/ post	PSR 79%; RTS 78%; RR 6%; sign. change in pain	Fasciotomy is recommended for CECS patients as there is no other treatment for this condition.
Irion	Retrospective chart review	surg	fasciotomy	14	19.7 (17-24)	ant/lat/ post	RTS 84.6%; RS 30.8%	RTS relatively high in elite-athletes RTS takes more time if 4 compartments involved, more research needed in this population
Islam	Prospective cohort study	surg	modified open fasciotomy	123	28 (18-53)	ant/lat/ post	RTS 90%; CRS 90%; CR 11%	CECS should be treated surgically, open fasciotomy = safe & effective
Isner-Horobeti	Case series	cons	BoNT-A injections	16	23 (18-36)	ant/lat	CRS 94%; sign. decrease in ICP; muscle strength reduced in 69%	BoNT-A injection ↘ ICP and EILP at ST for ant/lat CECS
Lohrer	Case series	surg	endoscopic fasciotomy	17	24 (14-43)	ant/lat/ post	PSR 58.7%; CRS 58.8%	endoscopic fasciotomy = feasible, but less effective and safe than open fasciotomy; dp CECS = critical (CR and outcomes)

Maffulli	Prospective case series	surg	minimally invasive fasciotomy	18	27 (18-35)	ant/lat	PSR 94.4%; RTS 94%; sign. changes: EQ-5D, SF-36	minimally invasive fasciotomy = safe, PSR & function OK, may be alternative to traditional open surgery
Maher	Retrospective case series	surg	bilateral simultaneous vs. staged fasciotomy	31	24.7±8.26	ant/lat/ post	PSR 76%; RTS 81%; CR 9.5% (details per group)	bilateral & staged fasciotomy both effective; better outcome for 4-compartment- than for 2-compartment-release
McCallum	Retrospective consecutive case series	surg	fasciotomy	46	30 (19-50)	ant/lat/ post	PSR 71.4%; RTFD 41.3%; CR 21.4%	fasciotomy: 41.4% chance of returning to full duty, PSR 71%
Meulekamp	Prospective cohort study	cons	rehabilitation, physiotherapy	160	23 (18-40)	nd	PSR 55.5%	conservative treatment: modest ST results, no sign. prognostic factors for this treatment
Micheli	Retrospective cohort study	surg	minimal incision fasciotomy	53	17 (13-21)	ant/lat/ post	PSR 76%; RTS 75%	females may respond less well than men to operative fasciotomy
Mouhsine	Retrospective consecutive case series	surg	minimal open fasciotomy	18	25 (19-38)	ant/lat	RTS 100%	minimal open double incision fasciotomy = effective for ant/lat CECS
Packer	Cohort study	mixed	fasciotomy vs. nonoperative treatment	73 vs. 27	26.3±11.7 (surg); 31±13.9 (cons)	ant/lat	PSR 81% (surg) vs. 56% (cons)	Better outcomes (PSR, function) in younger patients and only ant. CECS; lateral release should be avoided if not necessary
Pasic	Retrospective consecutive case series	surg	fasciotomy	89	30±13	ant/lat/ post	PSR 78%; RTS 63%; RR 11%	fasciotomy = safe & effective surgical treatment for CECS; good functional outcomes
Pierret	Prospective cohort study	surg	fasciotomy	234	24±5	ant/lat/ post	PSR 68.4%; CR 5.9%	Outcomes of this surgical technique: satisfactory with few surgical complications

Raikin	Case series	surg	bilateral simultaneous vs. staged fasciotomy	19	25 (14-50)	ant/lat	RTS 87%; CRS 81.25%	bilateral simultaneous fasciotomy = safe & effective, with early RTS and low CR
Roberts	Retrospective cohort study	surg	fasciectomy	98	28±6	ant/lat/ post	RTFD 42%; 53% improved medical grading; 11% deteriorated	in a military population, lots of patients do not return to full fitness after fasciectomy; lack of relationship between ICP and outcomes -> question role of ICP, investigate conservative options
Roscoe	Controlled case series	Surg	fasciotomy	20	30.35±4.7	ant	sign. decrease in ICP, return to normal values	fasciotomy: sign. ↘ ICP, values come close to asymptomatic controls; findings support traditional pathophysiological model of CECS with fasciotomy as appropriate treatment
Schepsis	Prospective case series	surg	ant & lat fasciotomy vs ant only	20	23 (16-37)	ant/lat	PSR 90% overall, ant release only higher PSR than ant&lat release	lat compartment release in addition to ant release is unnecessary if only signs and symptoms for ant CECS
Schepsis	Retrospective case series	surg	fasciotomy	28	ant: 26 (15-39); dp: 23 (16-34)	ant/lat/ post	PSR 96% for ant group; PSR 65% for dp group	fasciotomy for dp CECS has a lower success rate than for ant CECS
Simpson	Retrospective case series	surg	bilateral fasciectomy	41	nd	ant	RTFD 22%; 46% improved medical grading; 24% deteriorated	after more accurate diagnosis of CECS, outcomes from bilateral ant fasciectomy in militaries are at the lower and of those previously reported

Slimmon	Retrospective cohort study	surg	fasciotomy combined with partial fasciectomy	62	ant: 25.3±5.3; post: 26.3±6.6; combined 24.9±7.0	ant/lat/ post	PSR 60% overall; PSR 65% ant; PSR 75% post; PSR 31% combined surgery; RTS 42%; CR 90%	surgical technique combining fasciotomy with partial fasciectomy: good results at ST, less at LT; further research necessary
Tam	Retrospective cohort study	surg	mini-open fasciotomy	138	29.7±9.7	ant/lat/ post	decreased pain and higher activity in 98.5%; ICP correlated with pain	fasciotomy sign. ↘ pain & ↗ activity; ICP positively correlated with pain
Thein	Comparative study	mixed	fasciotomy vs. physiotherapy	31 vs. 12	23.8±7.6	ant	RTS 77.4% (surg) vs. 25% (cons); both groups improved in terms of pain & Tegner, surg>cons	surgery > conservative in terms of pain and RTS; but still not 100% RTS (surg) while 25% CSR (cons)
Turnipseed	Retrospective cohort study	surg	open fasciectomy	276	28.4 (12-71)	ant/lat/ post	CRS 92%; CR 10.7%; RS 6.1%	open fasciectomy has lower CR and RR than subcutaneous fasciotomy -> open surgery should be preferred
Van Zantvoort	Retrospective cohort study	surg	fasciotomy	30	25 (17-65)	lat	LT PSR 33%; RTS 30%	fasciotomy for lat CECS: PSR 33% at LT
Van Zoest	Retrospective cohort study	mixed	fasciotomy vs. inlays and physiotherapy	27 vs. 19	35±16 (surg); 43±12 (cons)	dp	surg: PSR 33%, cons: 84% improved	fasciotomy for dp CECS successful in only 52% at LT; cons. treatment and DD indicated if ICP below cut-off
Verleisdonk	Prospective study	mixed	fasciotomy vs. conservative treatment	53 vs. 53	23 (18-41)	ant	PSR 83% (surg), sign. decrease ICP, cons: effective in 70%	fasciotomy successful in 83% with elevated ICP, successful in 70% with ICP just below cut-off; further research necessary to identify ICP limits
Waterman	Retrospective cohort study	surg	fasciotomy	611	28	ant/lat/ post	RTFD 72.3%; CR 15.7%; RS 44.7%; RR 5.9%	CECS is common in militaries; fasciotomy: high RS, CR and military discharge; unsuccessful in 1/5 patients

Wieczorek	Retrospective case series	surg	surgical treatment	16	27.75 (15-61)	ant/lat/ post	PSR 62.5%; RTS 62.5%; CRS 37.5%; CR 44%; poorer results if atypical presentation or dp CECS	results of surgery are inconsistent (pain & RTS), depending on affected compartment & clinical presentation
Winkes	Case series	surg	open fasciotomy	52	33±14	dp	LT success 48%; ST success 52%; LT & ST not correlated	large area under pre-operative 4-point ICP curve predicts success; results for dp-fasciotomy are fair
Winkes	Prospective case series	surg	open fasciotomy	42	23 (17-52)	dp	LT PSR 47%; ST PSR 58%; CR 6.25%	after failure of cons. treatment options, fasciotomy for dp-CECS reduces all cardinal symptoms
Zimmermann	Historic cohort study	cons	gait-retraining & physiotherapy	37	21±4	ant	PSR 55%; CRS 50%; 70% active in duty; RR 20%	conservative treatment for militaries with ant CECS: 2/3 return to duty & avoiding surgery; if failure -> surgery
Zimmermann	Prospective cohort study	cons	gait-retraining & standard care	41	23±2.9 men; 22.9±3.3 women	nd	sign. increase in SANE, running shoes vs. military boots: similar changes in running kinematics	same gait retraining cues in running shoes & military boots; add gait retraining sessions in boots might improve outcome

ant: anterior compartment; BoNT-A: Botulinum Neurotoxin – A; Borg RPE: Borg Received Perception of Exertion ; CB: centre-based; CECS: chronic exertional compartment syndrome; cons: Conservative treatment; CR: complication rate ; CRS: complete relief of symptoms; DD: differential diagnosis; dp: deep posterior compartment; EILP: exercise-induced leg pain; EQ-5D: EuroQol-5 Dimensions; GROC: global rating of change; HB: home-based; ICP: intracompartmental pressures; lat: lateral compartment; LLOS: Lower Leg Outcome Survey; LT: long term; nd: not detailed; post: posterior compartment; PSC: Patient Specific Complaints; PSR: patient satisfaction rate; RR: revision surgery rate; RS: recurrence of symptoms; RTFD: return to fully deployable; RTS: return to sport; SANE: Single Assessment Numeric Evaluation; SF-12: Short Form 12; SF-36: Short Form 36; sign.: significant; ST: short term; surg: surgical treatment

Table 3. Study quality appraisal

Studies	Q1	Q2	Q3	Q4	Q5a	Q5b	Q6a	Q6b	Q9	Q10	Q11	Q12
Beck et al. (2016)	•	•	•	•	•	•	•	ST	•	•	•	•
Biedert et al. (1997)	•	•	•	•	•	•	•	LT	•	Dp	•	•
Breen et al. (2015)	•	•	•	•	•	•	•	ST	•	•	•	•
Cook et al. (2002)	•	•	•	•	•	•	•	LT	•	•	•	•
De Fijter et al. (2006)	•	•	•	•	•	•	•	LT	•	Ant	•	•
Diebal et al. (2012)	•	•	•	•	•	•	•	ST	•	•	•	•
Drexler et al. (2017)	•	•	•	•	•	•	•	LT	•	•	•	•
Finestone et al. (2014)	•	•		•	•	•	•	LT	•	•	•	•
García-Mata et al. (2001)	•	•	•	•	•	•	•	LT	•	•	•	•
Gatenby et al. (2017)	•	•	•	•	•	•	•	LT	•	Ant/lat	•	•
Helmhout et al. (2015)	•	•	•	•	•	•	•	ST	•	•	•	•
Howard et al. (2000)	•	•	•	•	•	•	•	LT	•	•	•	•
Irion et al. (2014)	•	•	•	•	•	•	•	ST	•	Elite-athletes	•	•
Islam et al. (2015)	•	•	•	•	•	•	•	ST	•	•	•	•
Isner-Horobeti et al. (2013)	•	•	•	•	•	•	•	ST	•	Ant/lat		•
Lohrer et al. (2007)	•	•	•	•	•	•	•	LT	•	•	•	•
Maffuli et al. (2016)	•	•	•	•	•	•	•	LT	•	•	•	•
Maher et al. (2018)	•	•	•	•	•	•	•	LT	•	•	•	•
McCallum et al. (2014)	•	•	•	•	•	•	•	LT	•	•	•	•
Meulekamp et al. (2017)	•	•	•	•	•	•	•	ST	•	•	•	•
Micheli et al. (1999)	•	•	•	•	•	•	•	LT	•	Females	•	•
Mouhsine et al. (2006)	•	•	•	•	•	•	•	ST	•	•	•	•
Packer et al. (2013)	•	•	•	•	•	•	•	LT	•	•	•	•
Pasic et al. (2015)	•	•	•	•	•	•	•	LT	•	•	•	•
Pierret et al. (2011)	•	•	•	•	•	•	•	LT	•	•	•	•
Raikin et al. (2005)	•	•	•	•	•	•	•	ST	•	•		•
Roberts et al. (2014)	•	•	•	•	•	•	•	ST	•	Ant	•	•
Roscoe et al. (2018)	•	•	•	•	•	•	•	ST+ LT	•	Ant	•	•
Schepsis et al. (1993)	•	•	•	•	•	•	•	LT	•	Ant VS Post	•	•
Schepsis et al. (1999)	•	•	•	•	•	•	•	LT	•	Ant	•	•
Simpson et al. (2019)	•	•	•	•	•	•	•	ST	•	Ant	•	•
Slimmon et al. (2002)	•	•	•	•	•	•	•	LT	•	•	•	•
Tam et al. (2019)	•	•	•	•	•	•	•	ST	•	•	•	•
Thein et al. (2017)	•	•	•	•	•	•	•	LT	•	Ant	•	•
Turnipseed et al. (2002)	•	•	•	•	•	•	•	LT	•	•	•	•
Van Zantvoort et al. (2018)	•	•	•	•	•	•	•	LT	•	Lat	•	•
Van Zoest et al. (2008)	•	•	•	•	•	•	•	LT	•	Dp	•	•
Verleisdonk et al. (2004)	•	•	•	•	•	•	•	LT	•	•	•	•
Waterman et al. (2013)	•	•	•	•	•	•	•		•	•	•	•
Wieczorek et al. (2012)	•	•	•	•	•	•	•	ST	•	•	•	•
Winkes et al. (2012)	•	•	•	•	•	•	•	LT	•	Dp	•	•
Winkes et al. (2016)	•	•	•	•	•	•	•	LT	•	Dp	•	•
Zimmermann et al. (2019)	•	•	•	•	•	•	•	LT	•	•	•	•
Zimmermann et al. (2019)	•	•	•	•	•	•	•	ST	•	•		•

Green dots represent a YES while red dot represent NO. not applicable question were left blank. Abbreviations: ST= short-term (<2 years) and LT= long-term (>2 years). Ant = anterior compartment CECS, Dp= deep posterior compartment CECS, Post= posterior compartment CECS, Lat= lateral compartment CECS

10) FIGURES

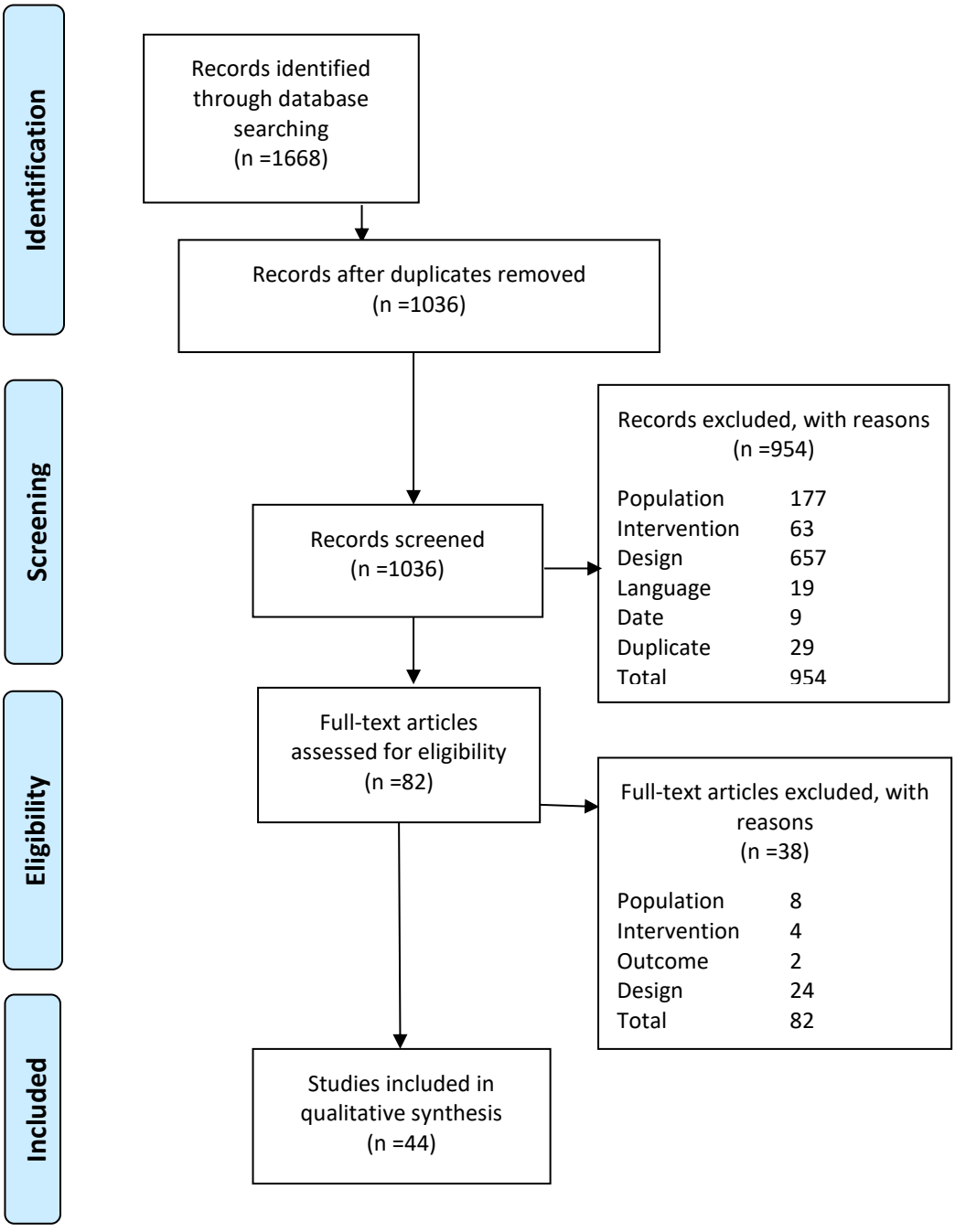

Figure 1. Study selection - Flow chart

11) The authors have no conflicts of interest to declare.