The Effectiveness of Surgical and Non-Surgical Management Strategies in Patients with Chronic Exertional Compartment Syndrome of the Anterior Compartment of the Leg: A Systematic Review and Meta-Analysis

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A dissertation submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in fulfilment of the requirements for the degree of MSc (Physiotherapy).

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Declaration

I, Sean Kaplan, declare that this Dissertation is my own, unaided work. It is being submitted for the MSc (Physiotherapy) degree at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

Sean Kaplan

Signed in Johannesburg on this 21st day of June 2021

Abstract

Objective: The objective of this review was to evaluate the effectiveness of surgical management versus non-surgical management on pain, range of motion, intracompartmental pressure (ICP) values, patient satisfaction, recurrence of symptoms, return to activity, function, strength, and sensation in patients diagnosed with Chronic Exertional Compartment Syndrome (CECS) of the anterior compartment of the leg.

Introduction: CECS is the most prevalent cause of exercise-induced leg pain in athletes. Current evidence suggests that the best methods for management of the condition include activity modification or cessation, injection of botulinum toxin into the affected compartment, or surgical intervention. However, no systematic review has been done to provide level one evidence of the effectiveness of surgical versus non-surgical management of CECS of the anterior compartment of the leg. Findings from this study will inform clinical practice and identify gaps for further research into this condition.

Study Design: Systematic review and meta-analysis of case reports, case series, cohort studies, case-control studies, quasi-experimental studies, and randomised controlled trials. Level of evidence: 1

Inclusion criteria: Studies were included if they assessed human participants that were diagnosed with CECS of the anterior compartment of the leg through a combination of elevated ICP values and patient history. Studies reporting patients with CECS in addition to diagnoses of another lower limb pathology were included. Studies that included patient reported outcome measures such as return to activity, pain, and those that use specific outcome measures related to function were included. Studies published in all languages were considered for inclusion. Studies were excluded if they included management of acute compartment syndrome or if they did not mention and specify the method of ICP measurement and/or other diagnostic parameters. Studies assessing multiple compartments of the leg were excluded if they do not separately report results for the anterior compartment.

Methods: MEDLINE via PubMed, SPORTDiscus, Physiotherapy Evidence Database (PEDro), EBSCOhost MasterFILE Premier, EBSCOhost CINAHL Complete, ProQuest Health and Medical Complete, SCOPUS and Science Direct were systematically searched from 1956 to December 2020. Grey literature databases were also searched. Included full-text studies were critically appraised using JBI SUMARI. Where statistical pooling was possible, results from the articles were synthesised for statistical analysis using JBI SUMARI and R. The findings of all included studies were presented in a narrative review, including results from studies that underwent meta-analysis.

Results: A total of 52 studies were included in the review, with a collective sample size of 1458 participants. The designs of the included studies were case reports (n=15), case series (n=24), cohort studies (n=8), quasi-experimental studies (n=3), case-control studies (n=1), and randomised controlled trials (n=1). Regardless of the type of management intervention, pain scores improved significantly across all studies (95% CI[1.73-4.11], $p<0.01$, $I^2=94\%$). ICP values improved following intervention in patients undergoing surgical fasciotomy, gait re-training, and botulinum toxin injection into the affected compartment (at rest 95% CI [9.74-17.83], $p<0.01$, $I^2=98\%$; at P_0 95% CI [12.08-49.79], $p<0.01$, $I^2=99\%$; at P_1 95% CI [13.95-40.63], $p<0.01$, $I^2=99\%$; at P_5 95% CI [11.43-30.15], $p<0.01$, $I^2=99\%$). Satisfaction rates for surgical fasciotomy were greater than both surgical fasciectomy and combination surgery, but comparable to those reported for non-surgical management (95% CI [2.20-10.70], $p<0.51$, $I^2=0\%$). Symptom recurrence was reported as 36% for fasciectomy and ranged from 0% to 23% for fasciotomy. Symptom recurrence was not expressly presented for non-surgical management. Range of motion for ankle dorsiflexion improved significantly for patients managed with botulinum toxin and manual therapy. Muscle strength initially decreased following intervention with botulinum toxin but did not affect function and returned to normal at follow-up. Sensory deficits were reported following fasciotomy and were either due to peroneal nerve entrapment, sural nerve damage, or pre-existing CECS. Rates of return to activity were 25-95% in patients that underwent fasciotomy and 57-100% for patients receiving gait-retraining (95% CI [0.40-0.79], $p<0.01$, $I^2=95\%$).

Conclusions: Non-surgical management strategies are a safe and effective intervention for CECS of the anterior compartment of the leg with low risk and should be exhausted prior to referral for surgical management, preferably in the form of surgical fasciotomy. If surgical management is unsuccessful, repeat fasciotomies including additional compartments may be necessary. A consensus needs to be reached regarding diagnostic parameters for CECS. Further research into non-surgical interventions and novel surgical interventions such as fascial fenestration is necessary.

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List of Abbreviations

CECS – Chronic exertional compartment syndrome

SANE – Single assessment numeric evaluation

LEFS – Lower extremity functional scale

SF-36 and SF-12 – Short-form 36 / Short-form12 survey

LLOS – Lower leg outcome survey

FAAM – Foot and ankle mobility measure

VAS – Visual analogue scale

EQ-5D - EuroQol-5 Dimension survey

NPRS – Numeric pain rating scale

VRS – Verbal pain rating scale

RoM – Range of motion

MRC – Medical research council

MTSS – Medial tibial stress syndrome

ICP – Intracompartmental pressure

EILP – Exercise-induced leg pain

PAES – Popliteal artery entrapment syndrome

MRI – Magnetic resonance imaging

NIRS – Near-infrared spectroscopy

P_0 – immediately post-exercise

P_1 – 1-minute post-exercise

P_5 – 5-minutes post-exercise

Chapter 1 Introduction

1.1 Background

Chronic exertional compartment syndrome (CECS) was first reported in 1956 as a condition with symptoms of pain, numbness, and tightness in the anterolateral leg with a gradual progression during activity and ceasing with rest (Mavor, 1956). There is a stark difference between acute and chronic compartment syndromes, where acute compartment syndrome is a surgical emergency requiring early diagnosis and urgent, appropriate surgical intervention for a good prognosis (Donaldson et al., 2014).

Broadhurst and Robinson (2020, p. 1) describe CECS as “a condition caused by a transient or reversible increase in compartmental pressure brought on by exercise” with pain or paraesthesia in a specific fascial compartment following activity and with total resolution of symptoms following 10 to 20 minutes of rest. Symptoms of CECS do not improve if the condition is untreated; in an observational study regarding the natural course of CECS symptoms conducted over 50 months, Van der Wal et al. (2015) found that symptoms persist over time without resolution if patients do not receive intervention.

Chronic exertional compartment syndrome is the most common form of exercise-induced leg pain (EILP) experienced in athletes, occurring in 27% of recorded EILP cases (Burrus et al., 2015, Tucker, 2010). Approximately 95% of all cases occur in the anterior compartment of the leg (Bonasia et al., 2015). The anterior and lateral compartments of the leg are usually assessed and treated simultaneously yet approximately 7% of all CECS cases may occur in the lateral compartment alone – it is difficult to differentiate between the two compartments with current knowledge (van Zantvoort et al., 2019).

Despite its prevalence in EILP, the pathophysiology of CECS remains poorly understood and subsequently the condition is often misdiagnosed which has led to underdiagnosis of a presumably large number of cases (Bonasia et al., 2015, Roberts and Franklyn-Miller, 2012). It is therefore essential to obtain a thorough history of the patient’s symptoms (Bonasia et al., 2015) and to exclude differential diagnoses (Broadhurst and Robinson, 2020) such as medial tibial stress syndrome, stress fractures, peripheral nerve entrapments, deep vein thrombosis, popliteal artery entrapment, and vascular claudication (Buerba et al., 2019).

It is largely accepted that young adults partaking in exercise in the form of running, team ball sports, and military service, with no clear discrimination between men and women, are most at risk of developing CECS (Bonasia et al., 2015). Research into the biomechanical factors that may be a contributory factor for developing CECS is lacking, however, Calvelli et al. (2020) has alluded to the role of biomechanics in the pathophysiology of CECS. The first diagnosed case of CECS in elite Nordic skiers appeared when free-technique skiing was introduced – biomechanical analysis of this technique found that more strain is placed on the anterior and lateral compartments of the leg during this skiing technique compared to other techniques (Calvelli et al., 2020).

Intracompartmental pressure (ICP) measurement is mandatory for making an accurate diagnosis of CECS (Broadhurst and Robinson, 2020). The most frequently used “gold standard” criteria for diagnosis of the condition (Ding et al., 2020) is the Pedowitz criteria (Pedowitz et al., 1990), which measures ICP using a handheld slit catheter. Prior to ICP measurement the patient must present with a history of EILP as well as reproduction of symptoms on exercise testing (Pedowitz et al., 1990). According to the Pedowitz criteria, ICP measurements required for a positive diagnosis in the affected compartment are: a pre-exercise reading of ≥15mmHg; 1-min post-exercise reading of ≥30mmHg; 5-min post-exercise reading of ≥20mmHg (Pedowitz et al., 1990). Recently, however, some researchers have found the Pedowitz criteria to be inadequate, finding that a broadening of the diagnostic values and inclusion of dynamic ICP measurements during a three-step exercise protocol using a catheter wire to be a more sensitive and specific diagnostic outcome measure than the Pedowitz criteria (Roscoe et al., 2015). There is currently no clear consensus regarding exact diagnostic criteria (Dyer and Hogrefe, 2018) or pathological ranges of ICP values (Aweid et al., 2012), therefore care must be taken when interpreting diagnostic criteria used in studies evaluating CECS.

The majority of patients with a positive CECS diagnosis who wish to return to activity are currently treated surgically with fasciotomy, which presents minimal risk of serious complication (Edmundsson and Toolanen, 2011) however symptom recurrence following surgical management ranges between 8.4% and 44.7% (Drexler et al., 2017, Roberts et al., 2015, Waterman et al., 2013a). The range in symptom recurrence may be due to a lack of consensus on catheter placement for measuring and positioning when assessing ICP (Aweid et al., 2012) as well as a lack of consensus on surgical technique (Tzortziou et al., 2006). Alternate surgical treatment options include piercing the fascia through fascial fenestration (Finnoff and Rajasekaran, 2016) and partial excision of fascia through fasciectomy (Roberts et al., 2015, Simpson et al., 2020). Following surgical management, between 41.3% and 90% of patients can return to their respective activities without impaired function (Gatenby et al., 2017, McCallum et al., 2014, Roberts et al., 2015).

Several non-surgical management options for treating CECS have been proposed. Gait-retraining, which involves altering gait mechanics to emphasise mid-foot strike or forefoot running, has shown excellent results – between 57% and 100% of patients were able to return to activity without surgical intervention following a minimum six-week intervention (Breen et al., 2015, Diebal et al., 2012, Zimmermann et al., 2019). This method of management may however be impractical for military personnel and certain athletes participating in sports where these gait changes could affect performance. Patients reported greater improvements in pain and function relative to the duration of the intervention (Diebal et al., 2012) and retained technical changes to their running technique at six-week follow-up (Breen et al., 2015). A novel non-surgical treatment for CECS management has been proposed by Isner-Horobeti et al. (2013) using Onabotulinum Toxin-A (Dysport, Ipsen) injected into the symptomatic compartment. Pain resolved completely in 94% of patients with no reported adverse effects, and ICP was measured at a level of 59-69% lower than pre-injection values at 4.4 month follow up (Isner-Horobeti et al., 2013). Baria and Sellon (2016) had similar results when treating a diagnosed CECS patient with botulinum toxin – pain following aggravating activity reduced from 9/10 to 1/10 on the VAS, paraesthesia resolved completely one week post injection, and no atrophy, weakness, or other adverse effects were identified at 14-month follow-up. Hutto et al. (2019) conducted a similar case study in a CECS patient who showed total pain resolution within two weeks of injection, and no recurrence of symptoms at 10-month follow-up. While these results are promising, the mechanism of action of intracompartmental botulinum toxin is not clearly defined and further research into this type of management is required (Baria and Sellon, 2016, Isner-Horobeti et al., 2013). Manual therapy, such as massage and myofascial release, has so far shown inconclusive results for the management of CECS (Rajasekaran and Hall, 2016).

1.2 Problem Statement

Chronic exertional compartment syndrome is the most common form of exercise-related leg pain experienced in athletes, occurring in 27% of recorded cases (Rajasekaran and Hall, 2016). There is increasing research into effective methods of non-surgical management for treating CECS, yet current best practice remains surgical management (Edmundsson and Toolanen, 2011).

The JBI Evidence Synthesis, Cochrane Database, MEDLINE, DARE, PROSPERO, EPISTEMONIKOS, and ACCESSSS databases were searched on 27 November 2020 for up-to-date available systematic reviews using the terms “chronic exertional compartment syndrome” AND “systematic review”. There is at present only one systematic review comparing outcomes of surgical and non-surgical management of CECS (Vogels et al., 2020b). However, all compartments of the lower leg were included in the review. Only six databases were searched for literature, grey literature was not included, search terms were limited, date ranges did not extend to the first reported use of the term “chronic exertional compartment syndrome” by Mavor in 1956 (Mavor, 1956), and not all types of studies were included for review (Vogels et al., 2020b). Aside from this review by Vogels et al. (2020b), only three other systematic reviews related to the management of CECS have been conducted to date. Two systematic reviews have been conducted on outcomes of surgical management. The first assessed outcomes at short- and mid-term follow up, with no long-term outcomes of surgical management (Campano et al., 2016). The second assessed outcomes for CECS of all fascial compartments and included long-term follow up, however, only two databases were searched (Medline and EMBASE) and the number of included articles were limited (Ding et al., 2020). The other systematic review, conducted by Rajasekaran and Hall (2016) only considered non-surgical management of CECS. These three systematic reviews did not include meta-analysis. There is currently no other systematic review comparing management outcomes for CECS of the anterior compartment of the leg.

1.3 Systematic Review Question

What is the effect of surgical management versus non-surgical management on pain, range of motion, ICP values, patient satisfaction, recurrence of symptoms, return to activity, function, strength, and sensation in patients diagnosed with CECS of the anterior compartment of the leg?

1.4 Aims and Objectives

The objective of this review was to compare the results of surgical management to non-surgical management in terms of clinical outcomes (e.g., pain, range of motion, ICP values, patient satisfaction, recurrence of symptoms, return to activity, function, strength, and sensation) for patients diagnosed with CECS of the anterior compartment of the leg and provide meta-analyses.

1.5 Significance

This review is the first to compare the outcomes of surgical and non-surgical management of CECS of the anterior compartment of the leg, as well as the first systematic review to conduct meta-analysis for CECS outcomes. The results of this study may inspire further research into the diagnosis and treatment of CECS by having identified gaps within the literature, as well as stressing the importance of facilitating the formulation of a consensus that may lead to effective non-surgical management of the condition. Understanding the relationship and effects of different types of management on patients diagnosed with CECS adds to the body of knowledge and will assist in informing clinicians and patients of alternate management strategies, their efficacy, and their application. Inclusion of all studies regardless of study type or number of participants allowed for evaluation of all available evidence to provide insight into consensus regarding study design and results.

1.6 Outline of this Dissertation

This dissertation is presented in the order depicted below in Figure 1.

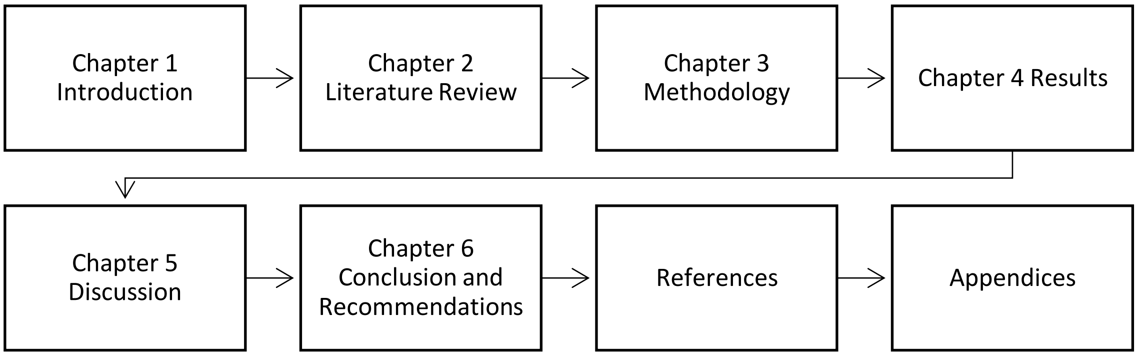

Figure 1 - Outline of Dissertation

Chapter 2 Literature Review

2.1 Introduction

The previous chapter provided a brief overview of the background, diagnosis, and management of CECS. This chapter will provide the reader with a comprehensive background understanding of CECS and its management, and further elucidate the need for additional research into the condition. The epidemiology, pathophysiology, diagnosis, treatment options and their respective outcomes for patients diagnosed with CECS will be discussed.

Epidemiological evidence for CECS is lacking, which may preclude current awareness of CECS in patients of all age groups and activity levels (de Bruijn et al., 2018b). There is no clear understanding of the exact background mechanisms of CECS (Edmundsson et al., 2018) as well as inconsistency regarding diagnostic criteria (Waterman et al., 2013b). In Europe, CECS is estimated to contribute to lifetime public expenses of up to 3.2 million US dollars per individual due to the condition's impact on physical ability and quality of life (Orlin et al., 2016).

Current treatment options for CECS are limited. Surgical management includes fasciotomy (Edmundsson and Toolanen, 2011), fasciectomy (Roberts et al., 2015), and ultrasound-guided fascial fenestration (Finnoff and Rajasekaran, 2016). Non-surgical treatment options include activity modification such as gait re-training (Breen et al., 2015), botulinum toxin (Isner-Horobeti et al., 2013), and manual therapy (Ragab et al., 2019). Studies investigating non-surgical management of CECS and its role in managing the condition are scarce and of low-quality design, prompting healthcare practitioners to recommend surgery as a first-line treatment (Tzortziou et al., 2006).

Intracompartmental pressure values according to the Pedowitz criteria (Pedowitz et al., 1990) are considered the "gold standard" for diagnosing CECS, however the proposed diagnostic values have come under much scrutiny in recent years due to a perceived inadequacy in diagnosing the condition (Roscoe et al., 2015). This is in part due to conditions such as popliteal artery entrapment syndrome (PAES) which presents with very similar symptomatology to CECS, including elevated ICP levels (Gaunder et al., 2017). Therefore, there is a high likelihood of either condition being misdiagnosed as the other if ICP values alone are used diagnostically (Gaunder et al., 2017). Some studies have attempted to diagnose CECS through MRI imaging rather than ICP with promising results (Eskelin et al., 1998, Johnson et al., 2020, Sigmund et al., 2014, Verleisdonk et al., 2001), however no large-scale studies have yet been performed to confirm its reliability as a diagnostic tool.

A standardised questionnaire for assessing outcomes of management of CECS does not yet exist (Orlin et al., 2016). There is great variability in outcomes measured (as well as outcome measures used) across studies. The most commonly used outcome measures are pain (Visual Analogue Scale (VAS), Numeric Pain Rating Scale (NPRS), ICP levels (mmHg), function (Single Assessment Numeric Evaluation (SANE), Lower Limb Outcome Survey (LLOS), Tegner Activity Scale, 36-Item Short-Form Survey (SF-36), range of motion (degrees), muscle strength (Oxford scale, MRC scale), return to previous activity level (yes/no), patient satisfaction (Excellent, Good, Fair, Poor), recurrence of symptoms(yes/no), and surgical complications (minor/major) (Anil et al., 2019, Beck et al., 2016, Helmhout et al., 2015, Isner-Horobeti et al., 2013, Ragab et al., 2019, Thein et al., 2019, Zimmermann et al., 2019).

2.2 Search Strategy

The search strategy for this literature review aimed to find both published and unpublished studies. Studies published in all languages were included. Due to the condition being first described by Mavor in 1956, studies published from 1956 to December 2020 were included. A three-step strategy was utilised in this review. An initial limited search of MEDLINE and CINAHL was undertaken followed by analysis of the text words contained in the title and abstract, and of the index terms used to describe the article. A second search using all identified keywords and index terms was then undertaken across all included databases. Thirdly, the reference lists of all reports and articles identified for inclusion in the review were searched for additional studies.

2.3 Epidemiology

Population prevalence of CECS is estimated to be as high as 7.6% (Orlin et al., 2016) however this is the only study reporting population prevalence at present. Prevalence in all compartments of the leg appears to increase with age and plateaus around the age of 50 (de Bruijn et al., 2018a). The incidence of CECS has been reported as 1 in

2000 persons per year, according to a study that assessed incidence in a US Military cohort (Waterman et al., 2013b) – suggesting that these results may better reflect incidence rates in military and athletic populations. There seems to be no correlation of positive diagnosis with gender, age, and duration of symptoms (Meulekamp et al., 2017) however; female sex, increasing chronological age, and white race may be influential factors (de Bruijn et al., 2018a, Orlin et al., 2016, Waterman et al., 2013b).

Chronic exertional compartment syndrome does not only affect athletes and active individuals (Orlin et al., 2016) and can affect sedentary, non-athletic individuals (Edmundsson et al., 2007) as well as adolescents (Garcia-Mata et al., 2001). In non-sporting populations, diagnosis is more likely to occur in the anterior compartment of the leg (de Bruijn et al., 2018a). Recent studies have shown patients between the ages of 14 and 81 testing positive for CECS (de Bruijn et al., 2018a, Johnson et al., 2020). A study conducted by de Bruijn et al. (2018b) demonstrated that 14% of patients diagnosed were over the age of 50, and this is hypothesised to be due to an increase in activity levels in this population due to increased leisure time with retirement.

Different sports appear to contribute to CECS in specific compartments depending on the demands of the sports; speed skating increases the likelihood of developing CECS in the anterior compartment of the leg while soccer players have an increased likelihood of developing CECS of the deep, posterior compartment of the leg (de Bruijn et al., 2018a). Controversially, in the cohort studied, running appears to be linked to a reduced likelihood of developing CECS in all compartments of the leg (de Bruijn et al., 2018a). It is believed that these increased likelihoods are due to intrinsic, sport-specific factors such as biomechanics of posture during activity, and an increasing intensity during sports (de Bruijn et al., 2018a).

Chronic exertional compartment syndrome can also occur after trauma to the affected compartment (Edmundsson et al., 2007, Tubb and Vermillion, 2001). Patients with unilateral complaints tend to have a higher prevalence of previous trauma or vascular pathology (de Bruijn et al., 2018a). In patients older than 50, complaints are more often unilateral and significantly more frequent in the anterior compartment of the leg compared to other compartments (de Bruijn et al., 2018b). Higher exposure to previous trauma and/or comorbidities may be a reason for development of CECS in older patients (de Bruijn et al., 2018b).

2.4 Pathophysiology

The pathophysiology of CECS remains unclear (Bonasia et al., 2015) and causes of elevated ICP are still unknown (Dahl et al., 2011, Verleisdonk et al., 2001). It is proposed that the compartment size is inadequate to cope with the increase in myovascular volume during activity (Mannarino and Sexson, 1989) due to abnormal muscle capillarisation, low fascial compliance, and muscle hypertrophy (Edmundsson et al., 2018, Edmundsson and Toolanen, 2010).

The prevalence of elevated ICP levels in asymptomatic individuals is yet to be determined (Orlin et al., 2016). No correlation has been found between ICP values and pain experience in patients diagnosed with bilateral CECS in all compartments of the leg (Orlin et al., 2013).

Tissue oxygenation and muscle fiber dilation appear diminished in CECS patients (Sigmund et al., 2014, van den Brand et al., 2004). Tissue deoxygenation is greater within the structures of the affected compartment of CECS patients during exercise compared to those of healthy volunteers (van den Brand et al., 2004). Also, muscle fiber dilation is present in the muscles of healthy volunteers, in CECS patients this dilation is not observed (Sigmund et al., 2014). Structural and mechanical properties of the fascia, such as stiffness and thickness, do not appear to be major contributing factors to CECS pathology (Dahl et al., 2011). Pathogenesis of CECS in diabetic patients appears to be different to that of non-diabetic patients – diabetic patients present with greater local capillary density and decreased cross-sectional area of the muscle fibers compared to non-diabetic patients (Edmundsson et al., 2018).

In order of distribution, patients with CECS will typically report pain as the main symptom, followed by a feeling of “tightness”, cramps, altered sensation, and muscle weakness (de Bruijn et al., 2019). Pain is related to the duration of the activity and is relieved with rest (Mannarino and Sexson, 1989). Sensitivity changes in CECS differ from those reported in other conditions such as polyneuropathy – changes in dermatomal sensitivity above the knee compared to below the knee seem to be less correlated with compartmental pain of the leg (Orlin et al., 2016). Another symptom that has recently been noted is nocturnal cramps with leg pain, occurring in as many as 31% of CECS patients (Orlin et al., 2016).

Patients are less likely to be diagnosed with CECS when they present with unilateral symptoms compared to those presenting with bilateral symptoms (de Bruijn et al., 2018a). As many as 74% - 88.7% of patients have bilateral complaints (de Bruijn et al., 2018a, Johnson et al., 2020). Bilaterality is type-dependent showing a greater correlation with CECS of the anterior compartment of the leg (de Bruijn et al., 2018a). ICP between legs is also highly correlated in bilateral CECS (Orlin et al., 2013). Oedema caused by rheumatic diseases, heart failure, and hormone medication is present in 40-50% of patients with bilateral presentations (Orlin et al., 2016).

2.5 Diagnosis

The "gold standard" diagnostic measure for CECS at present is ICP measurement according to the Pedowitz criteria which is as follows; a pre-exercise (resting) reading of ≥15mmHg; 1-min post-exercise reading of ≥30mmHg; and a 5-min post-exercise reading of ≥20mmHg (Pedowitz et al., 1990). Prior to publication of the Pedowitz criteria, Mannarino and Sexson (1989) had proposed that ICP readings above 100mmHg at any stage of testing are a predictive marker for CECS. Diagnostic thresholds have remained inconsistent among healthcare providers (Orlin et al., 2016, Tzortziou et al., 2006). Test protocols and ICP measurement techniques such as catheter placement also differ in the literature (Aweid et al., 2012), with exercise protocols varying between walking, running, speed, incline, and active ankle movement (Aweid et al., 2012, Maksymiak et al., 2020). Additionally, there is disagreement regarding diagnostic accuracy for the different stages of testing, with authors stating that; ICP values at rest are more valid than those after exertion (Orlin et al., 2013), measurements immediately after exercise are more reliable than at other stages (Verleisdonk, 2000), measurements 1-min after exercise are most significant (Aweid et al., 2012), only ICP during exercise demonstrates significant differences between patients and controls (Mannarino and Sexson, 1989). These conflicting observations add gravity to the statement that the diagnostic "gold standard" for CECS is flawed (Roberts and Franklyn-Miller, 2012).

To assess the reliability of the Pedowitz criteria, Pasic et al. (2015) conducted a study that found it to be sensitive (97%) but not specific (10%), with a positive predictive value (PPV) of 79%. More specific methods have been proposed such as measuring ICP immediately after exercise, which showed slightly lower sensitivity (93%), but significantly higher specificity (74%) and a higher PPV of 85% (Verleisdonk et al., 2004). Roscoe et al. (2015) proposed a three-phase exercise protocol; ICP measurements according to phase two with a cut-off value of 105mmHg show specificity of 95% and sensitivity of 63% and a PPV of 84.5%. Near-infrared spectroscopy (NIRS) has also demonstrated good reliability with 90% sensitivity and 63% specificity and has shown that tissue oxygenation saturation (StO2) cut-off values are comparable to those of ICP while being a less invasive test (van den Brand et al., 2004). These results are expressed graphically below in Figure 2.

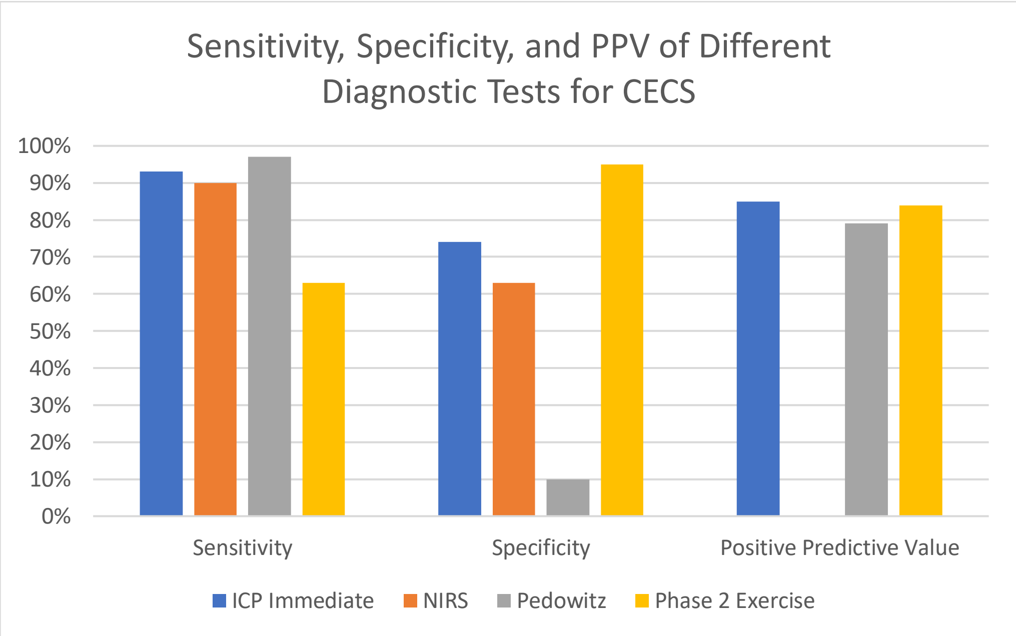

Figure 2 - Diagnostic Tests for CECS

Clinical parameters are therefore an especially important diagnostic requirement, as they are the only criteria that researchers agree upon (Aweid et al., 2012, Fouasson-Chailloux et al., 2018, Mannarino and Sexson, 1989). In addition to symptoms previously mentioned, absence of pain at rest, a decrease in pain following exercise, muscle hardness and palpable hernia after exercise are also useful for diagnosis (Fouasson-Chailloux et al., 2018).

A consistent finding to rule out CECS is the absence of tenderness directly over the tibia – this would raise the index of suspicion for the diagnosis of stress fracture (Mannarino and Sexson, 1989). Other differential diagnoses to be excluded in the case of suspected CECS of the leg include L5 nerve root impingement, tarsal tunnel syndrome, and peripheral nerve entrapment (Orlin et al., 2016). In adolescent patients, complaints symptomatically like CECS may be dismissed as “growing pains” if not appropriately investigated and followed up (Orlin et al., 2016).

A useful approach to differentiate CECS from other pathologies is through MRI imaging (Sigmund et al., 2014). One such diagnosis is that of Popliteal Artery Entrapment Syndrome (PAES) which may be present in up to 51.6% of patients with CECS of the anterior compartment of the leg (Johnson et al., 2020). Bilateral symptoms are present in 94% of patients with concurrent CECS of the anterior compartment of the leg and PAES (Johnson, 2020). Though symptoms are analogous between CECS of the anterior compartment of the leg and PAES, management of the conditions differ, and appropriate management must be performed to relinquish symptoms whether they occur independently or simultaneously (Johnson et al., 2020). Clinical differences to confirm a diagnosis of PAES and rule out CECS include reduced pulses in the affected compartment which diminish entirely on provocative movement, immediate reproduction of symptoms with a specific activity, and no resolution from intervention targeted at the fascia (Gaunder et al., 2017).

2.6 Treatment

2.6.1 Surgical Management

To date the most reported, successful surgical management of CECS is fascial incision through fasciotomy, being performed in approximately 88% of surgically managed patients (Campano et al., 2016). Patient satisfaction following fasciotomy is 48-94%, and 30-63% of patients can return to full activity (Ding et al., 2020). However, this is not without complications; haematoma occurs in 2.70-22.50% of patients, 2.00-18.60% of patients report nerve injuries, deep vein thrombosis occurs in 2.70% of cases, recurrence of symptoms ranges from 0.65-8.40%, and up to 10.40% of patients require revision surgery (Ding et al., 2020). Though this study is recent, there are certain limitations. The databases searched by Ding et al. (2020) were limited to MEDLINE, Embase, and clinical trial registries, therefore studies in other databases may have been missed. Most of the included studies are retrospective, lending themselves to recall bias, the quality of included studies is “very low”, and meta-analysis was not performed due to large heterogeneity of included studies (Ding et al., 2020).

Edmundsson et al. (2018) concluded that the success of fasciotomy is due to regeneration of muscle tissue even though there is no apparent regeneration of vascular tissue in the capillary bed. Patients who become asymptomatic following surgery demonstrate StO2 curves that are comparable to those of healthy volunteers (van den Brand et al., 2004) giving the impression that this improvement in tissue saturation occurs exclusively within muscular tissue. These findings require further research for generalisability primarily due to small sample sizes in both studies.

Fasciectomy involves partial excision of the fascia of the affected compartment and is performed in approximately 12% of surgically managed patients (Campano et al., 2016). Fasciectomy is more often conducted in the military setting where the outcomes are reported according to medical deployability grading. Research findings demonstrate relatively consistent outcomes with military patients showing a 46-52% improvement in grading following fasciectomy, 22-26% of patients improve to a fully deployable grade, 29-37% remain in the same grade, and 11-24% regress (Roberts et al., 2015, Simpson et al., 2020). Limitations of these two studies are retrospective design, small sample sizes, and limited availability of data for participants. Strengths of the studies are well-described ICP testing protocols; the value described by Roscoe et al. (2015) was used by Simpson et al. (2020) with a presumed greater reliability for diagnosis, and surgical techniques were standardised for both studies.

The latest pseudo-surgical management of CECS is fascial fenestration, described by Finnoff and Rajasekaran (2016) in a case study. Following positive CECS diagnosis using ICP measurement, ultrasound-guided, percutaneous needle fenestration was performed. The patient in this case series was able to resume full sports participation pain-free only one week after the procedure, and at 18-month follow-up the patient reported full participation in all activities without pain (Finnoff and Rajasekaran, 2016). This study is limited by its design as a retrospective case study. The described technique is limited to only superficial fascial compartments. Due to the study design only including one patient, generalisability of results from the study is not possible and complications may occur if a larger sample size is used.

2.6.2 Non-Surgical Management

While there is limited evidence available for non-surgical treatment options for CECS, the available literature reports few to no adverse effects with conservative approaches, supporting consideration of their use in clinical practice (Rajasekaran and Hall, 2016). Only one randomised controlled trial assessing the outcomes of non-surgical management exists at present. This trial, conducted by Ragab et al. (2019), randomised 30 participants into two even groups; the control groups received intermittent massage and the experimental group received manual therapy using a specialised instrument. Both groups showed improvements in pain, function, and dorsiflexion range, however greater improvements were noted in the experimental group (Ragab et al., 2019). Details of diagnosis of CECS for the participants was unfortunately not available, with the researchers stating simply that diagnosis were made clinically. Only patients without history of previous trauma to the leg and those with gradual cessation of provocative activity were enrolled.

Blackman et al. (1998) assessed the effect of a five-week intervention of intermittent massage such as myofascial release on seven patients diagnosed with CECS. Following the intervention, ICP values three minutes post-exertion showed a mild increase suggesting that massage has no effect on ICP values, however, the average work to onset of pain improved threefold from 147J to 532J (Blackman et al., 1998). Pressures were measured at the patients' reported point of fatigue and unfortunately the duration of exercise was not reported. Pain severity also improved for all patients both during and after exercise following the intervention. Regrettably, the small sample size and lack of control group do not lend great significance to the outcomes of this study.

Gait re-training appears to be an effective non-surgical management option for patients with CECS. A case series examining the effect of adopting a forefoot running technique in 10 CECS patients found that following a six-week intervention, participants were able to improve their running distance threefold with significant decrease in pain and post-exercise ICP, and significant improvements in functional outcomes (Diebal et al., 2012). These results are reinforced in a more recent cohort study where 19 CECS patients underwent the same six-week protocol described by Diebal et al. (2012) (Helmhout et al., 2015). All patients demonstrated significant improvements in pain, performance, and ICP values (Helmhout et al., 2015). Gait-retraining of marching by means of increasing cadence, decreasing stride length, and disengaging the muscles of the leg and foot, as well as implementation of an unspecified lower limb strengthening program over a five-week period produced moderate to fair improvements in six patients diagnosed with CECS of the anterior compartment of the leg (Helmhout et al., 2016). The largest study on the efficacy of gait-retraining for CECS patients is a case series of 75 patients with CECS of the anterior compartment with and without medial tibial stress syndrome (MTSS) (Zimmermann et al., 2019). The study protocol consisted of stretching, strengthening, massage, dry needling, vitamin D supplementation, evaluation of running shoes and orthotics, general fitness training, and gait re-training of both marching and running techniques (Zimmermann et al., 2019). Fasciotomy was avoided in 57% of patients who were able to return to active duty, 43% of all patients were able to return to their original specialty, and 48% still experienced symptoms (Zimmermann et al., 2019). Limitations of these studies are their small sample sizes, and all participants were pooled from a military cohort. Improvements in patient outcomes in all studies indicate that gait-retraining shows promising results and further high-quality studies assessing the effect of the intervention need to be performed.

A novel non-surgical CECS treatment option involves injection of botulinum toxin into the muscles of the affected compartment. Following administration of botulinum toxin, intra-compartmental pressure reduces to levels below pathological values in most patients and pain is eliminated in nearly all of them (Isner-Horobeti et al., 2013). The majority of patients showed a one-point decrease in strength post-intervention without subsequent loss of function (Isner-Horobeti et al., 2013). The mechanism of botulinum toxin in reducing pain ICP levels remains unknown however it is proposed that muscle atrophy, inhibition of nociceptors, and loss of contractile tissue are contributing factors (Hutto et al., 2019, Isner-Horobeti et al., 2013). Sample size in these studies is a limiting factor, although injection sites and dosages are well reported.

2.7 Outcome Measures

The lack of standardised outcome measures for assessing management outcomes of patients with CECS (Orlin et al., 2016) has led to great variety in the use of outcome measures and reported outcomes across studies. Outcome measures used in studies included in the literature review are discussed below.

Objective outcome measures include change in ICP values frequently reported in mmHg pre- and post-intervention (Beck et al., 2016, Diebal et al., 2012, Isner-Horobeti et al., 2013, Zimmermann et al., 2019); presence or absence of herniation (Beck et al., 2016); minor or major complications (Beck et al., 2016), muscle strength according to the Medical Research Council grading (Isner-Horobeti et al., 2013), and range of motion using the range of motion for ankle dorsiflexion in degrees (Ragab et al., 2019).

Subjective outcome measures are also commonly used to assess treatment effect: dichotomous values (yes/no) are used to assess outcomes such as return to activity (Anil et al., 2019, Beck et al., 2016, Howard et al., 2000, McCallum et al., 2014, Zimmermann et al., 2019), recurrence of symptoms (Beck et al., 2016, Howard et al., 2000, Zimmermann et al., 2019), and patient satisfaction with treatment outcomes (Anil et al., 2019, Howard et al., 2000, McCallum et al., 2014). Pain is also commonly reported using values from either the Visual Analog Scale (VAS) (Howard et al., 2000, Isner-Horobeti et al., 2013, Orlin et al., 2013, Ragab et al., 2019, Thein et al., 2019) or the Numeric Pain Rating Scale (NPRS) (Collins and Gilden, 2016, Meulekamp et al., 2017).

Outcome measures used to subjectively score function are erratic across the literature. The reported degree of improvement is most frequently measured, using the SANE score where patients report their ankle function on a single-item scale with points from 0 (no function) to 100 (normal function) (Helmhout et al., 2015, Helmhout et al., 2016, Zimmermann et al., 2019, McCallum et al., 2014, Diebal et al., 2012) and the Global Rating of Change (GROC) scale where, following treatment, patients report global ratings of change to their level of joint-specific (ankle) well-being on a single-item, 15-point scale ranging in value from -7 (a very great deal worse) to 7 (a very great deal better) (Collins and Gilden, 2016, Diebal et al., 2012, Helmhout et al., 2015, Helmhout et al., 2016). Function relating to daily activities is reported using the LLOS which assesses symptoms and limitations of the lower leg when performing activity on a 12-item, six-point scale ranging in value from 0 (unable to perform activity) to 5 (no difficulty) (Diebal et al., 2012, Helmhout et al., 2015, Helmhout et al., 2016) and the Lower Extremity Functional Scale (LEFS) where patients report their difficulties with activity due to their lower limb on a 20-item, five-point scale ranging in value from 0 (extreme difficulty or unable to perform activity) to 4 (no difficulty) (Collins and Gilden, 2016, Ragab et al., 2019). General activity levels are measured using the Tegner Activity Scale, which measures the highest level of activity participation on a single-item scale from Level 0 (sick leave or pension due to problems in the specific joint) to Level 10 (competitive sport at the national elite level) (Anil et al., 2019, Thein et al., 2019) and Short QUestionnaire to ASsess Health enhancing physical activity

(SQUASH) which measures the effort required to perform household, communal, and leisure activities as well as on average how many days per week, and how many minutes per day a patient was able to partake in these activities (Helmhout et al., 2016). The least stated outcomes are related to quality of life, which is measured using the EuroQol-5Dimension (EQ-5D) (Anil et al., 2019), SF-36 (Thein et al., 2019), and 8-Item Short Form Survey (SF-8) (Orlin et al., 2013).

2.8 Conclusion

There is a general lack of knowledge regarding the pathophysiology of CECS and the diagnostic criteria for CECS remains a much-debated topic with no clear consensus at present. Management options are currently limited to surgery focused on fascial release and non-surgical options with few available studies, and most available evidence for the management of CECS is of low-quality design. Furthermore, the outcome measure(s) used to assess the effects of management of CECS varies in the literature.

Additional research is necessary to compare the results of surgical and non-surgical management, to generalise outcomes for different types of management, and to formulate guidelines for transitioning from non-surgical to surgical management.

Chapter 3 Methodology

The systematic review was conducted in accordance with the JBI methodology for systematic reviews of effectiveness evidence (Tufanaru et al., 2020). An a priori protocol was developed and accepted for publication in JBI Evidence synthesis.

3.1 Study Design

This study is a systematic review and meta-analysis of case reports, case series, cohort studies, case-control studies, quasi-experimental studies, and randomised controlled trials. Level of evidence: 1

3.2 Inclusion Criteria

3.2.1 Participants

This review considered studies that included human participants of all ages that were diagnosed with CECS of the anterior compartment of the leg through a combination of patient history and elevated ICP values. Studies including patients presenting with diagnoses of other lower limb pathology (e.g., medial tibial stress syndrome) in addition to CECS of the anterior compartment of the leg, were also included.

Studies were excluded if they did not use or specify the diagnostic ICP testing using either the Pedowitz criteria or other quantifiable means of diagnosis, or if they included management of acute compartment syndrome. Studies assessing multiple compartments of the leg were excluded only if they did not separately report results for the anterior compartment.

3.2.2 Interventions

This review considered studies that evaluated the effectiveness of surgical management of patients diagnosed with CECS of the anterior compartment of the leg. Surgical fasciotomy is the current best and most frequently utilised surgical management of CECS; incisions are made to symptomatic fascial compartments and the fascia is dissected using laparotomy scissors – the surgical technique aims to release pressure within the compartment and allow for full weight-bearing immediately post-surgery (Drexler et al., 2017). Fascial fenestration is a minimally-invasive procedure that involves ultrasound-guided insertion of a high-gauge needle into the fascia within the borders of the fascial compartment. Fenestration is performed from the distal segment toward the proximal segment of the fascial compartment until the entire compartment has been fenestrated (Finnoff and Rajasekaran, 2016). Fasciectomy involves a longitudinal incision, wide enough to allow for division of the fascia of the affected compartment, followed by the excision of an approximately 1cm width of fascia along the length of the compartment (Roberts et al., 2015, Simpson et al., 2020).

3.2.3 Comparators

This review considered studies that evaluated the effectiveness of non-surgical management of CECS for patients diagnosed with CECS of the anterior compartment of the leg. Non-surgical treatment included injection of botulinum toxin, activity modification, and manual therapy. Injection of botulinum toxin is a relatively novel treatment method for CECS management. Onabotulinum Toxin-A (Dysport, Ipsen) is typically used; all muscles of a symptomatic compartment are injected with a solution of botulinum toxin and saline which reduces intramuscular pressure through a yet-unknown mechanism (Baria and Sellon, 2016). All agents and solutions of botulinum toxin used for intervention were included in the review. Activity modification includes altering running techniques, such as promoting a forefoot strike which in turn reduces eccentric activity in the anterior muscles of the leg, aims to increase step rate with running, and typically lasts a minimum of six weeks (Diebal et al., 2012). There were no limitations relating to duration, intensity, or person responsible for delivering the intervention. Manual therapy includes massage in the form of transverse and longitudinal gliding, myofascial release of the myofascial structures of the affected compartment, and a home-based isometric stretching program to be performed daily by patients (Blackman et al., 1998). All forms of manual therapy identified in the search strategy were included for review with no restriction relating to duration, intensity, or person delivering the intervention.

3.2.4 Outcomes

Outcomes analysed included primary outcomes of pain (numerical pain scale, visual analogue scale), range of motion (inclinometer, goniometer), muscle compartment pressure (ICP measurements expressed in mmHg), patient satisfaction, recurrence of symptoms, return to activity, and function via specific lower limb outcome measure surveys such as the Lower Leg Outcome Survey (LLOS) (Diebal et al., 2012) or Single Assessment Numeric Evaluation (SANE) (Williams et al., 1999) which numerically score function of the lower limb. Secondary outcomes included strength (Oxford scale, Medical Research Council scale, dynamometer, electromyography measurements) and sensation (absence or presence of paraesthesia, pinprick, light touch, two-point discrimination).

3.2.5 Types of Studies

This review considered both experimental and quasi-experimental study designs including randomised controlled trials, non-randomised controlled trials, before and after studies and interrupted time-series studies. In addition, analytical observational studies including prospective and retrospective cohort studies, case-control studies and analytical cross-sectional studies were considered for inclusion. This review also considered descriptive observational study designs including case series, individual case reports, and descriptive cross-sectional studies for inclusion.

3.3 Search Strategy

The search strategy aimed to find both published and unpublished studies. Studies published in all languages were included. Due to the condition being first described by Mavor (1956), studies published from 1956 to December 2020 were included. A three-step strategy was utilised in this review. An initial limited search of MEDLINE and CINAHL was undertaken using the MeSH terms for Anterior Compartment Syndrome/drug therapy, Anterior Compartment Syndrome/therapy, Anterior Compartment Syndrome/rehabilitation, and Anterior Compartment Syndrome/surgery, followed by analysis of the text words contained in the title and abstract, and of the index terms used to describe the article. A second search using all identified keywords and index terms was then undertaken across all included databases. Thirdly, the reference lists of all reports and articles identified for inclusion in the review was searched for additional studies.

3.4 Information Sources

Databases searched included: MEDLINE via PubMed, SPORTDiscus, Physiotherapy Evidence Database (PEDro), EBSCOhost MasterFILE Premier, EBSCOhost CINAHL Complete, ProQuest Health and Medical Complete, SCOPUS and Science Direct.

Additionally, Cochrane Controlled Trials Register, ClincalTrail.gov, EBSCO Academic Search Ultimate, OpenGrey (SIGLE), WorldCat, and Google Scholar were searched for unpublished studies and grey literature. It was not necessary to use Restoring Invisible and Abandoned Trials and All Trials to restore abandoned trials of relevance to the study, as no relevant abandoned trials were identified.

Initial keywords included: CECS, chronic exertional compartment syndrome, lower limb, treatment, exercise, exercise-induced leg pain, treatment, intervention, modality, surgical, conservative, non-surgical, botulinum toxin, physiotherapy, physical therapy. The initial search strategy via MEDLINE (PubMed) is listed in Appendix A – search string #6 was used to identify relevant studies.

3.5 Study selection

Following the search, all identified citations were collated and uploaded into EndNote X9.3.3 (Bld13966) (Clarivate Analytics, PA, USA) and duplicates removed. Titles and abstracts were then screened by two independent reviewers for assessment against the inclusion criteria for the review. Potentially relevant studies were retrieved in full, and their citation details were imported into the JBI System for the Unified Management, Assessment and Review of Information (JBI SUMARI) (JBI, Adelaide, Australia) (Munn et al., 2019). The full text of selected citations was assessed in detail against the inclusion criteria by two independent reviewers. Reasons for exclusion of full text studies that did not meet the inclusion criteria were recorded and reported in the systematic review. No disagreements arose between the reviewers at each stage of the study selection process, and resolution through discussion, or with a third reviewer was not necessary. The results of the search were reported in full and presented in a Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) (Moher et al., 2009) flow diagram which can be found in Figure 3 on page 25.

3.6 Assessment of methodological quality

Eligible studies were critically appraised by two independent reviewers for methodological validity prior to inclusion in the review using standardised critical appraisal instruments from JBI System for the Unified Management, Assessment and Review of Information (JBI SUMARI) (JBI, Adelaide, Australia) (Munn et al., 2019).

Authors of papers were contacted to request missing or additional data for clarification, where required. No disagreements arose between reviewers. All studies, regardless of the results of their methodological quality, underwent data extraction and synthesis (where possible). Experimental designs, quasi-experimental designs, and observational-analytical designs were synthesised in meta-analysis and narrative synthesis. Observational-descriptive studies underwent narrative synthesis. Results of the critical appraisal can be found in Appendix B. Studies scoring four or more "no" or "uncertain" scores in critical appraisal were excluded.

3.7 Data extraction

Data was extracted from papers included in the review using the JBI System for the Unified Management, Assessment and Review of Information (JBI SUMARI) (JBI, Adelaide, Australia) (Munn et al., 2019). The data extracted included specific details about the interventions, populations, study methods and outcomes of significance to the review question and specific objectives. The results of data extraction are presented in Appendix C.

3.8 Data synthesis

Quantitative data, where possible, was pooled in statistical meta-analysis using the JBI System for the Unified Management, Assessment and Review of Information (JBI SUMARI) (JBI, Adelaide, Australia) (Munn et al., 2019) . Where no comparison group was provided, studies were pooled for single-arm meta-analysis using the meta package v4.15-1 (Balduzzi et al., 2019) in R v4.0.5 (R Core Team, 2021). Individual groups from the studies undergoing statistical meta-analysis were included in single-arm meta-analysis. A random effects model was utilised for meta-analysis of studies with an I^2 value >50%, with the objective of improving statistical power to detect the effect of treatment. Inverse Variance and the DerSimonian and Laird method (DerSimonian and Laird, 1986) was followed for meta-analysis of data where appropriate sample size was obtained. For smaller sample sizes, the Mantel-Haenszel method (Mantel and Haenszel, 1959) was used. All results were subject to double data entry. Mean age across studies was calculated as the quotient of the sum of the provided mean values multiplied by their correlating sample size, divided by the sum of all sample sizes; $\frac{(\Sigma(\text{mean value x sample size})}{\Sigma(\text{sample sizes})}$. The value for median age was calculated in a similar manner. Effect sizes were expressed as odds ratio (for categorical data such as patient satisfaction, recurrence of symptoms, muscle compartment pressure (where expressed as elevated or reduced), return to activity, sensation) and weighted mean differences (for continuous data such as pain, range of motion, muscle compartment pressure (where expressed numerically), survey scores, muscle strength) and their 95% confidence intervals were calculated for analysis. Heterogeneity was assessed statistically using the I^2 value. Where statistical pooling was not possible the findings were presented in narrative review. Results from the meta-analysis were expressed graphically using forest plots.

3.9 Ethical Considerations

Neither ethical clearance nor an ethical clearance waiver was required due to the nature of the study in that no human or animal participants were enrolled.

Chapter 4 Results

4.1 Study Selection

The preliminary search yielded 2069 results. An additional six records were identified through the screening of reference lists. Following removal of duplicates, 1532 unique records remained. Screening of the title and abstract led to the exclusion of 1283 records. Full texts were assessed for eligibility in the 249 remaining records. Of these, 187 were excluded for reasons outlined in Appendix D. Critical appraisal was therefore performed for 62 studies. Following critical appraisal, 10 articles were excluded for receiving four or more "no" or "uncertain" scores. Ultimately, 52 studies were included in the systematic review. Study designs of the included studies consisted of case studies (n=15), case series (n=24), cohort studies (n=8), quasi-experimental studies (n=3), one case-control study, and one randomised controlled trial. The study selection process is presented as a PRISMA flow diagram in Figure 3 below.

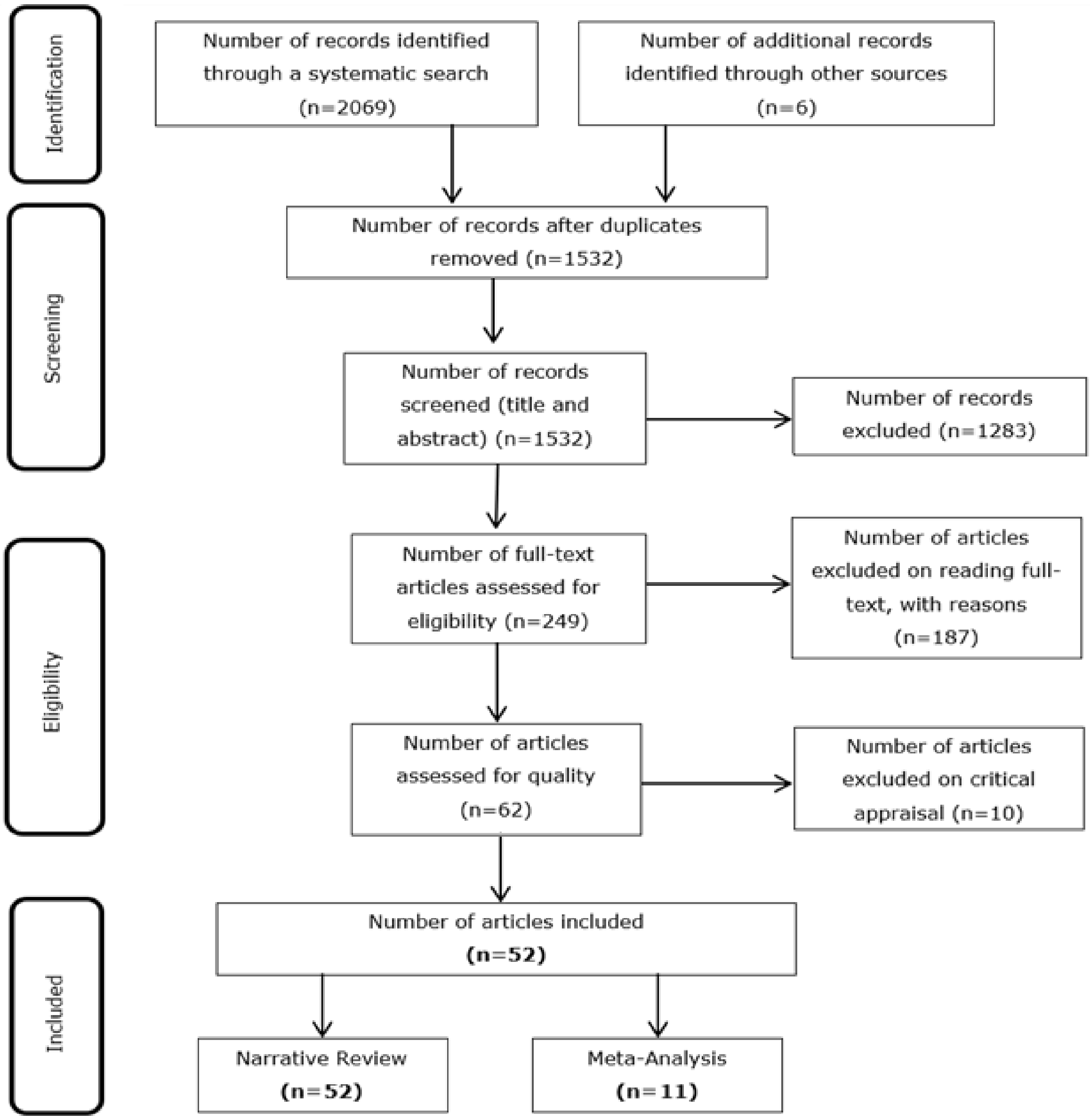

Figure 3 - PRISMA flow diagram

4.2 Study Characteristics

Data extracted from each of the included studies included the country in which the study was conducted, the study setting, participant characteristics, interventions, outcome measures, and results.

4.2.1 Countries of Origin

All included studies originated from a total of 12 countries, with most records originating from the United States of America and the Netherlands. All countries and the number of records from each are reflected below in Figure 4.

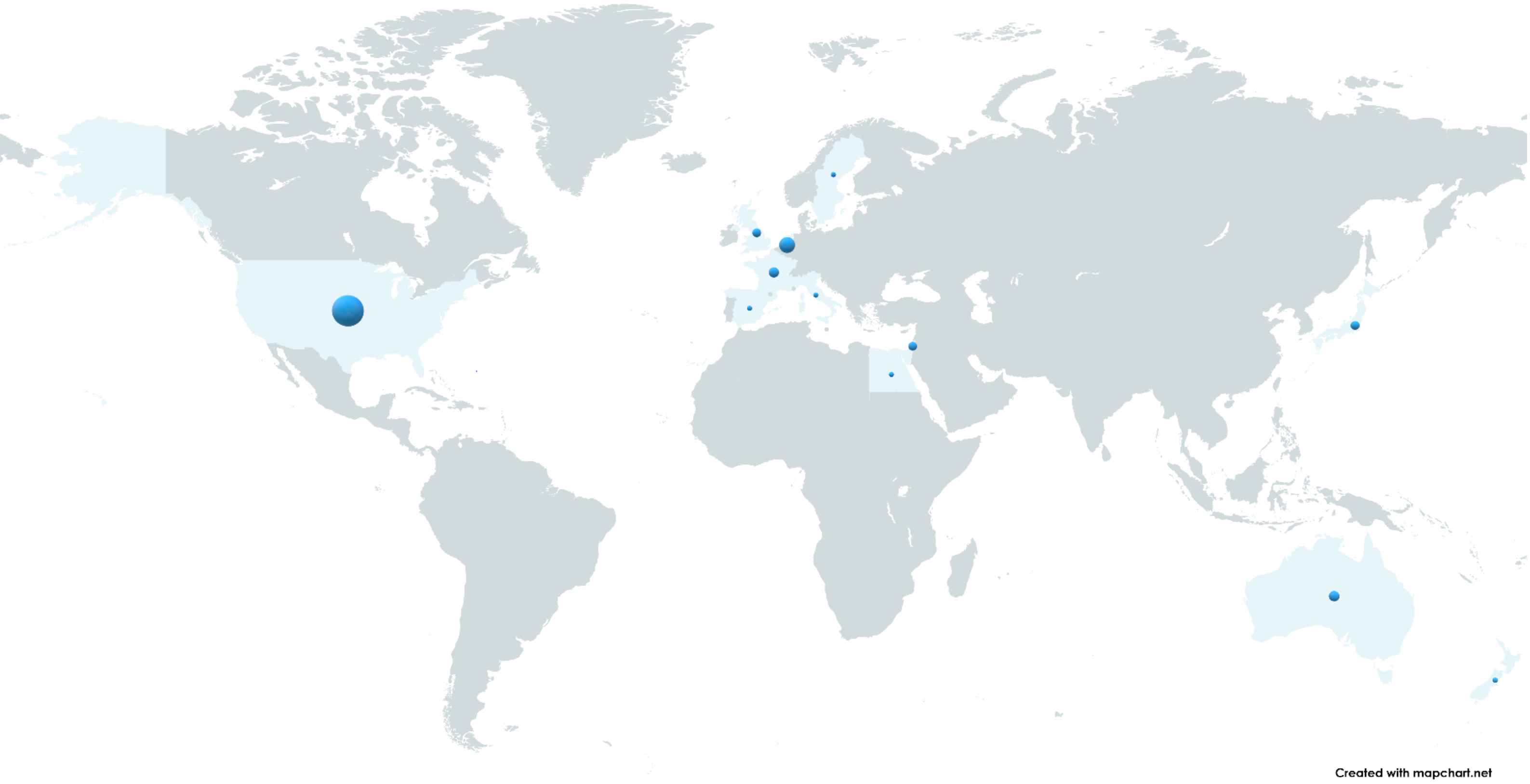

Figure 4 – Bubble Map – Records per Country

United States of America n=21; Netherlands n=9; Australia n=4; France n=4; Israel n=3; Japan n=3; United Kingdom n=3; Egypt n=1; Italy n=1; New Zealand n=1; Spain n=1; Sweden n=1

4.2.2 Study Setting

Twenty-six studies were performed in a hospital setting, 12 in clinics and outpatient facilities, 11 in a military setting, and three in athletic medical centres.

4.2.3 Participant Characteristics

4.2.3.1 Age

Fifty of the 52 included studies reported the ages of participants. No age data was available for one study (Simpson et al., 2020). In the other study, no mean or median ages were reported, and it was not possible to calculate these values due to the absence of a table of demographic information for the participants (Blackman et al., 1998). Forty-four studies provided mean ages and 22 studies provided median ages. Additionally, ages of the individual patients reported in 15 case reports were included. The ages of participants across all included studies (in years) ranged from 12 (Beck et al., 2016, Fronek et al., 1987) to 78 (van Zantvoort et al., 2017). Average mean age was 25 years, and the average median age was 21 years.

4.2.3.2 Sex

The 52 included studies reported a total of 1458 participants. Ten studies did not report on the sex of the included participants (Edmundsson et al., 2008, Diebal et al., 2012, Simpson et al., 2020, Ragab et al., 2019, Zimmermann et al., 2019, Wieczorek et al., 2012, Finestone et al., 2014, Balius et al., 2016, Schepsis et al., 1999, Bell, 1986). Sex data was available for 1234 participants, of which 704 (57%) were male and 530 (43%) were female.

4.2.4 Interventions

Surgical interventions were reported in 90.4% (n=47) of studies, with fasciotomy performed in 41/47 surgical interventions. Non-surgical interventions were reported in 53.8% (n=28) of studies, with strengthening included in the protocol in 7/28 non-surgical interventions. Further detail regarding specific interventions and the number of studies reporting these interventions are presented in Table 1 below.

Table 1 - Study Interventions

Intervention	Studies (n)	% of Total
Surgical	**47**	**90.4%**
Fasciotomy	41	78.8%
Fasciectomy	4	7.7%
Fascial Fenestration	1	1.9%
Non-Surgical	**28**	**53.8%**
Strengthening	7	13.5%

Stretching	6	11.5%
Manual Therapy	6	11.5%
Unspecified	4	7.7%
Gait Re-Training	3	5.8%
Botulinum Toxin	2	3.8%

4.2.5 Outcome Measures

The three most reported outcomes were return to activity, reported in 30/52 studies (58%), pain, reported in 15/52 studies (28.8%), and complications following surgical intervention, reported in 13/47 surgical intervention studies (27.7%). The number of studies reporting specific outcomes, and the percentage of studies reporting these outcomes are expressed in Table 2 and Figure 5 below.

Table 2 - Outcome Measures Reported

Outcome Measure	**Studies (n)**	**% of Total**
Return to Activity	30	57.7%
Pain	15	28.8%
Complications	13	25.0%
Satisfaction	12	23.1%
ICP	11	21.2%
Recurrence	10	19.2%
Success/Failure	6	11.5%
Symptom Intensity	6	11.5%
Work to Onset	5	9.6%
Hernia Presence	3	5.8%
Sensation	2	3.8%
Range of Motion	2	3.8%
Strength	1	1.9%
Service Evaluation	1	1.9%
Function	**16**	**30.8%**
SANE	3	5.8%
FAAM	3	5.8%
Tegner	2	3.8%
SF-36	2	3.8%
LEFS	2	3.8%
PFT	1	1.9%
EQ-5D	1	1.9%
SF-12	1	1.9%
LLOS	1	1.9%

ICP – intracompartmental pressure; SANE – single assessment numeric evaluation; FAAM – foot and ankle mobility measure; SF-36 – short-form 36 survey; LEFS – lower extremity functional scale; PFT – physical performance test; EQ-5D - EuroQol-5 Dimension; SF-12 – short-form 12 survey; LLOS – Lower leg outcome survey

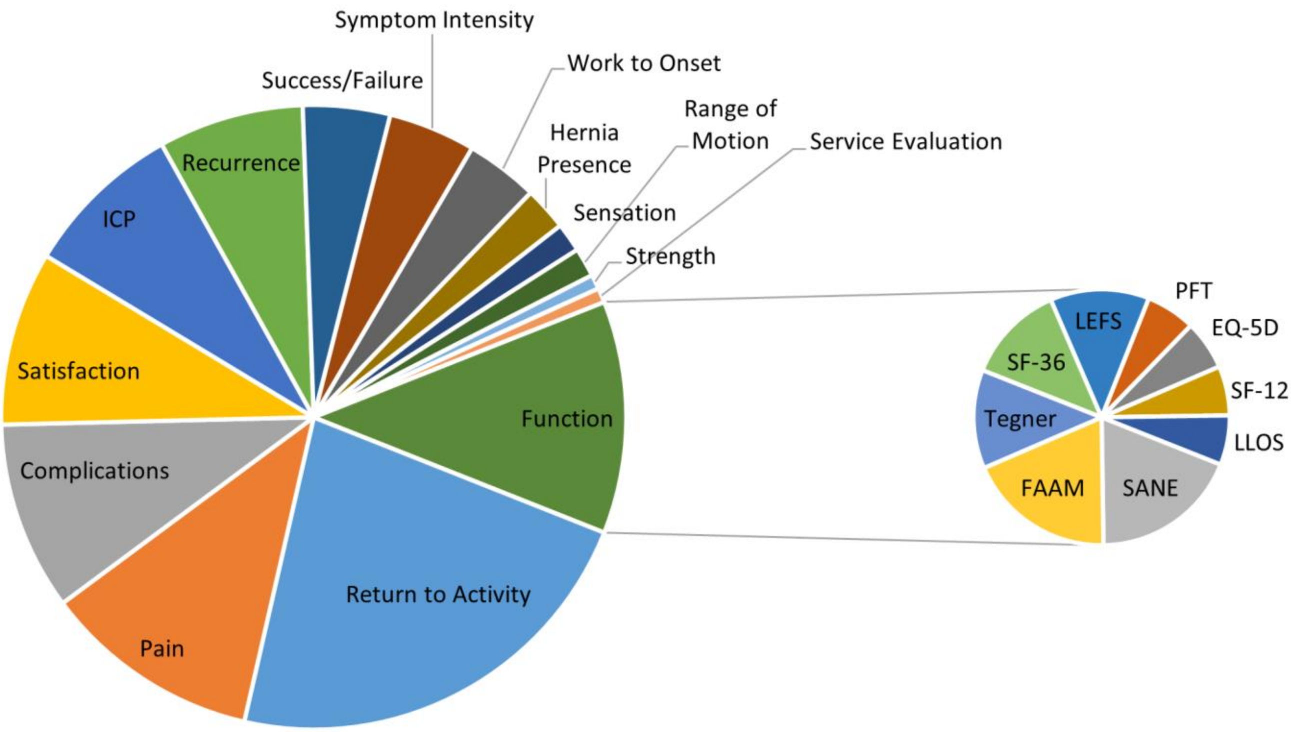

Figure 5 - Outcome Measures Reported

4.3 Review Results

Studies reporting appropriate outcome data were pooled for comparative meta-analysis using the JBI System for the Unified Management, Assessment and Review of Information (JBI SUMARI) (JBI, Adelaide, Australia) (Munn et al., 2019). Due to the lack of a comparative group in several studies, single-arm meta-analyses were performed with the statistical software R v4.0.5 (R Core Team, 2021) using the meta package v4.15-1 (Balduzzi et al., 2019). Studies and groups undergoing comparative or single-arm meta-analyses are reflected below in Table 3 and Table 4, respectively.

Table 3 - Comparative Meta-Analyses

Groups Compared	Outcome	Studies Compared
Surgical vs. Control	ICP at rest	Fronek, 1987 Roscoe, 2018
Surgical vs. Control	ICP 1-min post-exercise	Fronek, 1987 Roscoe, 2018
Surgical vs. Control	ICP 5-min post-exercise	Fronek, 1987

		Roscoe, 2018
Surgical vs. Non-Surgical	ICP at Rest	Packer, 2013 Vogels, 2020
Surgical vs. Non-Surgical	ICP Immediately Post-Exercise	Packer, 2013 Vogels, 2020
Surgical vs. Non-Surgical	Patient Satisfaction	Packer, 2013 Vogels, 2020
Surgical vs. Non-Surgical	Return to Activity	Packer, 2013 Thein, 2019 Vogels, 2020

Control – asymptomatic individuals with similar demographic characteristics to the intervention group

Table 4 - Single-Arm Meta-Analyses

Groups Compared	**Outcome**	**Studies Compared**
Surgical vs. Non-Surgical vs. Control	ICP at Rest	Fronek, 1987 Verleisdonk, 2004 Roscoe, 2018 Vogels, 2020 Vogels, 2020 (Non-Surgical) Fronek, 1987 (Control) Roscoe, 2018 (Control)
Surgical vs. Non-Surgical vs. Control	ICP Immediately Post-Exercise	Fronek, 1987 Verleisdonk, 2004 Roscoe, 2018 Vogels, 2020 Vogels, 2020 (Non-Surgical) Fronek, 1987 (Control) Roscoe, 2018 (Control)
Surgical vs. Non-Surgical vs. Control	ICP 1-min post-exercise	Fronek, 1987 Verleisdonk, 2004 Roscoe, 2018 Vogels, 2020 Vogels, 2020 (Non-Surgical) Fronek, 1987 (Control) Roscoe, 2018 (Control)
Surgical vs. Non-Surgical vs. Control	ICP 5-min post-exercise	Fronek, 1987 Verleisdonk, 2004 Roscoe, 2018

		Vogels, 2020 Vogels, 2020 (Non-Surgical) Fronek, 1987 (Control) Roscoe, 2018 (Control)
Surgical	Patient Satisfaction (Surgical)	Schepsis, 1999 Slimmon, 2002 Packer, 2013 Vogels, 2020
Surgical vs. Non-Surgical vs. Control	Pain	Slimmon, 2002 Thein, 2019 Thein, 2019 (Non-Surgical) Ragab, 2019 (Non-Surgical) Ragab, 2019 (Control)
Surgical	Hernia Presence	Fronek, 1987 Schepsis, 1993 Verleisdonk, 2004
Surgical	Complications (Surgical)	Fronek, 1987 Slimmon, 2002 Packer, 2013
Surgical	Complications (Major)	Fronek, 1987 Slimmon, 2002 Packer, 2013
Surgical vs Non-Surgical (Statistical analysis performed for combined results of both surgical and non-surgical groups)	Return to Activity (Total)	Schepsis, 1993 Packer, 2013 Thein, 2019 Calvelli, 2020 Vogels, 2020
Surgical	Return to Activity (Surgical)	Schepsis, 1993 Packer, 2013 Thein, 2019 Calvelli, 2020 Vogels, 2020
Non-Surgical	Return to Activity (Non-Surgical)	Packer, 2013 Thein, 2019 Vogels, 2020

Control – asymptomatic individuals with similar demographic characteristics to the intervention group

Heterogeneity

Heterogeneity was assessed using I^2 and p-values. I^2 values for determining heterogeneity were interpreted as “low” for values between 0-40%, “moderate” for values between 30-60%, “substantial” for values between 50-90 %, and “considerable” for values between 75-100% according to the Cochrane Handbook for Systematic Reviews of Interventions (Higgins et al., 2021). A p-value of <0.10 was used to indicate statistical significance of the overall findings (Deeks et al., 2021). Due to relatively small sample sizes and objectively low number of studies included in the meta-analysis, the overall direction of effect (whether the results of the studies visibly appeared to favour surgical or non-surgical management) was also considered in determining the relevance and significance of the findings regardless of heterogeneity (Deeks et al., 2021). In the included studies, heterogeneity varied greatly from 0% (for major complications, return to activity in the non-surgical subgroup, and comparing satisfaction between surgical and non-surgical interventions) to 99% (for ICP immediately post-exercise and at 1- and 5-minutes post-exercise) dependent on the outcome being assessed. P-values ranged from 0 (when assessing return to activity between surgical and non-surgical interventions as well as when assessing ICP values 1-minute post-exercise between a surgical and a control group) to 0.89 (when assessing return to activity for the non-surgical subgroup). Forest plots with low heterogeneity are marked with an asterisk (*) and are tabulated in Chapter 6.

4.3.1 Meta-Analysis Results

4.3.1.1 Comparative Meta-Analyses

Studies reporting results for surgical vs control groups (Fronek et al., 1987, Roscoe et al., 2018) and surgical vs non-surgical groups (Packer et al., 2013, Thein et al., 2019, Vogels et al., 2020a) were included for comparative meta-analysis. All comparative meta-analyses were conducted using the JBI System for the Unified Management, Assessment and Review of Information (JBI SUMARI) (JBI, Adelaide, Australia) (Munn et al., 2019).

ICP Values at Rest– Surgical vs Control

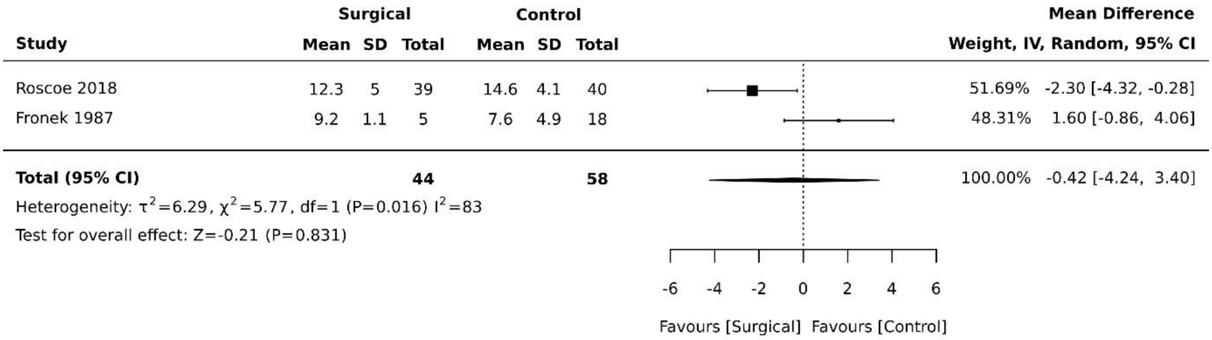

Figure 6 - ICP Values at Rest - Surgical vs Control

The 95% confidence interval of one study (Fronek et al., 1987) crossed the line of no effect indicating no statistical significance of individual findings. The 95% confidence interval of Roscoe et al. (2018) did not cross the line of no effect, indicating statistical significance for the results favouring the surgical group. The 95% confidence interval of the overall effect measure crossed the line of no effect with a P value of 0.83 indicating no statistical significance for overall effect. The studies in this meta-analysis showed considerable heterogeneity (I^2=83%).

ICP Values 1-Minute Post-Exercise – Surgical vs Control

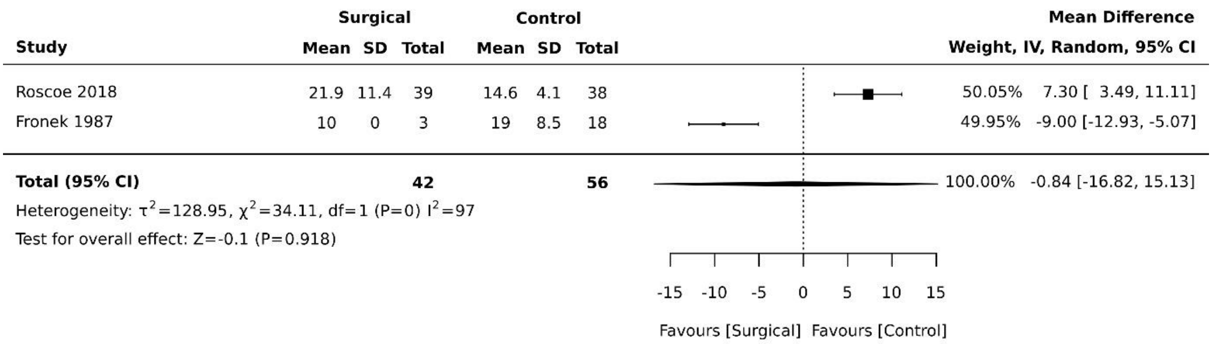

Figure 7 - ICP Values 1-Minute Post-Exercise – Surgical vs Control

The 95% confidence interval of each of the studies crossed the line of no effect indicating statistical significance of their individual findings; however, they fell on either side of the line of no effect, demonstrating conflicting results. The 95% confidence interval of the overall effect measure crossed the line of no effect with a P value of 0.92 indicating no statistical significance for overall effect. Considerable heterogeneity was observed in this meta-analysis, with an I^2 value of 97%.

ICP Values 5-Minutes Post-Exercise – Surgical vs Control

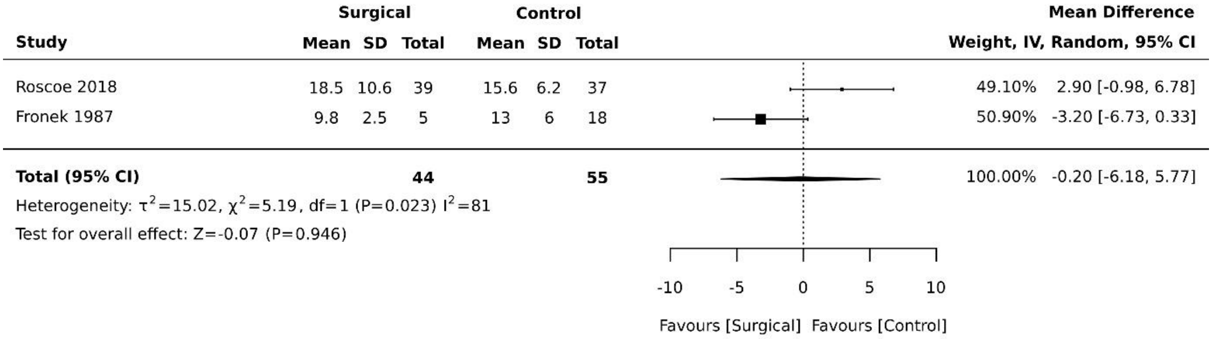

Figure 8 - ICP Values 5-Minutes Post-Exercise – Surgical vs Control

The 95% confidence interval of each of the studies crossed the line of no effect indicating no statistical significance of their individual findings. The 95% confidence interval of the overall effect measure crossed the line of no effect with a P value of 0.95 indicating no statistical significance for overall effect. Heterogeneity in this meta-analysis was considerable (I^2=81%).

ICP Values at Rest – Surgical vs Non-Surgical

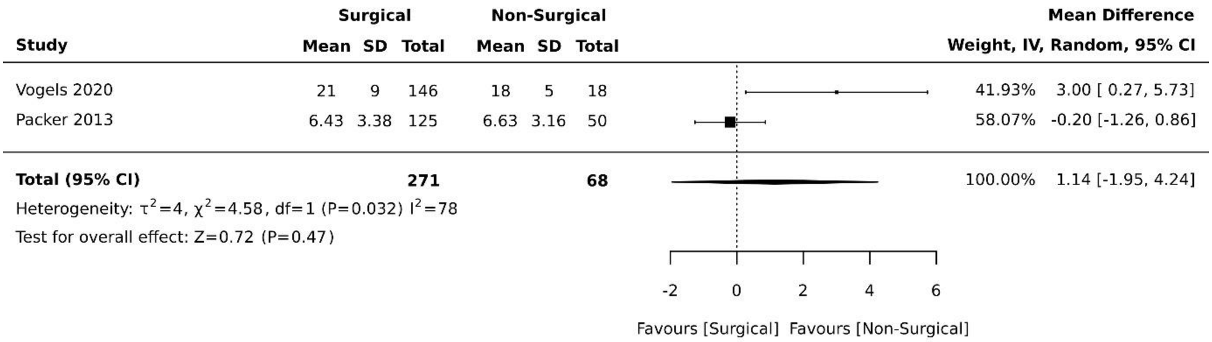

Figure 9 - ICP Values at Rest – Surgical vs Non-Surgical

The 95% confidence interval of one study (Packer et al., 2013) crossed the line of no effect indicating no statistical significance of individual findings. The 95% confidence interval of Vogels et al. (2020a) did not cross the line of no effect, indicating statistical significance for the results favouring the non-surgical group. The 95% confidence interval of the overall effect measure crossed the line of no effect with a P value of 0.47 indicating no statistical significance for overall effect. Considerable heterogeneity (I^2=81%) was observed in this meta-analysis.

ICP Values Immediately Post-Exercise – Surgical vs Non-Surgical*

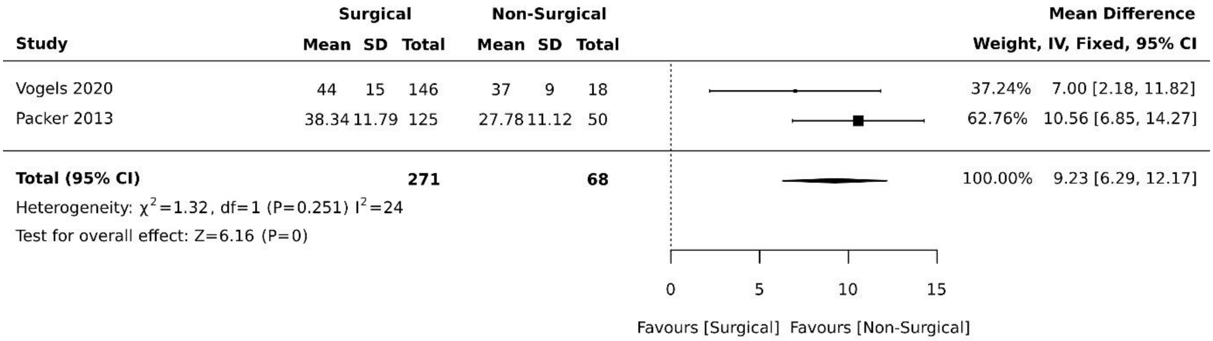

Figure 10 - ICP Values Immediately Post-Exercise – Surgical vs Non-Surgical

The 95% confidence interval of each of the studies fell to the right of the line of no effect, indicating statistical significance of both studies favouring the non-surgical groups. The 95% confidence interval of the overall effect measure fell to the right of the line of no effect with a P-value of 0, indicating substantial statistical significance of the findings that ICP values immediately post-exercise are lower in participants that received non-surgical intervention. The heterogeneity of this meta-analysis was low (I^2=24%).

Patient Satisfaction – Surgical vs Non-Surgical*

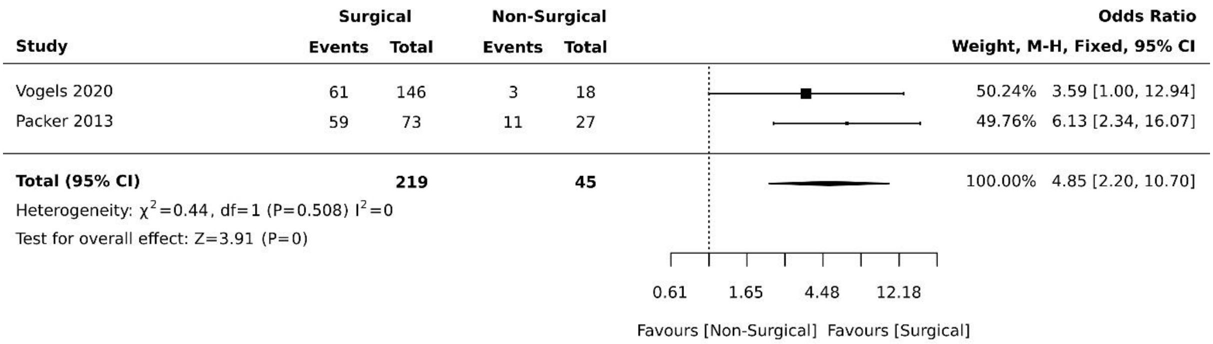

Figure 11 - Patient Satisfaction – Surgical vs Non-Surgical

The 95% confidence interval of one study (Vogels et al., 2020a) crossed the line of no effect, indicating no statistical significance of individual findings. The 95% confidence interval of one study (Packer et al., 2013) fell to the right of the line of no effect, indicating statistical significance for the results favouring the surgical group. The 95% confidence interval of the overall effect measure fell to the right of the line of no effect with a P-value of 0, indicating substantial statistical significance of the findings that higher satisfaction was achieved in patients receiving surgical intervention. The heterogeneity of this meta-analysis was low, with an I^2 value of 0%.

Return to Activity – Surgical vs Non-Surgical

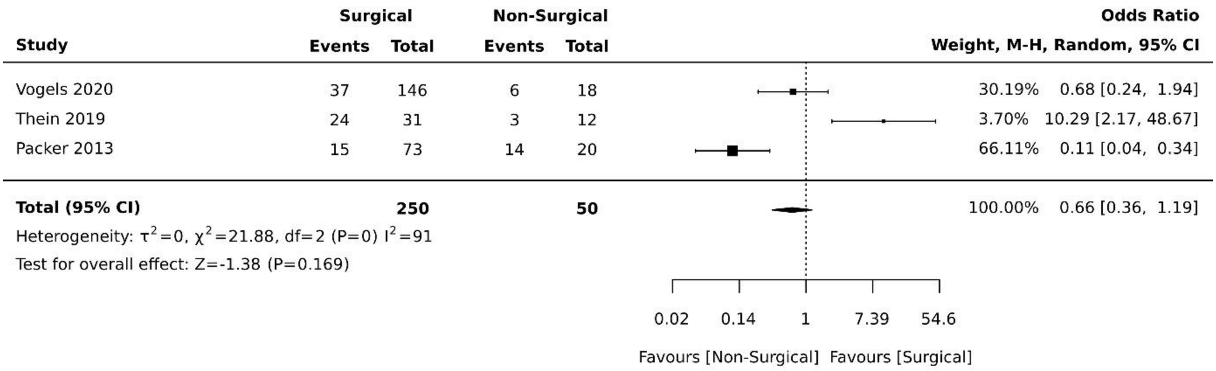

Figure 12 - Return to Activity – Surgical vs Non-Surgical

The 95% confidence interval of one study (Vogels et al., 2020a) crossed the line of no effect indicating no statistical significance of individual findings. The 95% confidence interval of Packer et al. (2013) and Thein et al. (2019) did not cross the line of no effect indicating statistical significance of their individual findings; however, they fell on either side of the line of no effect, demonstrating conflicting results. The 95% confidence interval of the overall effect measure crossed the line of no effect with a P value of 0.17 indicating no statistical significance for overall effect. The I^2 value of this meta-analysis was 91%, indicating considerable heterogeneity.

4.3.1.2 Single-Arm Meta-Analyses

Studies reporting results for individual groups (Calvelli et al., 2020, Packer et al., 2013, Schepsis et al., 1993, Schepsis et al., 1999, Slimmon et al., 2002, Verleisdonk et al., 2004) as well as those reporting results for both an intervention group and either a control or non-surgical group (Fronek et al., 1987, Ragab et al., 2019, Roscoe et al., 2018, Thein et al., 2019, Vogels et al., 2020a) were included in single-arm meta-analysis. Single-arm meta-analysis was conducted using the meta package v4.15-1 (Balduzzi et al., 2019) in R v4.0.5 (R Core Team, 2021). Study groups that were not labelled as "non-surgical" or "control" were all surgical intervention groups.

ICP Values at Rest

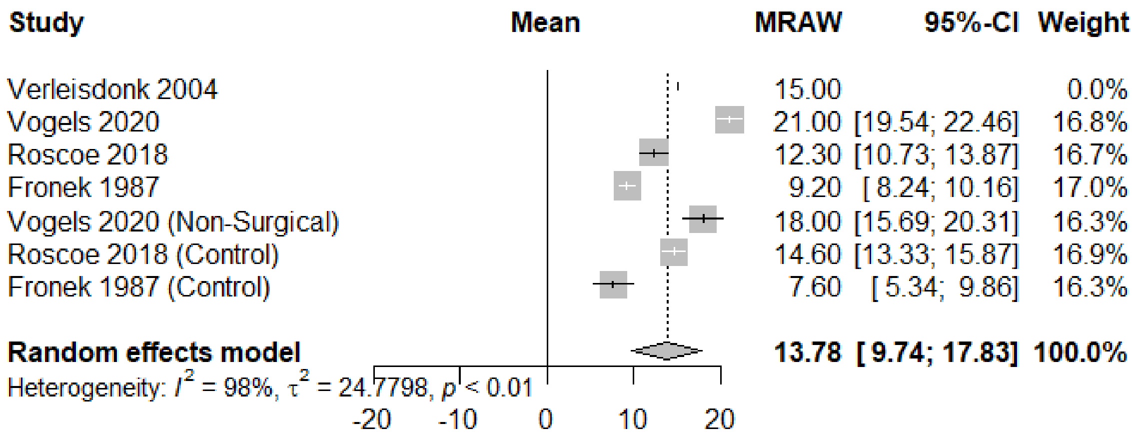

Figure 13 - ICP Values at Rest

Verleisdonk et al. (2004) reported mean ICP however did not report on standard deviation and therefore received no weighting in the forest plot. Two intervention groups (Fronek et al., 1987, Roscoe et al., 2018) fell to the left of the summary measure line indicating lower ICP values for surgical intervention compared to the non-surgical intervention of Vogels et al. (2020a) (Non-Surgical) and the control group reported by Roscoe et al. (2018) (Control), which fell to the right of the summary measure line. The surgical group in Vogels et al. (2020a) reported the highest mean ICP in this analysis (21mmHg), conflicting with the results of the other surgical groups with reported mean ICP of 12.3mmHg (Roscoe et al., 2018) and 9.2mmHg (Fronek et al., 1987). The summary measure indicates a mean ICP at rest of 13.78mmHg in all plotted studies. Heterogeneity of this meta-analysis was considerable, I^2=98%.

ICP Values Immediately Post-Exercise

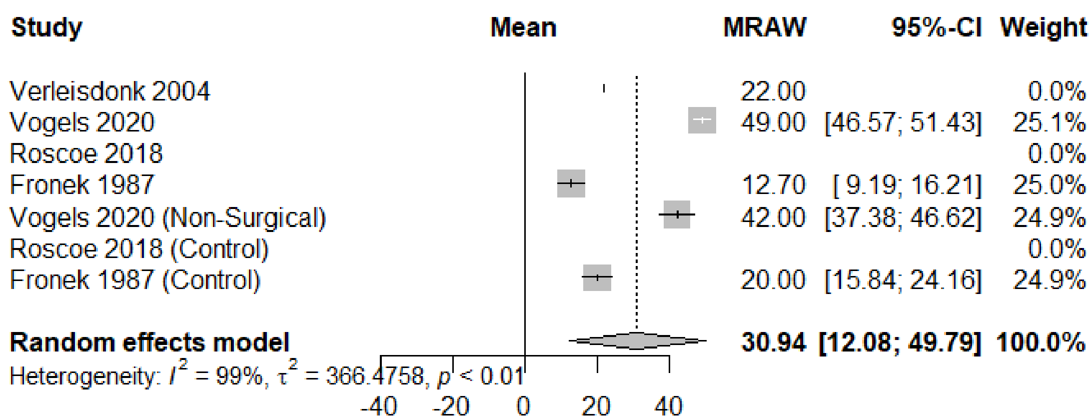

Figure 14 - ICP Values Immediately Post-Exercise

Verleisdonk et al. (2004) reported mean ICP however did not report on standard deviation and therefore received no weighting in the forest plot. ICP immediately post-exercise was not reported in one study (Roscoe et al., 2018) and therefore the study received no weighting in the forest plot. One intervention group (Fronek et al., 1987) fell to the left of the summary measure line indicating lower ICP values for surgical intervention compared to the control group of Roscoe et al. (2018) (Control), the non-surgical intervention of Vogels et al. (2020a) (Non-Surgical), and the surgical intervention of (Vogels et al., 2020a). One surgical group (Vogels et al., 2020a) and one non-surgical group (Vogels et al., 2020a) (Non-Surgical) fell to the right of the summary measure line, with the surgical group (Vogels et al., 2020a) reporting the highest mean ICP in this analysis (49mmHg), conflicting with the results of the surgical group reported by Fronek et al. (1987). The summary measure indicates a mean ICP immediately post-exercise of 30.94mmHg in all plotted studies. This meta-analysis had considerable heterogeneity (I^2=98%)

ICP Values 1-Minute Post-Exercise

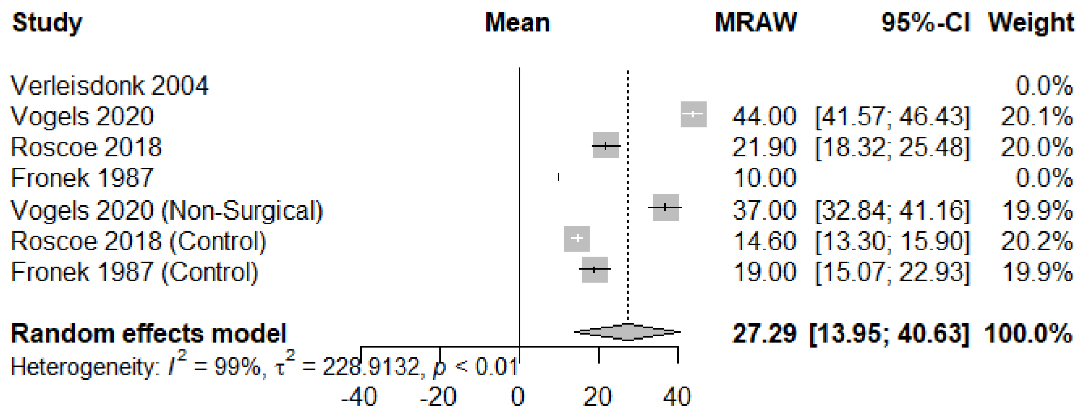

Figure 15 - ICP Values 1-Minute Post-Exercise

The surgical group in Fronek et al. (1987) reported mean ICP however did not report on standard deviation and therefore received no weighting in the forest plot. ICP 1-minute post-exercise was not reported in one study (Verleisdonk et al., 2004) and therefore the study received no weighting in the forest plot. One intervention group (Roscoe et al., 2018) fell to the left of the summary measure line indicating higher ICP values for surgical intervention compared to the control groups (Fronek et al., 1987, Roscoe et al., 2018) (Control) but lower ICP values compared to both the non-surgical intervention of Vogels et al. (2020a) (Non-Surgical), and the surgical intervention of

Vogels et al. (2020a). One surgical group (Vogels et al., 2020a) and one non-surgical group (Vogels et al., 2020a) (Non-Surgical) fell to the right of the summary measure line, with the surgical group (Vogels et al., 2020a) reporting the highest mean ICP in this analysis (44mmHg), conflicting with the results of the surgical group from Roscoe et al. (2018). The summary measure indicates a mean ICP 1-minute post-exercise of 27.29mmHg in all plotted studies. Heterogeneity in this meta-analysis was considerable according to the I^2 value of 99%.

ICP Values 5-Minutes Post-Exercise

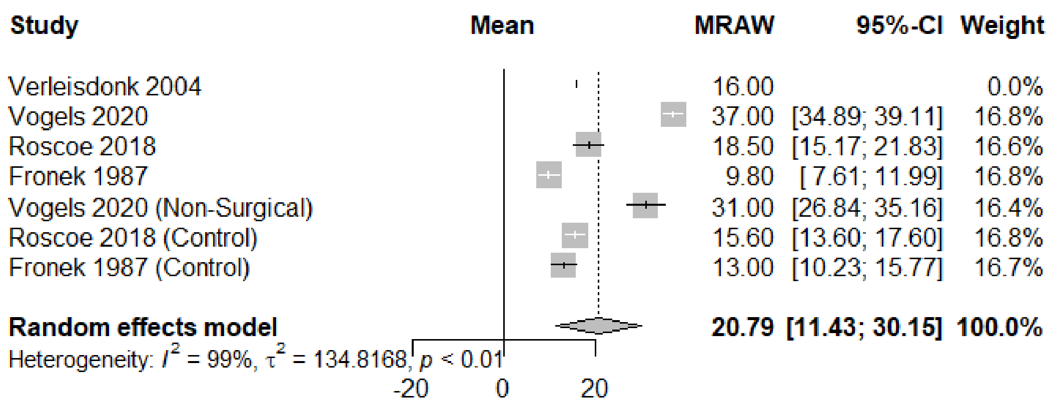

Figure 16 - ICP Values 5-Minutes Post-Exercise

Verleisdonk et al. (2004) reported mean ICP however did not report on standard deviation and therefore received no weighting in the forest plot. Two intervention groups (Fronek et al., 1987, Roscoe et al., 2018) fell to the left of the summary measure line indicating lower ICP values for surgical intervention compared to both the non-surgical intervention of Vogels et al. (2020a) (Non-Surgical), and the surgical intervention of Vogels et al. (2020a). One surgical group (Vogels et al., 2020a) and one non-surgical group (Vogels et al., 2020a) (Non-Surgical) fell to the right of the summary measure line, with the surgical group (Vogels et al., 2020a) reporting the highest mean ICP in this analysis (37mmHg), conflicting with the results of the other surgical groups (Fronek et al., 1987, Roscoe et al., 2018). The summary measure indicates a mean ICP 5-minutes post-exercise of 20.79mmHg in all plotted studies. In this meta-analysis I^2=99%, demonstrating considerable heterogeneity.

Patient Satisfaction (Surgical)

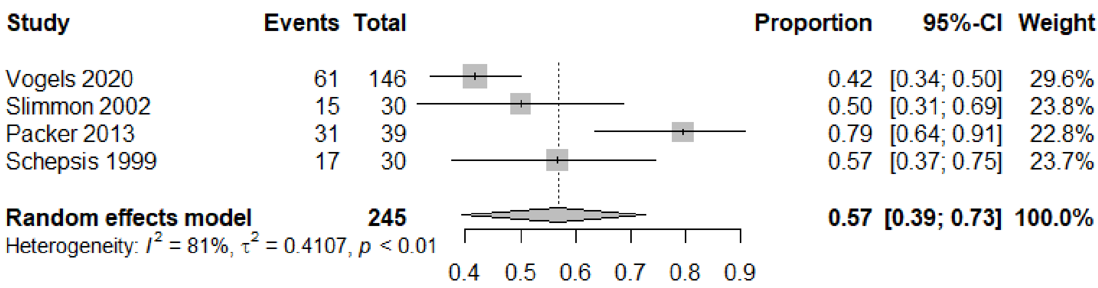

Figure 17 - Patient Satisfaction (Surgical)

Two studies (Slimmon et al., 2002, Vogels et al., 2020a) reported mean patient satisfaction of <50%. One study fell exactly on the summary measure line (Schepsis et al., 1999) reporting mean patient satisfaction of 57% and one study fell to the right of the summary measure line (Packer et al., 2013) reporting 79% patient satisfaction. The summary measure indicates that 57% of all patients were satisfied with surgical intervention. The I^2 value of this meta-analysis was 81%, indicating considerable heterogeneity.

Pain

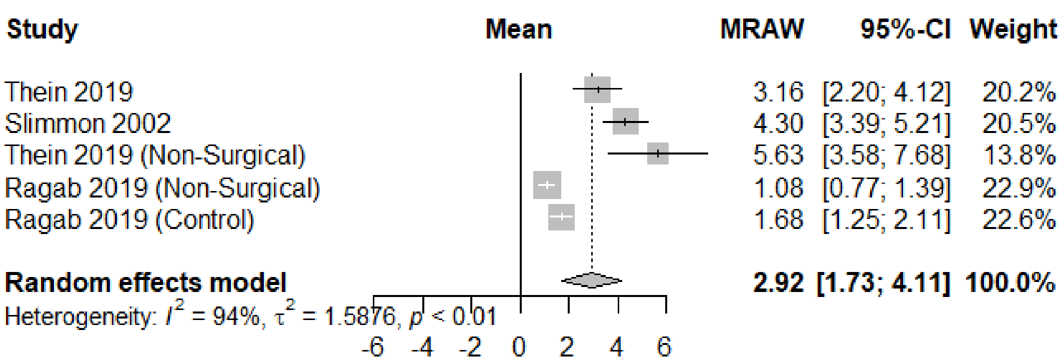

Figure 18 - Pain

Two groups (Ragab et al., 2019) (Non-Surgical & Control) fell to the left of the summary measure line and reported the lowest mean levels of pain post-intervention of 1.08 and 1.68, respectively. One group crossed the summary measure line (Thein et al., 2019) reporting post-intervention pain at 3.16. Two groups fell to the right of the summary measure line (Slimmon et al., 2002, Thein et al., 2019) (Non-Surgical) reporting mean post-intervention pain scores of 4.30, and 5.63, respectively. Ragab et al. (2019) (Non-Surgical) and (Thein et al., 2019) (Non-Surgical) reported the highest and lowest pain score values, indicating conflicting results for Non-Surgical management. The summary measure indicates a mean post-intervention pain score of 2.92 across studies. The heterogeneity in this study was considerable (I^2=94%).

Hernia Presence*

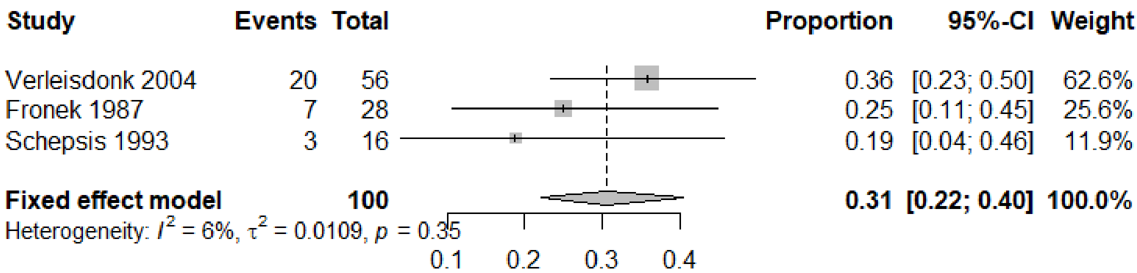

Figure 19 - Hernia Presence*

The 95% confidence interval of all studies (Fronek et al., 1987, Schepsis et al., 1993, Verleisdonk et al., 2004) crossed the summary measure line, reporting hernia presence in 36%, 25%, and 19% of patients, respectively. The summary measure indicates an average hernia presence of 31%. The heterogeneity of this meta-analysis was low (I^2=6%).

Complications (Surgical)

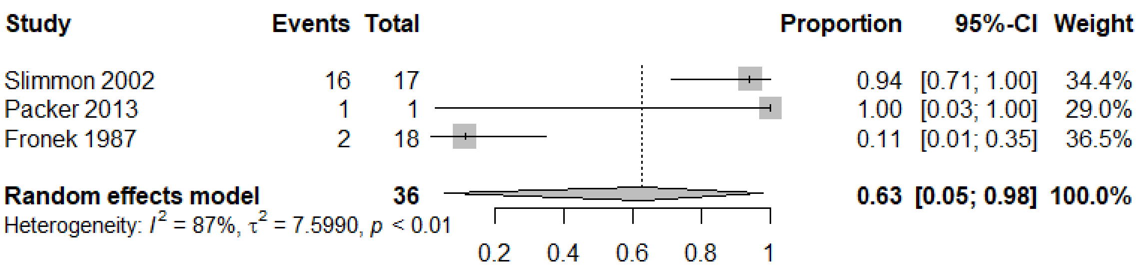

Figure 20 - Complications (Surgical)

Surgical complications were reported in all studies (Fronek et al., 1987, Packer et al., 2013, Slimmon et al., 2002). One study (Fronek et al., 1987) fell to the left of the summary measure line, reporting surgical complications in 11% of participants. Slimmon et al. (2002) and Packer et al. (2013) both fell to the right of the summary measure line and reported high event rates of 94% and 100%, respectively. The summary measure indicates a mean post-intervention surgical complication rate of 63%. Considerable heterogeneity was present in this meta-analysis, with an I^2 value of 87%.

Return to Activity (Total)

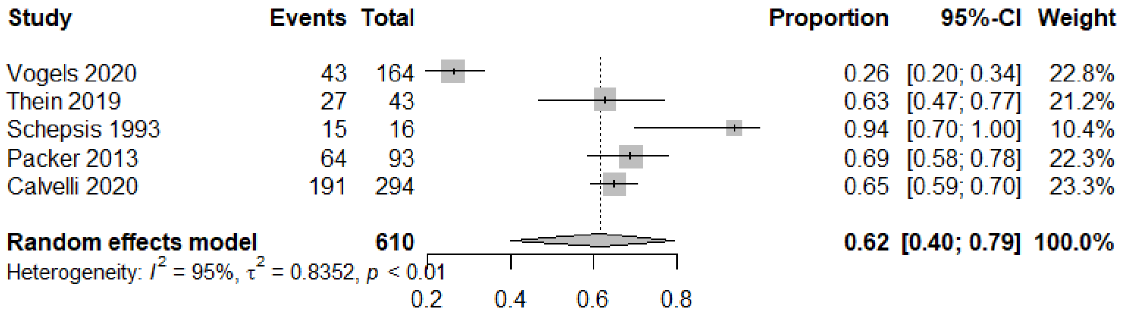

Figure 21 - Return to Activity (Total)

One group (Vogels et al., 2020a) fell to the left of the summary measure line and reported the lowest rate of return to activity of 26%. Three groups' 95% confidence intervals crossed the summary measure line (Calvelli et al., 2020, Packer et al., 2013, Thein et al., 2019) with 63%, 69%, and 65% return to activity, respectively. One group (Schepsis et al., 1993) fell to the right of the summary measure line, reporting the highest rate of return to activity at 94%. The summary measure indicates a mean return to activity of 62% in all participants, regardless of the intervention received. Considerable heterogeneity was found in this meta-analysis according to the I^2 value (95%).

4.3.1.3 Subgroup Single-Arm Meta-Analyses

Complications (Major)*

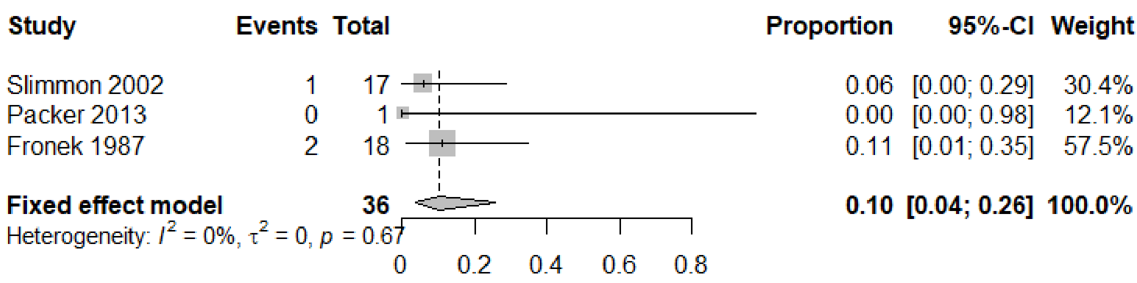

Figure 22 - Complications (Major)*

The confidence intervals of all groups (Fronek et al., 1987, Packer et al., 2013, Slimmon et al., 2002) crossed the summary measure line with major complications occurring in 6%, 0%, and 11% of participants, respectively. The summary measure indicates a mean rate of 10% for major complications across studies. There was no heterogeneity between studies in this meta-analysis (I^2=0%).

Return to Activity (Surgical)

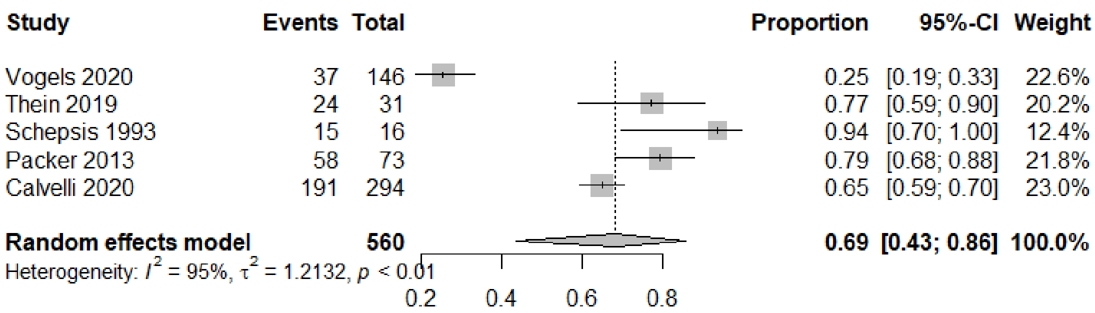

Figure 23 - Return to Activity (Surgical)

One group (Vogels et al., 2020a) fell to the left of the summary measure line and reported the lowest rate of return to activity of 25%. Three groups' 95% confidence intervals crossed the summary measure line (Calvelli et al., 2020, Packer et al., 2013, Thein et al., 2019) with 65%, 79%, and 77% return to activity, respectively. One group (Schepsis et al., 1993) fell to the right of the summary measure line, reporting the highest rate of return to activity at 94%. The summary measure indicates a mean return to activity of 69% in all participants receiving surgical intervention. Studies in this meta-analysis showed considerable heterogeneity (I^2=95%).

Return to Activity (Non-Surgical)*

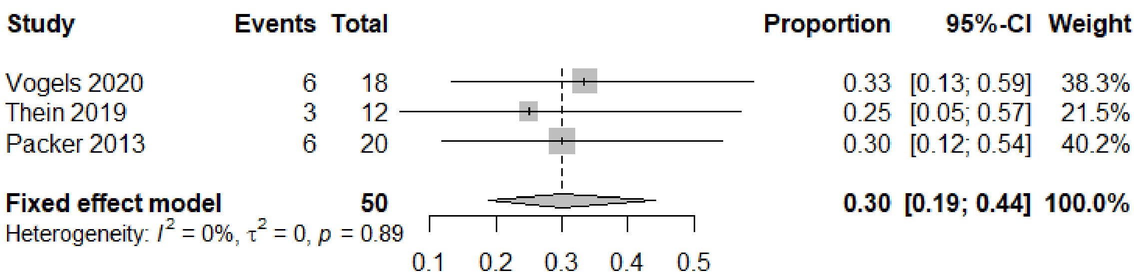

Figure 24 - Return to Activity (Non-Surgical)

The confidence intervals of all groups (Packer et al., 2013, Thein et al., 2019, Vogels et al., 2020a) crossed the summary measure line, reporting return to activity in in 33%, 25%, and 30% of participants, respectively. The summary measure indicates a mean return to activity of 30% in all participants receiving non-surgical intervention. The heterogeneity of this meta-analysis was low (I^2=0%)

4.3.2 Summary of Meta-Analysis Results

Intracompartmental pressure levels at all stages of testing were similar between surgical and non-surgical groups with significant differences compared to control groups, most notably at P_0 and P_1. Intracompartmental pressure values reported for all groups receiving surgical management, non-surgical management, or control groups at rest, P_0, P_1, and P_5 are presented in Figure 25 below.

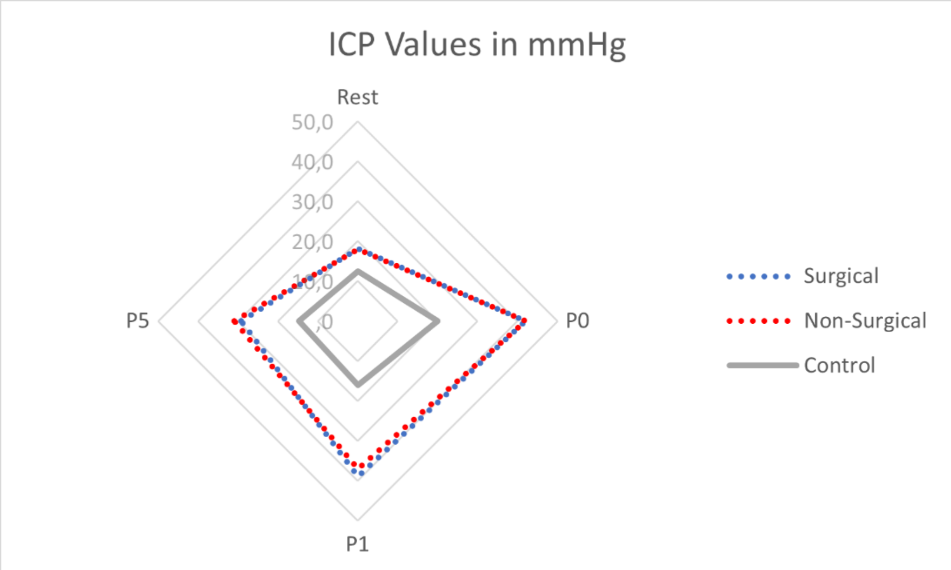

Figure 25 - Radar diagram of ICP values between surgical, non-surgical, and control groups

P_0 = immediately post-exercise; P_1 = 1-minute post-exercise; P_5 = 5-minutes post-exercise

Return to activity and patient satisfaction appeared significantly greater for groups receiving surgical intervention than for those receiving non-surgical intervention. Return to activity and patient satisfaction for all groups that received surgical or non-surgical management are shown in Figure 26 below.

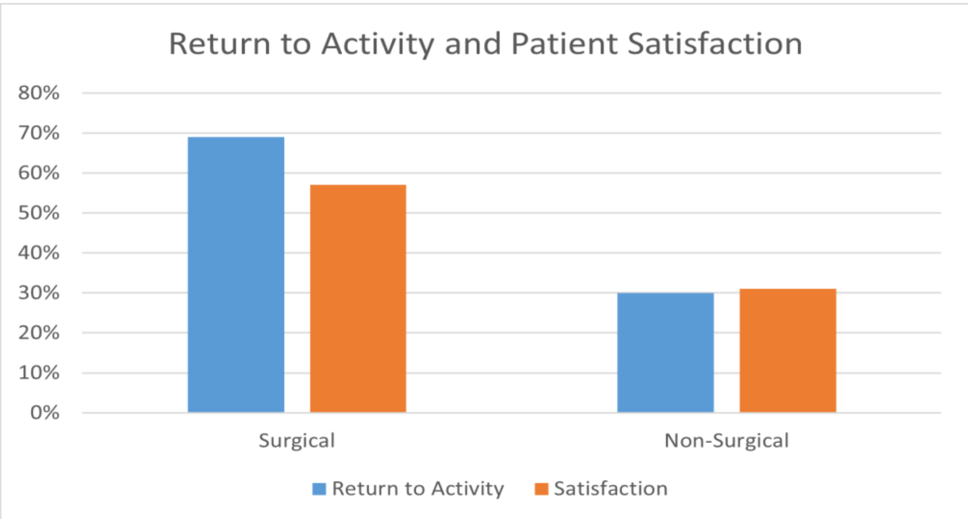

Figure 26 - Return to activity and patient satisfaction following surgical or non-surgical management

4.3.3 Narrative Review

Narrative review was performed for all studies, including those that were included in meta-analysis. The narrative review is presented according to the specific surgical or non-surgical interventions used and their respective outcomes. Due to the large number of case reports included for studies where fasciotomy was performed (n=12), the results of the case reports were discussed independently.

4.3.3.1 Surgical Intervention

Fasciotomy

By far the most reported treatment of CECS was surgical fasciotomy, reported in 41 (78.8%) of the included studies. Eight studies reported on the elevated pre-intervention ICP levels for participants (Fronek et al., 1987, Packer et al., 2013, van Zantvoort et al., 2017, Verleisdonk et al., 2004, Vogels et al., 2020a, Schepsis et al., 2005, Van der Wal et al., 2015). Significant improvements in ICP values following fasciotomy were reported in five studies (Verleisdonk et al., 2004, Van der Wal et al., 2015, Schepsis et al., 2005, Roscoe et al., 2018, Fronek et al., 1987) with the most significant difference noted at P_0 in one study (Verleisdonk et al., 2004). Mean ICP at all stages of testing were found to be lower in the non-surgical group compared to the surgical group in one study (Vogels et al., 2020a). One study found no correlation between the degree of increase in pre-surgical ICP levels and post-surgical outcomes (Packer et al., 2013).

Pain was assessed as present, relieved, or absent in three studies (Fronek et al., 1987, Verleisdonk et al., 2004, Wittstein et al., 2010) and all three studies found significant improvements in pain post-surgically. One study assessed pain by the duration of time participants were able to walk before having to stop due to pain and found that this parameter improved from <10 minutes to unlimited in 88.9% of patients following surgical intervention (Edmundsson et al., 2018). Four studies (Balius et al., 2016, de Bruijn et al., 2015, Drexler et al., 2017, Gatenby et al., 2017) found statistically significant improvements in pain for participants following fasciotomy using pain scales such as the VAS (Gatenby et al., 2017), the Numeric Pain Rating Scale (NPRS)(Drexler et al., 2017), and a verbal pain rating scale (VRS)(Balius et al., 2016, de Bruijn et al., 2015).

Patient satisfaction with fasciotomy ranged from 33% (van Zantvoort et al., 2017) to 100% (Van der Wal et al., 2015) and was reported in 13 studies in total. One study did not expressly report patient satisfaction however “technical operative success” was reported to be 100% (de Bruijn et al., 2015). Rates of return to activity after fasciotomy were reported in 15 studies and ranged from 25% (Vogels et al., 2020a) to 94% (Maffulli et al., 2016).

Measures of function were heterogenous amongst studies. The Tegner Activity Scale was used in two studies (Drexler et al., 2017, Thein et al., 2019). Physical Fitness Test (PFT) (Cook and Bruce, 2002), SF-12 (Drexler et al., 2017), SF-36 (Maffulli et al., 2016), and EQ-5D (Maffulli et al., 2016) scores were used in a single study each. All studies reported significant functional improvements following intervention, regardless of the outcome measure used (Cook and Bruce, 2002, Drexler et al., 2017, Maffulli et al., 2016, Thein et al., 2019).

Hernia presence was reported as primary hernia in between 31-39% of patients in three studies (Fronek et al., 1987, Kramer et al., 2013, Verleisdonk et al., 2004). One study reported the presence of post-surgical hernias as 31% (Kramer, 2013).

Surgical complications were reported in 11 studies. Major complications were reported in four studies (Gatenby et al., 2017, Packer et al., 2013, Schepsis et al., 2005, Thein et al., 2019) and occurred in between 2.3% (Thein et al., 2019) and 8.3% (Gatenby et al., 2017) of participants. Minor complications were reported in nine studies (Beck et al., 2016, Cook and Bruce, 2002, de Bruijn et al., 2015, de Bruijn et al., 2019, Drexler et al., 2017, Edmundsson et al., 2018, Finestone et al., 2014, Packer et al., 2013, Thein et al., 2019) and occurred in between 6.3% (de Bruijn et al., 2019) and 30.5% (Drexler et al., 2017) of participants.

Symptom recurrence of between 0% (Edmundsson et al., 2008) and 23.1% (Irion et al., 2014) was reported by seven studies (Beck et al., 2016, Cook and Bruce, 2002, Drexler et al., 2017, Edmundsson et al., 2008, Finestone et al., 2014, Gatenby et al., 2017, Irion et al., 2014). Re-operation was performed for 7.1% (Cook and Bruce, 2002) to 18.8% (Beck et al., 2016) of participants.

Fasciotomy was also used in 12 case reports that were included in the review: whose results were not discussed above. Eleven case reports mentioned that the participants had a full recovery and full return to activity following fasciotomy. One study reported that the patient had received a previous, failed fasciotomy and upon removing scar tissue from the site of the previous surgery and performing an additional fasciotomy, the patient had made a full recovery (Masukawa et al., 1992). One study reported that a previous two-compartment fasciotomy had failed; following a four-compartment fasciotomy the patient then made a full recovery (Truex and Menge, 2018). One study reported on a patient who had undergone nine weeks of non-surgical management and showed improvements in pain and function (using the FAAM score), however when the patient progressed to running on an asphalt surface their pain returned. The patient was subsequently referred for fasciotomy and was asymptomatic at follow-up (Snowden et al., 2014). One study reported great improvements in the patient's VAS pain score, however the patient experienced a bulging sensation throughout the anterior compartment of the leg that prevented them from returning to their pre-surgical activity levels (Tubb and Vermillion, 2001).

Fasciectomy

Four studies reported results on patients receiving fasciectomy (Bell, 1986, Roberts et al., 2015, Simpson et al., 2020, Slimmon et al., 2002). Outcomes following fasciectomy alone were reported in two studies (Roberts et al., 2015, Simpson et al., 2020). Between 46% (Simpson et al., 2020) and 48% (Roberts et al., 2015) of patients improved their military fitness grading following intervention. Full fitness was achieved in between 22% (Simpson et al., 2020) and 40% (Roberts et al., 2015) of patients.

Fasciotomy with partial fasciectomy was performed in two studies (Bell, 1986, Slimmon et al., 2002). Patients in one study had a significant decrease in VAS pain scores following intervention (Slimmon et al., 2002), and no pain was reported in the other study's patients (Bell, 1986). ICP levels were reported in one study (Bell, 1986) which found them to be significantly lower following intervention. Patient satisfaction (65%), return to activity (42%), symptom recurrence (36%) and re-operation (16.7%) were reported in one study (Slimmon et al., 2002).

Fascial Fenestration

One case report investigated outcomes following fascial fenestration (Finnoff and Rajasekaran, 2016). The patient was able to return to full activities with no pain from one week following intervention, and this improvement was maintained at 18-month follow-up (Finnoff and Rajasekaran, 2016).

4.3.3.2 Non-Surgical Intervention

Gait Re-Training

Gait re-training was investigated in three of the included studies (Diebal et al., 2012, Zimmermann et al., 2017, Zimmermann et al., 2019). One study reported that most patients were satisfied with gait-retraining intervention however this was not quantified (Zimmermann et al., 2017). All three studies reported that patients had improved function following intervention based on their SANE scores (Diebal et al., 2012, Zimmermann et al., 2017, Zimmermann et al., 2019). One study reported return to active duty in 57% of patients (Zimmermann et al., 2019), and one study reported full resumption of activities while avoiding surgical intervention for all participants (Diebal et al., 2012).

Botulinum Toxin

Two studies reported on the effect of the injection of botulinum toxin into the affected compartment (Hutto et al., 2019, Isner-Horobeti et al., 2013). Post-intervention ICP was reported in one study (Isner-Horobeti et al., 2013), with an average decrease in ICP values of 59-68%. Exertional pain was absent and activity levels had improved to pre-diagnostic levels in both studies at nine-month (Isner-Horobeti et al., 2013) and 10-month (Hutto et al., 2019) follow-up.

Manual Therapy

Manual therapy was used in the management of CECS in six studies (Blackman et al., 1998, Collins and Gilden, 2016, Ragab et al., 2019, Snowden et al., 2014, Zimmermann et al., 2017, Zimmermann et al., 2019). Manual therapy intervention was not specified for two studies (Zimmermann et al., 2017, Zimmermann et al., 2019). Manual therapy including myofascial release was unsuccessful for the patient, who was referred for fasciotomy, in a study which has been discussed previously in the surgical section of the narrative review (Snowden et al., 2014). One study reported the outcomes of specific manual therapy using a specialised instrument versus a control group in a randomised controlled trial (Ragab et al., 2019). Dorsiflexion range of motion, LEFS score, and VAS pain score improved significantly in both groups following intervention, however there were significantly greater improvements in all outcomes for the intervention group compared to the control group (Ragab et al., 2019). Two case reports assessed ICP levels pre- and post-intervention (Blackman et al., 1998, Collins and Gilden, 2016). One case report reported ICP measured at 3-minutes post-exercise that increased slightly following manual therapy intervention, however, all patients reported improvements in pain severity (VRS) during and after exercise, and work measured in Joules prior to onset of pain increased threefold even with the increase in ICP levels (Blackman et al., 1998). The other case report reported ICP using the Pedowitz criteria following intervention, which improved significantly for the patient (Collins and Gilden, 2016). In this study, the patient was able to return to full activity post-intervention and maintained pain-free activity at three-year follow-up (Collins and Gilden, 2016).

Chapter 5 Discussion

5.1 Introduction

The purpose of this review was to determine the effectiveness of surgical and non-surgical management strategies on clinical outcomes for patients diagnosed with CECS of the anterior compartment of the leg. Findings were grouped under two major categories: surgical management and non-surgical management. These categories were further subdivided into a total of three categories each, forming a total of six subcategories: fasciotomy, fasciectomy, fascial fenestration, gait-retraining, botulinum toxin, and manual therapy.

5.2 Designs of Included Studies

Most studies included in this systematic review were case series, which is of a relatively low level of evidence, while only one randomised controlled study met the inclusion criteria. It is important for future research that more randomised controlled trials are performed with large sample sizes to accurately reflect the outcomes of different types of management.

5.3 Participant Characteristics

Chronic exertional compartment syndrome is thought to occur most frequently in younger active individuals participating in sports, and military populations (Simpson et al., 2020) however there is also evidence that CECS may occur in individuals of all ages (de Bruijn et al., 2018a, Garcia-Mata et al., 2001, Johnson et al., 2020) as well as sedentary individuals (Edmundsson et al., 2007, Orlin et al., 2016). Correlations of age and gender on CECS diagnosis have been reported as either negligible (Meulekamp et al., 2017) or as positive factors leading to slightly higher prevalence in females and patients of increasing chronological age (de Bruijn et al., 2018a, Orlin et al., 2016, Waterman et al., 2013b), however the results of this study found that participants ranged in age from 12-years-old (Beck et al., 2016, Fronek et al., 1987) to 78-years-old (van Zantvoort et al., 2017) with an average mean age of 25-years-old, and an average median age of 21-years-old. Sex data for a total of 1234 participants across studies showed that 704 (57%) were male and 530 (43%) were female. The results of this study indicate that there is a significantly higher likelihood of diagnosis of CECS in young adult males.

5.4 Outcomes Across Studies

5.4.1 Pain

Exertional pain is considered an important diagnostic feature for patients with CECS (Fouasson-Chailloux et al., 2018), yet it was infrequently reported as an outcome in the studies included in this review (15/52)(28.8%). Outcome measures for pain were not standardised across studies and pain was reported using a variety of scales such as the VAS, NPRS, and VRS, amongst others (Balius et al., 2016, Bell, 1986, Blackman et al., 1998, Collins and Gilden, 2016, de Bruijn et al., 2015, Drexler et al., 2017, Fronek et al., 1987, Gatenby et al., 2017, Isner-Horobeti et al., 2013, Ragab et al., 2019, Slimmon et al., 2002, Snowden et al., 2014, Tubb and Vermillion, 2001, Verleisdonk et al., 2004, Wittstein et al., 2010). Due to the variety of pain scales used, it is not possible to compare pain scores between different outcome measures to compare overall effect of intervention on pain. Standardising a measure of pain for assessing outcomes of CECS management is therefore necessary.

5.4.2 Range of Motion

Only two studies reported on ankle dorsiflexion range of motion (Hutto et al., 2019, Ragab et al., 2019). Both studies noted significant improvements following intervention of both botulinum toxin (Hutto et al., 2019) and manual therapy using a specialised instrument (Ragab et al., 2019). Studies assessing biomechanical properties of patients with CECS of various anatomical compartment are necessary to understand both the pathophysiology of the condition and the influence of range of motion on prognostic and management outcomes.

5.4.3 ICP Values

The pathophysiological mechanisms of CECS are still poorly understood (Edmundsson et al., 2018). There appears to be no correlation between the degree of increase in pre-surgical ICP levels and post-surgical outcomes (Packer et al., 2013), suggesting that the cause of elevated pre-surgical ICP values is managed appropriately by reducing the restrictions imposed on the affected compartment by surgical release of the fascia, regardless of the extent of the restriction. Significant differences in pre-and post-intervention ICP values were found for patients that underwent surgical fasciotomy (Fronek et al., 1987, Roscoe et al., 2018, Schepsis et al., 2005, Van der Wal et al., 2015, Verleisdonk et al., 2004) and surgical fasciectomy

(Bell, 1986). Patients receiving non-surgical intervention in the form of botulinum toxin injection into the affected compartment (Isner-Horobeti et al., 2013) and manual therapy (Collins and Gilden, 2016) also demonstrated significant decrease in ICP values, indicating that there may be other mechanisms involved in the increased levels of intracompartmental pressure aside from fascial restriction. One study reported that manual therapy intervention led to a mild increase in ICP values at 3-minutes post-exercise, however this was accompanied with a threefold increase in work to onset of pain and does not reflect ICP following a standardised activity, duration, or intensity, which was not reported (Blackman et al., 1998).

The specific protocol for ICP measurements as well as the instrumentation used for measuring ICP differed across studies in terms of the use of dynamic (de Bruijn et al., 2018b, Roscoe et al., 2018, van Zantvoort et al., 2017) or static (Fronek et al., 1987, Verleisdonk et al., 2004, Vogels et al., 2020a) ICP measurements, specifics regarding catheter placement, and the type of electrode used for measurement. These differences may potentially lead to inaccuracies such as lower or higher values being reported due to variations in diagnostic technique. Guidelines on diagnostic technique and consensus regarding diagnostic protocol have not yet been established.

5.4.4 Patient Satisfaction

Patient satisfaction is an important outcome parameter for determining subjective success of the interventions used. Patient satisfaction reported in the studies ranged from 33% (van Zantvoort et al., 2018) to 100% (Van der Wal et al., 2015) for surgical interventions. This range in values is possibly due to different surgical techniques and different populations included for management. Only one non-surgical intervention study reported on patient satisfaction (Zimmermann et al., 2017), finding that most patients were satisfied with gait re-training intervention, however this value was not quantified. The use of patient satisfaction as an outcome should be reported in more non-surgical studies, although it is not yet a standardised outcome.

5.4.5 Recurrence of Symptoms

Symptom recurrence following intervention was rarely mentioned in the included studies. Rates of recurrence following surgical management was reported as between 0% (Edmundsson et al., 2008) and 36% (Slimmon et al., 2002), and recurrence rate was not reported in any of the non-surgical intervention studies. Reporting of symptom recurrence needs to be reported across studies, particularly surgical interventions due to their invasive nature, and standardised follow-up criteria must be established.

5.4.6 Function

Across all included studies, there was significant variation in outcome measures used to score function. Outcome measures for function and their corresponding parameters are presented below in Table 5. Significant functional improvements following intervention were reported in all studies, regardless of the outcome measure used. Comparison of improvements in function between different interventions to assess whether the type of intervention led to greater functional outcomes was not possible due to the use of inconsistent outcome measures, and a standardised measure needs to be implemented.

Table 5 - Outcome Measures for Function

Outcome Measure	Items	Points Per Item	Point Range Minimum	Point Range Maximum	Activities Measured
SANE	1	101	0	100	Percentage of function relative to what the patient considers normal
GROC	1	15	-7	7	Ankle well-being
LLOS	12	6	0	5	Activities of daily living, athletic activities
LEFS	20	5	0	4	Activities of daily living, advanced mobility (hopping, running, sharp turns while running)
Tegner	1	11	0	10	Highest level of activity participation
SQUASH	12	3	Light	Intense	Household, communal, leisure activities

SANE – single assessment numeric evaluation; GROC – global rating of change scale; LLOS – lower leg outcome survey; LEFS – lower extremity functional scale; Tegner – Tegner activity scale; SQUASH; short questionnaire to assess health-enhancing physical activity

5.4.7 Strength and Sensation

Only one study measured strength in the affected compartment following injection of botulinum toxin and noted a short-term 1-point decrease in MRC-scale strength scores that did not affect function for the participants, and strength had returned to normal at follow-up (Isner-Horobeti et al., 2013). Sensation was reported in two studies, both of which utilised fasciotomy as the intervention (de Bruijn et al., 2019, Tjeerdsma, 2016). Sensory deficits were found to be due to sural nerve injury, peroneal entrapment syndrome, superficial infection, and compartmental occlusion due to CECS (de Bruijn et al., 2019, Tjeerdsma, 2016). Due to the neurological symptoms that CECS patients may present with, studies measuring strength and sensation will offer more insight into neurological changes for patients with CECS following intervention.

Chapter 6 Conclusion and Recommendations

6.1 Conclusion

This systematic review aimed to assess the effectiveness of surgical and non-surgical management strategies on outcome parameters for patients diagnosed with CECS of the anterior compartment of the leg. Comparative meta-analyses were performed for five studies reporting results for an intervention group and either a control or non-surgical group. Additionally, single-arm meta-analyses were performed in 11 studies, due to the lack of a comparison group in six studies that had otherwise met the inclusion criteria. A narrative review was performed for all included studies and presented according to the interventions used.

The results from the meta-analyses showed that manual therapy appears to provide significant short-term improvements in pain and function for patients receiving the intervention, long-term data is not yet available. Patients receiving non-surgical intervention in the form of either gait-retraining or injection of botulinum toxin into the affected compartment had significant improvements in pain and return to activity, as well as a significant decrease in ICP levels. A summary of the results of forest plots with low heterogeneity are presented in Table 5 below.

Table 6 – Major results from the meta-analyses with low heterogeneity

Outcome	**Heterogeneity (P-value)**	**Finding**	**Studies**
ICP at P_0	24% (0)	Lower ICP at P_0 in participants that received non-surgical management compared to surgical management	(Vogels, 2020) (Packer, 2013)
Satisfaction	0% (0)	Higher satisfaction rate for patients treated surgically than non-surgically	(Vogels, 2020) (Packer, 2013)
Hernia Presence	6% (0.35)	Primary hernia presence reported in 31% of patients undergoing surgical management	(Verleisdonk, 2004) (Fronek, 1987) (Schepsis, 1993)
Complications (Major)	0% (0.67)	Major complications occurred in 11% of surgically managed patients	(Slimmon, 2002) (Packer, 2013) (Fronek, 1987)
Return to Activity (Non-Surgical)	0% (0.89)	Return to activity of 30% in patients receiving non-surgical management	(Vogels, 2020) (Thein, 2019) (Packer, 2013)

ICP – intracompartmental pressure; P_0 – immediately post-exercise

Strong statistical significance (P=0) was found in meta-analysis for patient satisfaction and ICP at P^0. Only findings with low heterogeneity are shown.

Most patients that underwent fasciotomy were satisfied with the outcomes following surgery. They also experience significant improvements in pain, function and return to activity. However, they were at risk of recurrence, re-operation, and surgical complications. Fasciotomy with partial fasciectomy appeared to be the least successful form of surgical management of CECS. Fasciectomy alone appeared to provide satisfactory results, however military grading is a vague interpretation of functional improvement, and fasciotomy offers seemingly preferential outcomes than fasciectomy. Fascial fenestration may provide significant improvements in both the short and long term, but further research is required to confirm the results of fascial fenestration in larger sample sizes and populations.

6.2 Clinical/Practical Recommendations

Increased ICP should be considered alongside clinical parameters to confirm a diagnosis of CECS, and the diagnosis of PAES should be excluded or treated if concurrently present. Non-surgical management strategies are a safe and effective intervention for CECS of the anterior compartment of the leg with low risk and should be exhausted prior to referral for surgical management, preferably in the form of surgical fasciotomy. If surgical management is unsuccessful, repeat fasciotomies including additional compartments may be considered.

6.3 Recommendation for Future Research

The background mechanisms of CECS require extensive research to pave the way for more targeted management strategies that may potentially negate the need for invasive management entirely. Consensus regarding diagnostic criteria for CECS is imperative. Standardised outcome measures for CECS must be established for future research to accurately report on patient outcomes for any type of management and to allow greater statistical analysis of studies in a comparative format. The authors recommend the use of outcome measures of the visual analogue scale for pain, maximal ICP values as well as those at rest, P_0, P_1, and P_5, range of motion of the joints above and below the effected compartment, binary patient satisfaction, return to activity should be monitored prospectively, and the SANE score for function. Reporting patient demographics and participant characteristics for groups according to their symptomatic compartments will allow more specific analytical research to be conducted in future studies.

6.4 Strengths and Limitations

This is the first study to report on the effectiveness of surgical and non-surgical management strategies for CECS of the anterior compartment of the leg, as well as the first study to perform meta-analyses of management outcomes for CECS in general. Many included studies were of low research quality, which reduces the generalisability of the results of the review. High heterogeneity was detected for most of the studies undergoing meta-analysis. The greatest difference between studies that contributed to this was inconsistency in both the reported outcomes, and outcome measures used. Single-arm meta-analyses were performed to provide graphical interpretation of the results where comparative groups were unavailable in some studies, this allowed for further analysis and review than would have been possible with only comparative meta-analysis. Many studies were excluded for not separately presenting results for the anterior compartment specifically, which influenced the number of included studies as well as the results of the statistical analysis.

6.5 Summary

Clinical parameters and the exclusion of differential diagnoses should be considered along with ICP levels when diagnosing a patient with CECS. Once diagnosed, non-surgical management options such as manual therapy, gait re-training, and botulinum toxin injection offer safe, effective management of the condition. Should non-surgical management fail, surgical fasciotomy appears to confer good clinical outcomes such as patient satisfaction and return to activity. Further research into the pathophysiology of CECS as well as non-surgical management options is necessary.

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Appendices

Appendix A - Example Search Terms

MEDLINE (PubMed) conducted December 2020

Search	Query	Records retrieved
#1	("CECS" OR "Chronic compartment syndrome" OR "chronic exertional compartment syndrome" OR "exertional compartment syndrome" OR "Anterior Compartment Syndrome/drug therapy"[Mesh] OR "Anterior Compartment Syndrome/therapy"[Mesh] OR "Anterior Compartment Syndrome/rehabilitation"[Mesh] OR "Anterior Compartment Syndrome/surgery"[Mesh])	2,298
#2	("EILP"[Text Word] OR "anterior compartment"[Title/Abstract] OR "lateral compartment"[Title/Abstract] OR "exercise neuropraxia"[Text Word] OR "fascial herniation"[Text Word] OR "compartment pressure"[Title/Abstract] OR "Post-exercise leg pain"[Text Word] OR "Exercise-related leg pain"[Title/Abstract] OR "Exercise-induced leg pain"[Title/Abstract])	3,048
#3	("Non-surgical"[Title/Abstract] OR "Physical Therapy" OR "Physiotherapy" OR "Manual therapy" OR "rehabilitation" OR "Exercise"[Text Word] OR "Cessation"[Text Word] OR "modification" OR "botox"[Title/Abstract] OR "botulinum toxin"[Title/Abstract] OR "non-operative"[Title/Abstract] OR "conservative"[Title/Abstract] OR "management")	2,550,015
#4	("surgery" OR "fasciotomy"[Title/Abstract] OR "fasciectomy"[Title/Abstract] OR "Fascial fenestration" OR "open fasciotomies"[Text Word] OR "surgical" OR "open fasciotomy"[Text Word])	3,746,624
#5	("strength"[Text Word] OR "range of motion"[Text Word] OR "pain"[Text Word] OR "recurrence"[Text Word] OR "function"[Text Word] OR "return to play"[Text Word] OR "Patient-reported outcomes"[Text Word] OR "ICP"[Text Word] OR "muscle compartment pressure" OR "intracompartmental pressure testing")	3,592,281
#6	#1 AND #2 AND #5 AND (#3 OR #4)	86
Limited from January 1956 to December 2020, no other limits applied.		

Appendix B – Results of Critical Appraisal

Table A - Case-Control Study Designs

Citation	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10
Fronek J, Mubarak SJ, Hargens AR, Lee YF, Gershuni DH, Garfin SR, et al. 1987.	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A
%	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	0.0

Table B - Case Report Study Designs

Citation	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8
Berg K, Cuppett M. 2002.	Y	Y	Y	Y	N	Y	Y	Y
Bresnahan JJ, Hennrikus WL. 2015.	Y	Y	Y	Y	Y	Y	U	Y
Collins CK, Gilden B. 2016.	Y	Y	Y	Y	Y	Y	N	Y
Drigny J, Reboursiere E, Desvergee A, Ruet A, Hulet C. 2019.	Y	Y	Y	Y	N	N	Y	Y
Finnoff JT, Johnson W. 2020.	Y	Y	Y	Y	Y	Y	N	Y
Finnoff JT, Rajasekaran S. 2016.	Y	Y	Y	Y	Y	U	N	Y
Flautt W, Miller J. 2013.	Y	Y	Y	Y	U	Y	N	Y
Hutto WM, Schroeder PB, Leggit JC. 2019.	Y	Y	Y	Y	Y	Y	N/A	Y
Joubert SV, Duarte MA. 2016.	Y	Y	Y	Y	N	N	Y	Y
Kitajima I, Tachibana S, Hirota Y, Nakamichi K, Miura K. 2001.	Y	Y	Y	Y	Y	Y	N/A	Y
Masukawa S, Watanabe H, Tsuruta T. 1992.	Y	Y	Y	Y	Y	Y	N/A	Y
Ota Y, Senda M, Hashizume H, Inoue H. 1999.	Y	Y	Y	Y	Y	Y	N/A	Y
Pierrart J, Croutzet P, Gregory T, Masmejean EH. 2015.	Y	N	N	N	Y	N	N/A	Y
Schissel DJ, Godwin J. 1999.	Y	Y	Y	Y	N	N	N/A	Y
Snowden J, Becker JA, Brosky JA, Hazle C. 2014.	Y	Y	Y	Y	U	U	Y	Y
Tjeerdsma J. 2016.	Y	Y	Y	Y	Y	Y	N/A	Y
Truex N, Menge TJ. 2018.	Y	Y	Y	Y	Y	Y	Y	Y
Tubb CC, Vermillion D. 2001.	Y	Y	Y	Y	Y	N	U	Y
Naito M, Ogata K, Kuroki T, Naito H. 1985.	Y	U	U	Y	N	U	N/A	Y
%	100.0	89.47	89.47	94.73	63.15	57.89	26.31	100.0

Table C - Case Series Study Designs

Citation	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10
Zimmermann WO, Hutchinson MR, Van den Berg R, Hoencamp R, Backx FJG, Bakker EWP. 2019.	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A
Balius R, Bong DA, Ardèvol J, Pedret C, Codina D, Dalmau A. 2016.	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A
Beck JJ, Tepolt FA, Miller PE, Micheli LJ, Kocher MS. 2016.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Bell S. 1986.	Y	Y	Y	Y	Y	Y	Y	Y	U	N/A
de Bruijn JA, van Zantvoort AP, Winkes MB, Raaymakers L, van der Cruijsen-Raaijmakers M, Hoogeveen AR, et al. 2015.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Diebal AR, Gregory R, Alitz C, Gerber JP. 2011.	N	N	Y	N	N	Y	Y	Y	Y	N/A
Diebal AR, Gregory R, Alitz C, Gerber JP. 2012.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Drexler M, Rutenberg TF, Rozen N, Warschawski Y, Rath E, Chechik O, et al. 2017.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Finestone AS, Noff M, Nassar Y, Moshe S, Agar G, Tamir E. 2014.	N	Y	Y	Y	Y	Y	Y	Y	Y	Y
Gatenby G, Haysom S, Twaddle B, Walsh S. 2017.	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A
Irion V, Magnussen RA, Miller TL, Kaeding CC. 2014.	U	Y	Y	Y	Y	Y	Y	Y	Y	Y
Isner-Horobeti ME, Dufour SP, Blaes C, Lecocq J. 2013.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Kramer DE, Pace JL, Jarrett DY, Zurakowski D, Kocher MS, Micheli LJ. 2013.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Micheli LJ, Solomon R, Solomon J, Plasschaert VF, Mitchell R. 1999.	U	Y	Y	Y	Y	U	U	Y	Y	U
Rorabeck CH, Fowler PJ, Nott L. 1988.	N	Y	Y	Y	Y	N	N	N	Y	N/A

Rosfors S, Eriksson M. 1993.	N	Y	Y	Y	Y	N	N	N	Y	N/A
Schepsis AA, Fitzgerald M, Nicoletta R. 2005.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Sebik A, Dogan A. 2008.	N	U	U	N	N	N	Y	N	N	N/A
Van der Wal WA, Heesterbeek PJ, Van den Brand JG, Verleisdonk EJ. 2015.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
van Zantvoort APM, de Bruijn JA, Hundscheid HPH, van der Cruijsen-Raaijmakers M, Teijink JAW, Scheltinga MR. 2018.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
van Zantvoort APM, de Bruijn JA, Winkes MB, Hoogeveen AR, Teijink JAW, Scheltinga MR. 2017.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Wieczorek V, Luciani JF, Brunet-Guedj E, Feugier P, Thevenon A. 2012.	N	Y	Y	Y	Y	Y	Y	Y	Y	Y
Wittstein J, Moorman CT, Levin LS. 2010.	N	Y	Y	Y	Y	Y	Y	Y	Y	N/A
Edmundsson D, Svensson O, Toolanen G. 2008.	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A
Roberts AJ, Krishnasamy P, Quayle JM, Houghton JM. 2015.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Allen MJ, Barnes MR. 1986.	Y	Y	Y	Y	Y	U	U	N	N	N/A
Maffulli N, Loppini M, Spiezia F, D’Addona A, Maffulli GD. 2016.	U	Y	Y	Y	Y	Y	Y	Y	Y	Y
Simpson C, Roscoe D, Hughes S, Hulse D, Guthrie H. 2020.	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A
Turnipseed WD, Hurschler C, Vanderby R. 1995.	N	Y	Y	Y	Y	U	U	Y	N	Y
Wijand Marnixde de F, Scheltinga MR, Luiting MG. 2006.	N	Y	Y	Y	Y	U	U	Y	N	N/A
Zimmermann W, Linschoten C, Beutler A. 2017.	Y	Y	Y	Y	Y	Y	Y	Y	U	Y
de Bruijn JA, van Zantvoort APM, Hundscheid HPH, Hoogeveen AR, Teijink JAW,	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

Scheltinga MR. 2019.										
%	62.5	93.75	96.87	93.75	93.75	78.12	81.25	87.5	78.12	56.25

Table D - Cohort Study Designs

Citation	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11
Verleisdonk EJ, Schmitz RF, van der Werken C. 2004.	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y
Calvelli N, Verges S, Rousseaux-Blanchi MP, Edouard P, Guinot M. 2020.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Cook S, Bruce G. 2002.	N/A	N/A	Y	Y	Y	U	N	Y	Y	N/A	N/A
Packer JD, Day MS, Nguyen JT, Hobart SJ, Hannafin JA, Metzl JD. 2013.	U	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y
Schepsis AA, Martini D, Corbett M. 1993.	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y
Slimmon D, Bennell K, Brukner P, Crossley K, Bell SN. 2002.	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y
Thein R, Tilbor I, Rom E, Herman A, Haviv B, Burstein G, et al. 2019.	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y
Vogels S, Ritchie ED, Hundscheid HP, van Someren K, Janssen L, Hoencamp R, et al. 2020.	Y	Y	Y	Y	Y	Y	Y	Y	N	N	Y
%	75.0	87.5	100.0	100.0	100.0	87.5	87.5	100.0	87.5	12.5	87.5

Table D - Quasi-Experimental Study Designs

Citation	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9
Blackman PG, Simmons LR, Crossley KM. 1998.	Y	N/A	N/A	N	Y	Y	Y	Y	Y
Schepsis AA, Gill SS, Foster TA. 1999.	Y	Y	Y	N	Y	Y	Y	Y	Y
Roscoe D, Roberts AJ, Hulse D, Shaheen AF, Hughes MP, Bennet AN. 2018.	Y	Y	N/A	Y	Y	Y	Y	Y	Y
%	100.0	66.66	33.33	33.33	100.0	100.0	100.0	100.0	100.0

Table E - Randomised Controlled Trials

Citation	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13
Ragab IM, Ali OI, Hamada HA, Radwan R, Mosaad D. 2019.	Y	Y	Y	Y	N	U	Y	N	Y	Y	Y	Y	Y
%	100.0	100.0	100.0	100.0	0.0	0.0	100.0	0.0	100.0	100.0	100.0	100.0	100.0

Appendix C – Results of Data Extraction

Table F - Characteristics of Included Case Control Study Designs

Study	Country	Setting/context	Participant characteristics	Group A description and sample	Group B description and sample	Exposures/variables measured	Description of main results
Fronek J, Mubarak SJ, Hargens AR, Lee YF, Gershuni DH, Garfin SR, et al. 1987.	United States of America	Hospital	Patients with exertional leg pain managed surgically with fasciotomy (one patient opted for fascial closure due to muscle hernia)	N=18, 10F 8M (28 compartments), mostly runners, (12 patients - 22 compartments - underwent fasciotomy)	N=14	ICP Pain Function Complications	Good results from surgery in almost all patients, few complications

Table G - Characteristics of Included Case Report Study Designs

Study	Country	Setting/ context	Participant characteristics	Patients	Description of main results
Berg K, Cuppett M. 2002.	United States of America	Hospital	55-year-old male with anterolateral leg tightness induced by exercise.	Patient with long history of exertional leg pain. He had been diagnosed with Type 1 diabetes at age 12. No complications or sequelae of diabetes had developed since the diagnosis. His diabetes was well controlled.	Full return to normal running 5 weeks post-surgery
Bresnahan JJ, Hennrikus WL. 2015.	United States of America	Clinic	A 15-year-old female soccer player	Patient was diagnosed with CECS of anterior compartment through ICP measurement and underwent surgical fasciotomy	Patient returned to normal activity 12 weeks following surgery
Collins CK, Gilden B. 2016.	United States of America	Outpatient Clinic	Male with CECS of bilateral anterior and posterior compartments	34-year-old male competitive triathlete underwent 14 weeks of functional manual therapy (23 visits over 3.5 months)	At discharge, the patient had returned to running pain free as well as training for an Olympic distance triathlon. ICP measures improved, 3 year follow-up patients remained pain-free
Drigny J, Reboursiere E, Desvergee A, Ruet A, Hulet C. 2019.	France	Clinic	Male with chronic exertional leg pain in both legs	Patient presented with PAES and CECS, and underwent fasciotomy of two compartments	Full recovery at 6 months.
Finnoff JT, Johnson W. 2020.	United States of America	Clinic	Female runner with exertional leg pain	Patient underwent ultrasound-guided fasciotomy	Full recovery at 9 month follow-up

Finnoff JT, Rajasekaran S. 2016.	United States of America	Clinic	Female lacrosse player with history of bilateral exertional leg pain	Patient underwent ultrasound-guided fascial fenestration	Back to sport at 1/52 with no pain, 18/12 follow-up all activities with no pain
Flautt W, Miller J. 2013.	United States of America	Military	25 year old male with painful pressure and tightness	Patient underwent 8 weeks of conservative management followed by fasciotomies	Full recovery at 12 week follow-up
Hutto WM, Schroeder PB, Leggit JC. 2019.	United States of America	Military	23 year old male active duty officer with progressive bilateral exertional lower limb pain	Patient received BoNT-A injections into affected compartments	Full recovery at 10/12 follow up, foot-drop at 1/52 post which resolved at 6/12
Kitajima I, Tachibana S, Hirota Y, Nakamichi K, Miura K. 2001.	Japan	Hospital	17-year-old female badminton player with exertional leg pain	Patient underwent 1-portal endoscopic fasciotomy	full recovery at 2/12 post surgery
Masukawa S, Watanabe H, Tsuruta T. 1992.	Japan	Clinic/Hospital	17-year-old female with bilateral leg pain	Patient previously received fasciotomy twice per leg. Afterward she received conservative treatment with orthosis for 7/12, followed by another fasciotomy, and 3/12 an additional fasciotomy was performed of the right ankle joint.	Initial failed fasciotomies, and an additional failed fasciotomy of the right side. On re-operation, it appeared that previous surgery had scarred to the point that it produced similar tension.
Tubb CC, Vermillion D. 2001.	United States of America	Military	24-year-old female army officer with exertional left leg pain following a direct blow to the leg	Patient underwent single-incision anterior compartment fasciotomy	2/52 post-op patient reported great improvement in pain (2/10 VAS) but with c/o a bulging sensation throughout the anterior compartment that inhibited her return to vigorous exercise.
Truex N, Menge TJ. 2018.	United States of America	Clinic	24-year-old-female with acute-on-chronic progressive right leg pain.	Patient underwent minimally-invasive four-compartment fasciotomies on right leg, followed by the left leg approximately 6/52 post op.	6/52 following second procedure, patient returned to full activity without complications.
Tjeerdsma J. 2016.	United States of America	Hospital	27-year-old Male with bilateral exertional leg pain	Patient underwent complete 4-compartment fasciotomy of right leg, anterior+lateral compartments on left	Significant improvements in LEFS score and FAAM outcomes in first 9 days following surgery. Similar results in range of motion of knee and ankle. Complete fasciotomy resulted in decreased sensation due to incision and infection. Full return to function at 18/12 post-op
Ota Y, Senda M, Hashizume H, Inoue H. 1999.	Japan	Clinic	19-year-old female basketball player with bilateral exertional leg pain	Patient underwent bilateral endoscopic fasciotomies	Full recovery and normal ICP 3/12 post-op

Snowden J, Becker JA, Brosky JA, Hazle C. 2014.	United States of America	Clinic	18-year-old female field hockey player with bilateral chronic lower leg pain	Patient underwent 9 weeks of conservative therapy. followed by bilateral fasciotomy of anterior+lateral compartments	Patient showed good improvement with conservative therapy, however when progressing to running on asphalt her symptoms recurred (at 9 weeks post-intervention). 2/12 post-surgery the patient was asymptomatic and able to run 2-3 miles per week. 6/12 post-surgery she had shown excellent improvements in FAAM scores.

Table H – Characteristics of Case Series Study Designs

Study	**Country**	**Setting/ context**	**Participant characteristic s**	**Groups**	**Outcomes measured**	**Description of main results**
Zimmermann WO, Hutchinson MR, Van den Berg R, Hoencamp R, Backx FJG, Bakker EWP. 2019.	Netherlands	Military	Military patients diagnosed with ant-CECS or ant-CECS+MTSS	CECS - N=37 - CECS+MTSS - N=38	Symptom recurrence SANE score Failure/success/return to activity	57% of patients able to return to active duty without surgery at 2 year follow-up
de Bruijn JA, van Zantvoort APM, Hundscheid HPH, Hoogeveen AR, Teijink JAW, Scheltinga MR. 2019.	Netherlands	Hospital	Patients with CECS of the anterior compartment	N=64 (120 legs), 36F 28M, underwent semi-blind fasciotomy of the anterior compartment	Symptom intensity (including pain, weakness, tightness, etc) Sensation at rest	SPN Not injured in any of the patients involved in the study General good results.
Zimmermann W, Linschoten C, Beutler A. 2017.	Netherlands	Military	Soldiers with exercise-related leg pain	CECS - N=2, 1M 1F,CECS + MTSS - N=13, 9M 4F,	SANE Score Patient satisfaction Recurrence	Good results obtained in majority of all patients
Simpson C, Roscoe D, Hughes S, Hulse D, Guthrie H. 2020.	United Kingdom	Military	Patients diagnosed with bilateral CECS of the anterior compartment through ICP measurement	N=41 patients underwent fasciectomy for anterior CECS	Military grading for locomotion FAAM FAAM SS EILP-G	46% of patients improved military fitness grading 22% returned to "full fitness"
Maffulli N, Loppini M, Spiezia F, D'Addona A, Maffulli GD. 2016.	Italy	Hospital	Patients diagnosed with CECS of the Ant or Ant+Lat compartment(s)	Anterior compartment - N=10(16 legs), 7M(12 legs) 3F(4 legs) - underwent single minimal incision fasciotomy of affected compartmentsAnt+Lat compartments - N=8(11 legs), 5M(8 legs) 3F(3 legs) - underwent single minimal	Short-Form Healthy Survey-36 (SF-36) European Quality of Life-5 Dimension (EQ-5D) Return to sport Relief of symptoms	High overall satisfaction, all patients able to continue sport following surgery at mid-term.

				incision fasciotomy of affected compartments		
Roberts AJ, Krishnasamy P, Quayle JM, Houghton JM. 2015.	United Kingdom	Military	Military patients diagnosed with CECS of the anterior compartment of the leg	N=98 (189 legs), M=170 F=19, underwent fasciectomy of the anterior compartment	Service evaluation Effect of pre-surgery ICP on outcome	48% of patients showed either no change or worsening of lower limb function following intervention Less than 40% patients graded as fully fit 2 years after surgery
Edmundsson D, Svensson O, Toolanen G. 2008.	Sweden	Hospital	Patients with diabetes and CECS of the leg	9 (responding) patients underwent fasciotomy of the anterior and lateral compartment	Walking time to stop due to pain Patient satisfaction/outcome (Schepsis 1994)	Walking time improved to unlimited in 8/9 patients Most patients reported good or excellent outcomes
Wittstein J, Moorman CT, Levin LS. 2010.	United States of America	Hospital	Patients with CECS of the anterior compartment of the leg	Anterior Isolated - N=2 (3 legs), 1M (1 leg) 1F (2legs) - underwent endoscopic compartment releaseAnterior and lateral - N=3 (6 legs), 2M (4 legs) 1F (2legs) - underwent endoscopic compartment releaseAnterior and posterior(sup&/ deep) - N= 4 (5 legs), 1M (1 leg) 3F (4 legs) - underwent endoscopic compartment release	Symptom recurrence return to sport	All patients had symptoms alleviated one patient was not able to return to play
Wieczorek V, Luciani JF, Brunet-Guedj E, Feugier P, Thevenon A. 2012.	France	Hospital	Patients diagnosed with CECS of the leg	n=12, Anterior compartment, underwent surgical decompression through fasciotomy	Satisfaction Return to activity Correlation with BMI	BMI may play a role in patient satisfaction post-op
van Zantvoort APM, de Bruijn JA, Winkes MB, Hoogeveen AR, Teijink JAW, Scheltinga MR. 2017.	Netherlands	Hospital	Patients with recurrent or ongoing CECS	Total N68, 42F, 26MSuspected Recurrent CECS after fasciotomy for ant-CECS - N=28, received re-ICP measurementRe-ICP Measurement	Activity cessation/modification ICP levels	5 surgical and 3 non-surgical ant-CECS patients retained elevated ICP

				for Ongoing Suspicion of CECS After a Previously Normal ICP - N=13, received re-ICP measurement		
van Zantvoort APM, de Bruijn JA, Hundscheid HPH, van der Cruijsen-Raaijmakers M, Teijink JAW, Scheltinga MR. 2018.	Netherlands	Hospital	Patients diagnosed with CECS through ICP values	Lateral and Anterior CECS - N=14(25 legs), 5F(9 legs) 9M(16 legs), underwent fasciotomyLateral, Anterior, and Posterior CECS - N=4(5 legs), 3F(4 legs) 1M(1 leg), underwent fasciotomy	Operative outcome Symptom severity Return to sport	4 years after surgery 1 in 3 patients with lateral CECS rated their outcomes as excellent or good
Van der Wal WA, Heesterbeek PJ, Van den Brand JG, Verleisdonk EJ. 2015.	Netherlands	Hospital - Military	Patients with CECS of the lower leg who underwent ICP of the anterior compartment	Overall: N=12 (21 legs), 11M 1FFasciotomy - N=6 (10 legs) - patients received fasciotomy of the anterior compartment No Fasciotomy - N=6 (11 legs) - patients underwent non-surgical management	Patient satisfaction ICP (average) Presence of surgical complications	Surgical patients - 3 free of complaints and 3 had significant decrease in complaints at 6/52 post-op Mean ICP of 36 immediately after exercise at 6/52 post-op No Fasciotomy - no significant change in ICP at follow-up
Schepsis AA, Fitzgerald M, Nicoletta R. 2005.	United States of America	Hospital	Athletes with unilateral ant-CECS who had previously had surgery for the affected compartment	N=18, 13F 5M - underwent repeat fasciotomy	Symptom recurrence Return to activity	Generally good satisfaction and return to activity - patients with SPN entrapment showed best results
Kramer DE, Pace JL, Jarrett DY, Zurakowski D, Kocher MS, Micheli LJ. 2013.	United States of America	Hospital	Patients with symptomatic muscle herniation	Primary herniaPostsurgical herniaUnderlying ant-CECS - N=6, 2F 4M, who underwent surgical decompression via fasciotomy	Satisfaction with surgery Return to sport Residual symptoms	CECS group showed best satisfaction with intervention, residual symptoms in 50% of ant-CECS patients following surgery
Isner-Horobeti ME, Dufour SP, Blaes C, Lecocq J. 2013.	France	Hospital	Moderately trained patients with anterior or anterolateral CECS	N=16, 13M 3F (25 legs - 25 anterior and 17 lateral compartments) received BoNT-A injections into the anterior or anterior and	ICP (IMP) Exertional pain Muscle strength (MRC)	One patient had no change following intervention and was referred for a successful fasciotomy - full recovery after 5/12 IMP; one patient became asymptomatic but IMP remained high.

				lateral compartment		The other 14 patients had 59 to 68% decrease in IMP Exertional pain; disappeared completely in the follow-up period (9/12) in 15 patients - less than 1/12 in 10 patients. All could exercise more at follow-up than initially. Strength; no correlation between BoNT-A dose and muscle strength. Muscle strength rated normal for all muscle at 4.4(±1.6)/12 follow up.
Irion V, Magnussen RA, Miller TL, Kaeding CC. 2014.	United States of America	Athletic Cohort	Elite athletes with CECS of the leg	Anterior and lateral compartment release - N=11, 5M 6F (16 legs)4 Compartment release - N=2, 1M 1F (4 legs)	Return to activity at previous level Symptom recurrence	4 compartment release group - able to return to previous level of sport with no return of symptoms Ant + lat release group - 2 unable to return to sport and had symptom recurrence. 2 others able to return to sport and had some return of symptoms but were able to maintain elite level of play.
Gatenby G, Haysom S, Twaddle B, Walsh S. 2017.	New Zealand	Hospital	Active patients diagnosed with anterolateral compartment syndrome	n=20, 8M 12F, Patients underwent isolated anterolateral fasciotomy.	Return to activity Level of activity Pain Satisfaction Ongoing symptoms CECS recurrence Major complications	90% of participants able to return to previous levels of activity or higher.
Finestone AS, Noff M, Nassar Y, Moshe S, Agar G, Tamir E. 2014.	Israel	Clinic	Patients who underwent elective anterior compartment fasciotomy for CECS	N=35 - patients had received surgical intervention - elective anterior compartment fasciotomy for CECS .	Complications Satisfaction Pain	Complications - SPN injury in 3 legs (3 patients), one requiring reoperation Mean pain score improved significantly 29% of patients would have declined surgery had they known their outcomes
Drexler M, Rutenberg TF, Rozen N, Warschawski Y, Rath E, Chechik O, et al. 2017.	Israel	Hospital	Patients diagnosed as having CECS	n= 54 (95 legs), 49M 4F, underwent single minimal incision fasciotomy of the anterior and lateral compartment	Numerical analog scale (NAS) Tegner activity score quality-of-life (SF-12)	75.5% of patients reported satisfactory outcomes Overall improvement in all scores average of 50.1/12 follow-up 25 surgical complications identified - symptom recurrence =8
Diebal AR, Gregory R, Alitz C, Gerber JP. 2012.	United States of America	Military	Patients diagnosed with CECS who were enrolled for surgical	10 patients underwent gait retraining to adopt forefoot strike technique	kinematic and kinetic measurements LLOS SANE ICP Pain (VAS) Running performance	All patients showed great improvements in all outcomes measured at 6/52 follow-up All patients reported even

			intervention (fasciotomy)			further improvement at 1 year follow-up All patients avoided surgical intervention
de Bruijn JA, van Zantvoort AP, Winkes MB, Raaymakers L, van der Cruijsen-Raaijmakers M, Hoogeveen AR, et al. 2015.	Netherlands	Athletic Medical Center	Patients with leg complaints suggestive of bilateral ant-CECS	N=14, 5M 9F (28 legs) underwent fasciotomy	Pain, tightness, cramps, muscle weakness, sensibility measured via a questionnaire Current functional status and symptoms assessed using questionnaire	1 leg had complications - superficial infection treated with a 7 day course of antibiotics 2/52 post-op no other cases of disturbed wound healing. self-reported recovery in the 14 responders was 4 weeks on average (1-8 weeksrange) 21/12 post-op all outcomes measured had improved significantly Overall outcomes reported by patients were; excellent=4, good=4, fair=3, poor=1, bad=1
Bell S. 1986.	Australia	Hospital	Males with symptoms 6/12 following decompression of the anterior compartment of the leg	N=5, all underwent fasciotomy and fasciectomy.	Presence of leg pain ICP	Decrease in ICP values and absence of pain in the three patients with follow-up at 6 months
Beck JJ, Tepolt FA, Miller PE, Micheli LJ, Kocher MS. 2016.	United States of America	Paediatric Hospital	Patients 18 years and younger that underwent fasciotomy for CECS	Total= 155, 136F 19M - Reoperation - N=27 (47 legs - 43F 4M)No Reoperation - N=108 (203 legs - 175F 28M)	Laterality Symptom type (pain, cramping, numbness) Symptom duration Primary sport(s) Herniation Previous treatment attempt	Negative correlation between isolated anterior compartment release and outcomes - higher rate of recurrence than in 4-compartment release. Worse results in patients with initial lower pressures 28 of 250 legs had wound complications 33% of 4-compartment releases had infection/dehisence compared to 8% of anterior/lateral alone
Balius R, Bong DA, Ardèvol J, Pedret C, Codina D, Dalmau A. 2016.	Spain	Hospital	Elite national athletes with chronic exertional compartment syndrome involving the anterior compartment confirmed by intracompartmental pressure testing, who had failed	7 Patients - 9 lower extremities with ant-CECS underwent Ultrasound-Guided Fasciotomy in affected anterior compartment	Final Pain Score Activity Level Return to play	Most patients returned to pre-surgical activity and had improved pain

			conservative (cessation of the provocative activity and stretching under the guidance of physical therapy)			

Table I - Characteristics of Included Cohort Study Designs

Study	**Country**	**Setting/ context**	**Participant characteristic s**	**Groups**	**Outcomes measured**	**Description of main results**
Verleisdonk EJ, Schmitz RF, van der Werken C. 2004.	Netherlands	Hospital	Adults with exertional pain in the lower leg	N=53 (100 legs) , 47M 6F, Patients with CECS diagnosed through ICP measurement that underwent fasciotomy of the anterior compartment	ICP Measures Pain Herniation presence/absence	83% success rate Significant change in post-exercise pressure measures following fasciotomy
Vogels S, Ritchie ED, Hundscheid HP, van Someren K, Janssen L, Hoencamp R, et al. 2020.	Netherlands	Hospital Cohort	Patients Presenting with CECS (additional data received for ant-CECS) diagnosed with Pedowitz criteria, who underwent Fasciotomy or Conservative treatment (non-standardised)	Surgical Intervention ant-CECS- N=146, 74M 72FConservativ e Intervention ant-CECS - N=18, 10M 8F	Patient reported satisfaction Success or Failure (based on above) Return to activity	Majority return to activity at lower level in both groups higher return in conservative vs surgical patients
Thein R, Tilbor I, Rom E, Herman A, Haviv B, Burstein G, et al. 2019.	Israel	Hospital	Patients with positive CECS results of the anterior compartment of the leg who underwent fasciotomy or conservative management	No Surgery - N=12, M10 F2 - 20 legs Surgery - N=31, M26 F5 - 54 legs	Pain, Tegner score, SF-36 form, Return to pre-symptomatic activity	Greater results overall for surgery vs conservative group

Slimmon D, Bennell K, Brukner P, Crossley K, Bell SN. 2002.	Australia	Hospital Cohort	Patients diagnosed with CECS who underwent unilateral or bilateral compartment fasciotomy with partial fasciectomy	Anterior compartment surgery only - N=21, 7M 14FCombined Surgery - N=15, 7M 8F	Subject perception of surgical outcome Pain Exercise levels Effect of Symptom Duration on Surgical Outcome Multiple operations Surgical complications	Surgical technique involving fasciotomy with partial fasciectomy for chronic exertional compartment syndrome is generally successful in the short term but less so in the long term
Schepsis AA, Martini D, Corbett M. 1993.	United States of America	Hospital	Patients diagnosed with CECS who underwent fasciotomy	Ant-CECS - N=16 (26 limbs) - 10M 6F	Return to activity subjective questionnaire	15/16 patients had excellent results and return to prior activity levels
Packer JD, Day MS, Nguyen JT, Hobart SJ, Hannafin JA, Metzl JD. 2013.	United States of America	Outpatient Facility	Patients with positive ant-CECS diagnoses who had failed nonoperative management and chose to either continue nonoperative management or undergo fasciotomy	No Surgery - N=27 (50 legs), 16F 11MSurgery - N=72 (125 legs), 52F 21M	Success rate return to sport satisfaction complications	Better outcomes with surgical vs conservative Mx younger age and single compartment release associated with greater outcomes
Cook S, Bruce G. 2002.	Australia	Military	Military personnel who underwent surgical decompression via fasciotomy and had failed nonsurgical management	Anterior Compartment surgery - N=8 (16 legs), 2F 6MAnterolateral - N=1 (2 legs), 1MFour compartments - N=5 (9 legs), 2F 3M	Clinical results PFT result Complications	Decompressive fasciotomy is effective treatment of compartment syndrome after failure of conservative treatment
Calvelli N, Verges S, Rousseaux-Blanchi MP, Edouard P, Guinot M. 2020.	France	Athletic Cohort	Elite Nordic Skiers who underwent Fasciotomy for CECS of the anterior compartment of the leg	Biathletes - 12 CECS cases 6F 6M - all underwent fasciotomy Cross-Country Skiers - 6 CECS cases 3F 3M - all underwent fasciotomy	Functional outcomes of CECS surgery and return to competition based on three criteria; subjective evaluation, objective comparison of French Ski Federation classification of the skier, and evolution of the skier's selection in French national teams (e.g. junior -> senior A/B)	The functional outcomes of the surgery, which was performed in all athletes with CECS, was satisfactory and allowed early return to performance in these elite Nordic skiers.

Table J – Characteristics of Included Quasi-Experimental Study Designs

Study	Country	Setting/ context	Participant characteristics	Groups	Outcomes measured	Main description of results
Roscoe D, Roberts AJ, Hulse D, Shaheen AF, Hughes MP, Bennet AN. 2018.	United Kingdom	Military	Adult males (age 18-40) in active military service, with symptoms of CECS or those who had undergone surgical management for CECS	PT - 20 males with symptoms consistent with ant-CECS who had yet to undergo formal treatmentCON - 20 male controls who were asymptomaticPTSURG 20 males who had undergone surgical fasciotomy for CECSPTSURG-NR 8 of the males who had undergone surgical fasciotomy for CECS - Subdivided as "non-responders" to surgical interventionPTSURG-R 12 of the males who had undergone surgical fasciotomy for CECS - Subdivided as "responders" to surgical intervention	Dynamic Intramuscular Compartment Pressure using a precalibrated Millar Mikro-Cath electronic transducer-tipped catheter which was inserted into the tibialis anterior muscle	Patients with successful fasciotomy demonstrate ICP values like those of asymptomatic controls.
Schepsis AA, Gill SS, Foster TA. 1999.	United States of America	Hospital	Athletes involved in running sports who had documented exertional anterior compartment syndrome without any suspicion of lateral compartment syndrome	Group 1 - 15 limbs that received anterior compartment release onlyGroup 2 - 15 limbs that received both anterior and lateral compartment releases	Satisfaction according to subjective questionnaire results	Overall, 90% satisfactory outcome. Greater satisfaction in single compartment release group compared to ant+lat (93% vs 87%)
Blackman PG, Simmons LR, Crossley KM. 1998.	Australia	Clinic	Athletes with suspicion of CECS.	7 Patients - 6 men and 1 woman, aged 21-29 years. All described running as most provocative.	ICP Total work to onset of pain (J) Pain	Improvements reported for all patients

Table K – Characteristics of Included Randomised Controlled Trial Study Designs

Study	**Country**	**Setting/ context**	**Participant characteristics**	**Groups**	**Outcomes measured**	**Description of main results**
Ragab IM, Ali OI, Hamada HA, Radwan R, Mosaad D. 2019.	Egypt	University Clinic	30 participants aged between 18 to 35 years, diagnosed clinically with bilateral exertional anterior compartment syndrome of the lower leg. for more than 3 months, with a Visual analog scale (VAS) Pain score > 4.	Group A - 15 people who received ASTM therapy Group B - 15 people who received intermittent massage (effleurage and cross fiber frictions)	Pain using the visual analogue scale Function using the lower extremity functional scale Range of motion of ankle dorsiflexion	Both groups showed improvement following intervention Significant difference in all outcome measures for group A versus group B following intervention

Appendix D – Reasons for Exclusion of Full Text

Reason for Exclusion	# Articles Excluded (n=187)
No separate information for ant-CECS	25
No follow-up following intervention	12
Author unable to provide further information	17
Outcomes do not fit inclusion criteria	153
Not diagnosed using ICP	19

ant-CECS – Chronic exertional compartment syndrome of the anterior compartment of the leg