The Effects of Anterior Compartment Fasciotomy on Intramuscular Compartment Pressure in Patients with Chronic Exertional Compartment Syndrome.

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ABSTRACT

Background

Patients with Chronic Exertional Compartment Syndrome (CECS) have pain during exercise that usually subsides at rest. Diagnosis is usually confirmed by measurement of intramuscular compartment pressure (IMCP) following exclusion of other possible causes. Management usually requires fasciotomy but reported outcomes vary widely. There is little evidence of the effectiveness of fasciotomy on IMCP. Testing is rarely repeated post-operatively and reported follow-up is poor. Improved diagnostic criteria based on pre-selection and IMCP levels during dynamic exercise testing have recently been reported.

Objectives

1. To compare IMCP in 3 groups, one with classical symptoms and no treatment and the other with symptoms of CECS who have been treated with fasciotomy and an asymptomatic control group.
2. Establish if differences in IMCP in these groups as a result of fasciotomy relate to functional and symptomatic improvement.

Methods

Twenty subjects with symptoms of CECS of the anterior compartment, 20 asymptomatic controls and 20 patients who had undergone fasciotomy for CECS were compared. All other possible diagnoses were excluded using rigorous inclusion criteria and MRI. Dynamic IMCP was measured using an electronic catheter wire before, during and after participants exercised on a treadmill during a standardised 15-minute exercise challenge. Statistical analysis included t-tests and ANOVA.
Results

Fasciotomy results in reduced IMCP at all time points during a standardised exercise protocol compared to pre-operative cases. In subjects responding to fasciotomy there is a significant reduction in IMCP below that of pre-operative groups (p<0.001). Post-operative responders to fasciotomy have no significant differences in IMCP from asymptomatic controls (p=0.182).

Conclusion

Fasciotomy reduces IMCP in all patients. Larger studies are required to confirm that the reduction in IMCP accounts for differences in functional outcomes and pain reductions seen in post-operative patients with CECS.

Key Findings

1. Post-fasciotomy subjects demonstrate lower IMCP values compared to pre-operative symptomatic subjects at all time points.

2. Subjects who improve function and reduce pain after fasciotomy demonstrate no significant differences in dynamic IMCP measurement to normal controls.
INTRODUCTION

Exercise Induced Leg Pain (EILP) accounts for a significant clinical burden for those practitioners dealing with exercising populations particularly military recruits, service personnel and athletes in running and jumping sports.[1-4] Various studies estimate the prevalence of Chronic Exertional Compartment Syndrome (CECS) in patients with EILP as ranging from 10-60% depending on the diagnostic criteria adopted although it has been suggested to be even higher in military populations[1-8]. The pathology is proposed to occur as a result of tissue ischaemia caused by oedematous muscle swelling within a relatively inextensible myofascial compartment resulting in elevated pressure and decreased tissue perfusion.[9]

The patient with CECS complains of a crescendo of pain triggered by activity that is relieved within minutes of rest sometimes accompanied by temporary neurological impairments.[2,4-6,10,11] Patients report fullness, tightness, or increased girth over the antero-lateral aspect of the leg and often describe gait disturbances when symptoms are fulminant.[12-17] Observation and examination of the patient at rest is frequently unrewarding.[16,18-21]
Diagnosis of CECS usually rests upon the measurement of intramuscular compartment pressure (IMCP). The most widely adopted criteria for diagnosis are those of Pedowitz whereby IMCP is measured at discrete time points before (supine) and after a non-standardised exercise challenge. One of; Pre-exercise >15mmHg, 1 minute post-exercise >30mmHg, 5 min post-exercise >20mmHg[22] are required for a positive diagnosis. Barnes described the dynamic measurement of IMCP during exercise recommending a diagnostic cut-off of over 50mmHg[23] although in practice this is rarely adopted.[21,24] Systematic reviews of the published literature have repeatedly questioned the validity of these existing criteria in confirming the diagnosis of CECS and highlighted the lack of control and normative IMCP data.[25,26] Significantly improved diagnostic criteria using standardised patient selection criteria and dynamic IMCP measurement during a phased treadmill protocol have recently been published. These improved criteria demonstrated a positive likelihood ratio (LR+) of 12.5 when a cut-off of 105mmHg was used during phase 2 of an incremental exercise protocol or LR+ of 6.8 when 89mmHg is used across all phases of testing.[27]

In accordance with this pathophysiological model, the goal of treatment in CECS is the reduction in pain symptoms and improved exercise tolerance. When IMCP testing is positive; patients are usually offered surgical fasciotomy to decompress the affected compartment.[9,28-30] Various different fasciotomy techniques have been described, but all involve the division of the fascia overlying the affected compartment either with or without the removal of a fascial window[9,31-35]. A successful response to fasciotomy for CECS can thus be defined as minimal or no pain associated with good functional recovery.[1,36-38]

Reported outcomes from surgery vary widely. Irion et al reported that 84.6% of elite athletes were able to return to previous activity levels[38] and Howard reported a
success rate of 81%[39], but concerns have been expressed that military populations typically have worse outcomes. Waterman reported post-operative data for CECS in the U.S. military demonstrating a 45% rate of symptom recurrence, a 28% chance of not being able to return to full activity, a 6% rate of revision surgery, and a 16% complication rate whilst 17% required a medical discharge from the military due to persistent symptoms of CECS.[40,41] This corresponds with recently published data from the UK military.[42] Unfortunately the literature also suggests that follow-up periods in mainstream clinical practice are frequently insufficient to detect complications[1,21] resulting in a possible overestimation of success rates.[26] Where follow-up studies have been reported, no validated outcome measure has been used.

The aim of this study was therefore to investigate the effect of surgical management of CECS of the anterior compartment by examining the changes in dynamically measured IMCP and establishing if these relate to post-operative functional and symptomatic improvement.

METHODS

Twenty consecutive male cases (mean age 27.5, sd= 4.9) with symptoms consistent with CECS of the anterior compartment of the leg that had yet to undergo any formal treatment (PT), 20 cases (mean age 30.35, sd=4.7) that had undergone surgical fasciotomy for CECS (PTSURG), and 20 asymptomatic male controls (mean age 28.25, sd=7.4) (CON) were recruited. Measurements were taken from both legs by a single clinician. The diagnosis of CECS was established from typical symptoms, with other pathologies excluded using clinical examination and MRI. Cases were recruited from the Lower Limb Pain clinic at the Defence Medical Rehabilitation Centre, Headley Court (DMRC) and a database of post-surgical cases. Controls were
recruited from the UK Armed Forces. All participants gave informed consent. The Ministry of Defence Research Ethics Committee granted ethical approval.

The inclusion criteria were: Male; Aged 18-40 (representing the typical age-range of UK military service personnel), in ongoing military service. PT cases required the following: symptoms of EILP consistent with a diagnosis of anterior compartment CECS, a negative MRI of the affected limb(s) and lumbar spine, no diagnosis other than CECS more likely, absence of multiple lower limb pathologies, and, no previous lower limb surgery. A detailed comparison of PT and CON subjects has been previously reported. [27] CON subjects were included when they had: no lower limb pain in previous 12 months; no current pain at any site, including during exercise; no reliance on orthotics; and, could run pain-free for up to 20 minutes. PTSURG cases were included if they: underwent fasciotomy within the UK Defence Medical Services between 6 and 60 months previously and remained in military service.

**Dynamic Compartment Pressure Testing**

Hair was removed and skin cleansed with alcohol at an insertion site 3cm distal and 3cm lateral to the tibial tuberosity, prior to infiltration of the overlying skin with 10mL 1% lidocaine local anaesthetic. A pre-calibrated electronic Millar Mikro-Cath™ catheter wire was inserted into the *Tibialis Anterior* muscle.

Participants were placed in a supine position with the knee extended and the ankle in neutral dorsiflexion. The catheter was then inserted at 30-45 degrees to the skin in an inferior direction using a modified Seldinger technique. The tip was advanced in order to lie in the centre of the muscle belly approximately 3cm beyond the point of penetration of the fascia where a large body of uniform pressure has been shown to exist.[43] Tip location was then checked through manual palpation of the overlying

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Participants then followed a standardised exercise protocol with IMCP recorded throughout the following phases:

a. Resting supine for 2 minutes.

b. Standing in a relaxed resting state for 30 seconds.

c. Exercising on a treadmill (Woodway Desmo, USA) as per the following protocol:
   1. Carrying a standard military issue 15kg-weighted backpack wearing their usual footwear, walking pace set at 6.5km/h for 5 minutes on a level treadmill.
   2. Carrying 15kg backpack the treadmill incline increased to 5 degrees and walking pace set at 6.5km/h for 5 minutes.
   3. Backpack weight removed, treadmill incline set at 5 degrees and running pace set at 9.5km/h for 5 minutes.

   d. Resting supine for 5 minutes post-exercise recovery

Participants were encouraged to continue the test for as long as tolerated but were allowed to terminate the test at any time if pain became excessive. Pain scores were recorded every minute throughout the test for each leg using a numerical rating scale of 0 (no pain) to 10 (worst pain imaginable). On completion of the exercise challenge, participants lay supine in a relaxed position for five minutes. At the end of this time, the catheters were removed. Participants were monitored throughout for bleeding from the catheter site.
Allocation of group membership

PTSURG were sub-defined as responders (PTSURG-R, n=12) or non-responders (PTSURG-NR, n=8) to surgical intervention. Responders were defined as being able to complete the entire protocol reporting pain scores less than or equal to 5/10 with post-protocol pain scores of less than 5/10. This was based on the maximal reported pain values within the CON group.

Statistical analyses

The mean IMCP was calculated for each phase described above using a custom Labchart script (ADInstruments, UK). The mean pressure over a 5 second period at 1-minute and 5-minutes post-exercise was recorded. The maximum pain score experienced during each phase was used for analysis. If participants stopped early, only completed time periods were used.

Descriptive statistics were obtained for all variables. All values are described as mean (sd) unless otherwise stated. Independent t-tests and ANOVA were carried out on parametric variables to compare variables between groups. Results were consistent between both methods. The assumption of equal variance was tested using Levene’s test and the resulting test result adjusted if this was significant. The comparison of the CON and PT groups leading to the generation of the new diagnostic values has been reported previously.[27]

Alpha for all analyses was set to 0.05. SPSS (v.20, Chicago, USA) was used for all analyses.
RESULTS

Compartment pressure testing

All participants completed the exercise protocol to the end or the point of maximal pain. No further exercise testing was carried out after this point of maximal pain. Only 7 of 20 PT cases were able to complete the full graduated exercise challenge as the others experienced significant provocation of their symptoms. Thirteen PTSURG were able to fully complete the exercise protocol. Four PT and 2 PTSURG stopped early due to pain during exercise phase 2; a further 9 PT and 2 PTSURG cases stopped during exercise phase 3. One PTSURG stopped just after phase 1 for technical reasons and 2 PTSURG and 2 CON stopped during phase 3 for reasons unrelated to their condition or the testing procedure. No further testing was then conducted.

All PT and 3 CON described some degree of pain during the first phase in at least one leg. All PT, 13 PTSURG and 2 CON described some pain during phases 2 and 3 in at least one leg.
Table 1. Mean(number of legs tested, sd) for each group at each phase/ timepoint.

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unknown error resulted in loss of 4 participant data sets in calculating values for ex-

As per tables 1 and 2:

**PTSURG vs. CON**

PTSURG had significantly lower IMCP supine pre-exercise and significantly higher IMCP during phases 2 and 3 as well as during all phases combined. There were no differences in IMCP standing, during phase 1 or supine post-exercise.

**PTSURG-R vs. CON**
There were no significant differences in IMCP between PTSURG-R and CON for all phases/time points.

PTSURG-NR vs. CON
PTSURG-NR had significantly lower IMCP supine pre-exercise than CON. PTSURG-NR had significantly higher IMCP during phases 2 and 3. There were no significant differences in IMCP during standing or phase 1, across all exercise phases combined, or supine post-exercise although there was a trend towards significance in three of these.

PTSURG vs. PT
PTSURG had significantly lower IMCP than PT for all phases and time points.

PTSURG-R vs. PT
PTSURG-R had significantly lower IMCP than PT for all phases/time points.

PTSURG-NR vs. PT
PTSURG-NR had significantly lower IMCP than PT supine pre-exercise, standing, during phase 1 and 2, and during all phases combined. There were no significant differences during phase 3, and supine post-exercise.

PTSURG-R vs. PTSURG-NR
There were no significant differences supine pre-exercise, standing, during phase 1 or 2, during all phases combined, or supine post-exercise. Responders had significantly lower IMCP during phase 3.
<table>
<thead>
<tr>
<th></th>
<th>Supine</th>
<th>Stand</th>
<th>Ph 1</th>
<th>Ph 2</th>
<th>Ph 3</th>
<th>Ex-all</th>
<th>1-min post</th>
<th>5-min post</th>
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<td>0.400</td>
<td>0.020</td>
<td>0.006</td>
<td>0.050</td>
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<td>0.389</td>
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<td>0.182</td>
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<td>&lt;0.001</td>
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<td>0.008*</td>
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<td>PT vs PTSURG-NR</td>
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<td>0.549*</td>
<td>0.009</td>
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<td>0.476</td>
<td>0.144</td>
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Table 2 – p-values of Students’ t-test for comparisons between IMCP variables

*indicates that an adjusted value was used.
DISCUSSION

The currently accepted gold standard for the diagnosis of CECS is IMCP measurement however there is considerable criticism of the most commonly adopted diagnostic criteria. This is due to the lack of healthy controls and methodological limitations identified in previous studies.[26] When IMCP testing is considered positive, fasciotomy is usually recommended. Post-operative follow-up periods are typically short and often insufficient to identify complications, failures or recurrences. These factors likely result in an overestimation of the positive outcomes from fasciotomy in the literature. The most widely reported reasons for surgical failure include multiple pathologies within the same leg, misdiagnosis and poor surgical technique.[1,42]

The most widely accepted pathological model of CECS depending upon a rise in IMCP due to fascial restriction. Despite this, IMCP is rarely measured post-operatively in routine clinical practice and very few studies have investigated the change in IMCP that occurs after fasciotomy. Only one previous study has done this dynamically during an ambulant exercise protocol. However this study used the wick-catheter technique that had previously been identified as flawed (due to low frequency response) in this context[45,46]. Despite this limitation, the results reported in the dynamic setting were comparable with those identified previously. A standardised exercise protocol using dynamic IMCP testing was recently reported which has significantly improved the criteria for the diagnosis of CECS.[27]

Detmer et al.[32] reported that more than 90% of patients were “cured or significantly improved” with fasciotomy which is in accordance with rates reported by Styf and Schepsis.[47,48] In contrast, outcomes from surgery in military populations appear to be significantly lower.[41,42] Waterman et al.[40] retrospectively reported on a group of 611 military recruits (754 procedures), 44.7 % had symptom recurrence, 27.7 %
were unable to return to full activity, and 17.3% were referred for medical discharge. Recent data on a group of elite athletes reported an 86.4% return to sport at the same level as pre-operatively. However, a 30.8% recurrence of symptoms was also reported and it was acknowledged that the follow-up period of the study was relatively short and that success had been defined only on the basis of an initial return to activity[38]. It is worth considering however that, due to the nature of military service and the requirement for comprehensive data collection and long-term occupational follow-up, it might be the case that these figures are more representative of the ‘ground truth’ in CECS.

In line with the proposed pathophysiological model of CECS (i.e. restrictive anterior compartment fascia resulting in elevation of IMCP during activity), these data demonstrate that: fasciotomy results in a significant reduction of IMCP to a level not significantly different to normal controls; and below that of pre-operative cases in the resting states, both supine and standing. Post-operative IMCP is significantly lower than pre-surgical levels in those subjects with symptoms of CECS regardless of functional outcome from surgery. This is in line with previous studies using older techniques, less robust inclusion criteria and follow-up periods considered insufficient to detect complications.[1,3,45,47]

Responders to fasciotomy were defined as those post-operative cases able to complete the exercise protocol with tolerable pain levels at or below the highest of those of asymptomatic volunteers and with only mild residual post-protocol pain. This study demonstrates that in those cases responding to fasciotomy, in terms of both pain and treadmill running there is a significant reduction in IMCP that tends to revert cases towards the state of asymptomatic controls. There is a significant difference in IMCP at all time points and phases of the protocol between the pre-operative (PT) and post-operative responder (PTSURG-R) groups; however, there were no time
points at which there were any significant differences between the asymptomatic control (CON) group and the responders. We believe that this finding further advances the evidence for the intrinsic role of IMCP as the key driver of symptoms as well as diagnostic and treatment target in CECS.

In considering possible alternative reasons for failure to respond to fasciotomy in PTSRG-NR, work published by Mathis et al. since the completion of this study may provide useful insight. Their work investigating the effects of fasciotomy in swine models demonstrated that the length of incision of the fascia correlates to the subsequent post-operative IMCP. They suggested that an incision length of 90% of the compartment length likely represents a breakpoint zone beyond which IMCP is returned to near baseline values. [49]

It is likely that the low number of non-responders to fasciotomy and the failure of several of these to complete the protocol beyond phase 2 has played a key role in the failure to detect widespread significant differences in IMCP between PTSURG-R and PTSURG-NR in this study. Phase 2 is recognised as the most valuable diagnostic time point with the greatest discriminating potential in CECS [27]; and lower IMCP in PTSURG-R compared to PTSURG-NR was observed (although not significant in this relatively small sample). The lower IMCP overall meant that both group means were below the suggested 105mmHg diagnostic cut-off. During all other phases IMCP in PTSURG-R was lower than PTSURG-NR suggesting that a more powerful observation might be made with a larger study in the future.

**LIMITATIONS**

It is acknowledged that the availability of non-responders for this study may have itself have been influenced by non-continuance in military service due to ongoing symptoms. However, the aim of this study was to establish the effect of fasciotomy
on IMCP rather than compare outcomes rates per se. Due to the timing and nature of
the study (i.e. using a newly described diagnostic method and criteria) there was
insufficient time and numbers of potential participants available to conduct a
longitudinal study using the same cohort.

CONCLUSIONS

This is the first study to use the newly described IMCP testing technique to compare
post fasciotomy IMCP with controls and pre-fasciotomy CECS patients. The results
add further support for the traditional pathophysiological model of CECS and the role
of IMCP and fasciotomy in the management of CECS.

COMPETING INTERESTS

None

FUNDING

UK Ministry of Defence
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b. Standing in a relaxed resting state for 30 seconds.

c. Exercising on a treadmill (Woodway Desmo, USA) as per the following protocol:
   1. Carrying a standard military issue 15kg-weighted backpack wearing their usual footwear, walking pace set at 6.5km/h for 5 minutes on a level treadmill.
   2. Carrying 15kg backpack the treadmill incline increased to 5 degrees and walking pace set at 6.5km/h for 5 minutes.
   3. Backpack weight removed, treadmill incline set at 5 degrees and running pace set at 9.5km/h for 5 minutes.

d. Resting supine for 5 minutes post-exercise recovery

Participants were encouraged to continue the test for as long as tolerated but were allowed to terminate the test at any time if pain became excessive. Pain scores were recorded every minute throughout the test for each leg using a numerical rating scale of 0 (no pain) to 10 (worst pain imaginable). On completion of the exercise challenge, participants lay supine in a relaxed position for five minutes. At the end of this time, the catheters were removed. Participants were monitored throughout for bleeding from the catheter site,
Allocation of group membership

PTSURG were sub-defined as responders (PTSURG-R, n=12) or non-responders (PTSURG-NR, n=8) to surgical intervention. Responders were defined as being able to complete the entire protocol reporting pain scores less than or equal to 5/10 with post-protocol pain scores of less than 5/10. This was based on the maximal reported pain values within the CON group.

Statistical analyses

The mean IMCP was calculated for each phase described above using a custom Labchart script (ADI Instruments, UK). The mean pressure over a 5 second period at 1-minute and 5-minutes post-exercise was recorded. The maximum pain score experienced during each phase was used for analysis. If participants stopped early, only completed time periods were used.

Descriptive statistics were obtained for all variables. All values are described as mean (sd) unless otherwise stated. Independent t-tests and ANOVA were carried out on parametric variables to compare variables between groups. Results were consistent between both methods. The assumption of equal variance was tested using Levene’s test and the resulting test result adjusted if this was significant. The comparison of the CON and PT groups leading to the generation of the new diagnostic values has been reported previously.[27]

Alpha for all analyses was set to 0.05. SPSS (v.20, Chicago, USA) was used for all analyses.
RESULTS

Compartment pressure testing

All participants completed the exercise protocol to the end or the point of maximal pain. No further exercise testing was carried out after this point of maximal pain. Only 7 of 20 PT cases were able to complete the full graduated exercise challenge as the others experienced significant provocation of their symptoms. Thirteen PTSURG were able to fully complete the exercise protocol. Four PT and 2 PTSURG stopped early due to pain during exercise phase 2; a further 9 PT and 2 PTSURG cases stopped during exercise phase 3. One PTSURG stopped just after phase 1 for technical reasons and 2 PTSURG and 2 CON stopped during phase 3 for reasons unrelated to their condition or the testing procedure. No further testing was then conducted.

All PT and 3 CON described some degree of pain during the first phase in at least one leg. All PT, 13 PTSURG and 2 CON described some pain during phases 2 and 3 in at least one leg.
<table>
<thead>
<tr>
<th></th>
<th>Supine (mmHg)</th>
<th>Stand (mmHg)</th>
<th>Ph 1 (mmHg)</th>
<th>Ph 2 (mmHg)</th>
<th>Ph 3 (mmHg)</th>
<th>Ex-all (mmHg)</th>
<th>1-min post (mmHg)</th>
<th>5-min post (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PT</td>
<td>16.0 (40.4, 8)</td>
<td>36.1 (40.14, 8)</td>
<td>92.5 (40.25, 3)</td>
<td>113.4 (40.31, 3)</td>
<td>92.9 (40.28, 7)</td>
<td>99.5 (40.39, 25.1)</td>
<td>37.1 (39.19, 8)</td>
<td>27.4 (39.19, 8)</td>
</tr>
<tr>
<td>PTSURG</td>
<td>12.3 (39.5, 0)</td>
<td>22.0 (39.8, 3)</td>
<td>66.6 (39.19, 9)</td>
<td>64.3 (39.23, 7)</td>
<td>67.4 (33.23, 5)</td>
<td>72.5 (31.18, 5)</td>
<td>21.9 (39.11, 4)</td>
<td>18.5 (39.10, 6)</td>
</tr>
<tr>
<td>PTSURG-NR</td>
<td>11.1 (16.4, 6)</td>
<td>23.0 (16.7, 6)</td>
<td>68.3 (16.20, 5)</td>
<td>92.3 (16.23, 3)</td>
<td>80.6 (12.24, 2)</td>
<td>75.5 (12.18, 7)</td>
<td>25.1 (16.14, 7)</td>
<td>20.8 (16.14, 1)</td>
</tr>
<tr>
<td>PTSURG-R</td>
<td>13.1 (23.5, 1)</td>
<td>21.3 (23.8, 9)</td>
<td>65.4 (23.19, 9)</td>
<td>78.7 (23.22, 9)</td>
<td>60.0 (21.19, 9)</td>
<td>70.5 (19.18, 6)</td>
<td>19.7 (23.8, 0)</td>
<td>17.0 (23.7, 1)</td>
</tr>
<tr>
<td>CON</td>
<td>14.6 (40.4, 1)</td>
<td>24.6 (40.10, 8)</td>
<td>62.4 (40.24, 0)</td>
<td>71.7 (40.23, 3)</td>
<td>53.4 (40.18, 9)</td>
<td>62.6 (40.22, 0)</td>
<td>19.5 (38.7, 4)</td>
<td>15.6 (37.6, 2)</td>
</tr>
</tbody>
</table>

Table 1. Mean(number of legs tested, sd) for each group at each phase/ timepoint.

*unknown error resulted in loss of 4 participant data sets in calculating values for ex-all.

As per tables 1 and 2:

**PTSURG vs. CON**

PTSURG had significantly lower IMCP supine pre-exercise and significantly higher IMCP during phases 2 and 3 as well as during all phases combined. There were no differences in IMCP standing, during phase 1 or supine post-exercise.

**PTSURG-R vs. CON**
There were no significant differences in IMCP between PTSURG-R and CON for all phases/time points.

PTSURG-NR vs. CON

PTSURG-NR had significantly lower IMCP supine pre-exercise than CON. PTSURG-NR had significantly higher IMCP during phases 2 and 3. There were no significant differences in IMCP during standing or phase 1, across all exercise phases combined, or supine post-exercise although there was a trend towards significance in three of these.

PTSURG vs. PT

PTSURG had significantly lower IMCP than PT for all phases and time points.

PTSURG-R vs. PT

PTSURG-R had significantly lower IMCP than PT for all phases/time points.

PTSURG-NR vs. PT

PTSURG-NR had significantly lower IMCP than PT supine pre-exercise, standing, during phase 1 and 2, and during all phases combined. There were no significant differences during phase 3, and supine post-exercise.

PTSURG-R vs. PTSURG-NR

There were no significant differences supine pre-exercise, standing, during phase 1 or 2, during all phases combined, or supine post-exercise. Responders had significantly lower IMCP during phase 3.
<table>
<thead>
<tr>
<th></th>
<th>Supine</th>
<th>Stand</th>
<th>Ph 1</th>
<th>Ph 2</th>
<th>Ph 3</th>
<th>Ex-all</th>
<th>1-min post</th>
<th>5-min post</th>
</tr>
</thead>
<tbody>
<tr>
<td>CON vs</td>
<td>0.022</td>
<td>0.232</td>
<td>0.400</td>
<td>0.020</td>
<td>0.006</td>
<td>0.050</td>
<td>0.287</td>
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<td>PTSURG</td>
<td>0.006</td>
<td>0.595</td>
<td>0.389</td>
<td>0.004</td>
<td>&lt;0.001</td>
<td>0.073</td>
<td>0.069</td>
<td>0.068</td>
</tr>
<tr>
<td>CON vs</td>
<td>0.185</td>
<td>0.214</td>
<td>0.613</td>
<td>0.252</td>
<td>0.207</td>
<td>0.182</td>
<td>0.952</td>
<td>0.435</td>
</tr>
<tr>
<td>PTSURG-R</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PT vs</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.008</td>
<td>&lt;0.001</td>
<td>0.001</td>
<td>0.017</td>
</tr>
<tr>
<td>PTSURG</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PT vs</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.001</td>
<td>0.018</td>
<td>0.549</td>
<td>0.009</td>
<td>0.033</td>
<td>0.232</td>
</tr>
<tr>
<td>PTSURG-NR</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PT vs</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.005</td>
</tr>
<tr>
<td>PTSURG-R</td>
<td>0.222</td>
<td>0.525</td>
<td>0.659</td>
<td>0.077</td>
<td>0.013</td>
<td>0.476</td>
<td>0.144</td>
<td>0.276</td>
</tr>
<tr>
<td>PTSURG-NR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Table 2 – p-values of Students’ t-test for comparisons between IMCP variables

*indicates that an adjusted value was used.
DISCUSSION

The currently accepted gold standard for the diagnosis of CECS is IMCP measurement however there is considerable criticism of the most commonly adopted diagnostic criteria. This is due to the lack of healthy controls and methodological limitations identified in previous studies.[26] When IMCP testing is considered positive, fasciotomy is usually recommended. Post-operative follow-up periods are typically short and often insufficient to identify complications, failures or recurrences. These factors likely result in an overestimation of the positive outcomes from fasciotomy in the literature. The most widely reported reasons for surgical failure include multiple pathologies within the same leg, misdiagnosis and poor surgical technique.[1,42]

The most widely accepted pathological model of CECS depending upon a rise in IMCP due to fascial restriction. Despite this, IMCP is rarely measured post-operatively in routine clinical practice and very few studies have investigated the change in IMCP that occurs after fasciotomy. Only one previous study has done this dynamically during an ambulant exercise protocol. However this study used the wick-catheter technique that had previously been identified as flawed (due to low frequency response) in this context[45,48]. Despite this limitation, the results reported in the dynamic setting were comparable with those identified previously. A standardised exercise protocol using dynamic IMCP testing was recently reported which has significantly improved the criteria for the diagnosis of CECS.[27]

Detmer et al.[32] reported that more than 90% of patients were “cured or significantly improved” with fasciotomy which is in accordance with rates reported by Styf and Schepsis.[47,48] In contrast, outcomes from surgery in military populations appear to be significantly lower [41,42] Waterman et al.[40] retrospectively reported on a group of 611 military recruits (754 procedures), 44.7 % had symptom recurrence, 27.7 %
were unable to return to full activity, and 17.3 % were referred for medical discharge. Recent data on a group of elite athletes reported an 86.4% return to sport at the same level as pre-operatively. However, a 30.8% recurrence of symptoms was also reported and it was acknowledged that the follow-up period of the study was relatively short and that success had been defined only on the basis of an initial return to activity[38]. It is worth considering however that, due to the nature of military service and the requirement for comprehensive data collection and long-term occupational follow-up, it might be the case that these figures are more representative of the ‘ground truth’ in CECS.

In line with the proposed pathophysiological model of CECS (i.e. restrictive anterior compartment fascia resulting in elevation of IMCP during activity), these data demonstrate that: fasciotomy results in a significant reduction of IMCP to a level not significantly different to normal controls; and below that of pre-operative cases in the resting states, both supine and standing. Post-operative IMCP is significantly lower than pre-surgical levels in those subjects with symptoms of CECS regardless of functional outcome from surgery. This is in line with previous studies using older techniques, less robust inclusion criteria and follow-up periods considered insufficient to detect complications.[1,3,45,47]

Responders to fasciotomy were defined as those post-operative cases able to complete the exercise protocol with tolerable pain levels at or below the highest of those of asymptomatic volunteers and with only mild residual post-protocol pain. This study demonstrates that in those cases responding to fasciotomy, in terms of both pain and treadmill running there is a significant reduction in IMCP that tends to revert cases towards the state of asymptomatic controls. There is a significant difference in IMCP at all time points and phases of the protocol between the pre-operative (PT) and post-operative responder (PTSURG-R) groups; however, there were no time
points at which there were any significant differences between the asymptomatic control (CON) group and the responders. We believe that this finding further advances the evidence for the intrinsic role of IMCP as the key driver of symptoms as well as diagnostic and treatment target in CECS.

In considering possible alternative reasons for failure to respond to fasciotomy in PTSRG-NR, work published by Mathis et al. since the completion of this study may provide useful insight. Their work investigating the effects of fasciotomy in swine models demonstrated that the length of incision of the fascia correlates to the subsequent post-operative IMCP. They suggested that an incision length of 90% of the compartment length likely represents a breakpoint zone beyond which IMCP is returned to near baseline values. [49]

It is likely that the low number of non-responders to fasciotomy and the failure of several of these to complete the protocol beyond phase 2 has played a key role in the failure to detect widespread significant differences in IMCP between PTSURG-R and PTSURG-NR in this study. Phase 2 is recognised as the most valuable diagnostic time point with the greatest discriminating potential in CECS [27]; and lower IMCP in PTSURG-R compared to PTSURG-NR was observed (although not significant in this relatively small sample). The lower IMCP overall meant that both group means were below the suggested 105mmHg diagnostic cut-off. During all other phases IMCP in PTSURG-R was lower than PTSURG-NR suggesting that a more powerful observation might be made with a larger study in the future.

LIMITATIONS

It is acknowledged that the availability of non-responders for this study may have itself have been influenced by non-continuance in military service due to ongoing symptoms. However, the aim of this study was to establish the effect of fasciotomy
on IMCP rather than compare outcomes rates per se. Due to the timing and nature of the study (i.e. using a newly described diagnostic method and criteria) there was insufficient time and numbers of potential participants available to conduct a longitudinal study using the same cohort.

CONCLUSIONS
This is the first study to use the newly described IMCP testing technique to compare post fasciotomy IMCP with controls and pre-fasciotomy CECS patients. The results add further support for the traditional pathophysiological model of CECS and the role of IMCP and fasciotomy in the management of CECS.

COMPETING INTERESTS
None

FUNDING
YYYYYY
REFERENCES


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Reviewer(s) Reports:

Reviewer: 1

Comments to Author

Overall this is an interesting and relevant study. The authors clearly explain their objectives and the unique contributions their study makes to the literature available on CECS.

Introduction:

- Nice summary of the relevant available literature on this topic and explanation of the motivation for the study.

Thank you

Methods:

- Please comment on who performed the dynamic compression pressure testing. How many testers? If more than one, did you assess inter-rater reliability?
- Page 7, Line 22: Limiting the PTSURG cases to those that remained on military service in the 6-60 month post-fasciotomy timeframe introduces selection bias, since it potentially eliminates those who were unable to return to duty or left the service due to continued symptoms. This likely contributed to the low number of non-responders (PTSURG-NR). This should be mentioned as a limitation in the Discussion section.
- The following has been added to the discussion: It is acknowledged that the availability of non-responders for this study may have itself been influenced by non-continuance in service due to ongoing symptoms however the primary aim of the study was to establish the effect of fasciotomy on IMCP rather than compare outcomes per se.
- Was a power analysis performed?
- No, there was insufficient evidence from the available literature to guide effect size calculation and the use of the electronic caliper has only recently been described by this research group with no prior data to inform calculation. The sample size used was the same used for the previously published study describing the new technique and improved diagnostic accuracy which had sufficient statistical size. A larger sample was also not possible due to the limitations of remaining in service with ongoing symptoms. Prospective studies are now in place to address the limitations of retrospective sample identification.
- For transparency, in Table 1 and 2, include the number (n) of data points used to determine the means for each phase, for each group.
- Table 1 has been amended to include numbers of legs tested for each group. Unfortunately further review of data identified loss of 4 participant data sets in the calculation of PTSURG values for EX-ALL. Combined values for table 2 are easily calculated from table 1 information. As described in the methods, this is taken from continuously collected IMCP data and a mean taken across the selected time periods using a lab chart script. The mean pressure over a 5 second period at 1 minute and 5 minutes post-exercise was recorded.
- Clarify how you defined “functional and symptomatic improvement” for the second objective of the study – i.e. Ability to complete entire protocol, pain level, etc. How did you specifically assess for correlation between IMCP improvement and functional improvement?
- The objective was to compare responders to non-responders and the other groups. Not paired data so not directly measured and correlations cannot be calculated as no individual data for IMCP “improvement”. But was compared on a group basis through comparison of responders and non-responders. “Responders to fasciotomy were defined as those post-operative cases able to complete the exercise protocol with tolerable pain levels at or below the highest of those of asymptomatic volunteers and with only mild residual post-protocol pain.” A larger longitudinal study to investigate this is currently underway.
- Why did the authors use a different group of subjects for Pre-fasciotomy IMCPs and Post-fasciotomy IMCPs, rather than gathering this data from the same group of subjects? This not only increased the number of subjects required for the study (and in turn invasive diagnostic testing), it also potentially introduced unnecessary confounding factors. Please explain in Discussion of study limitations.
- This would have been a preferred approach however due to the timing and nature of the study i.e. using a newly described diagnostic method and criteria there was insufficient time and study participants available to conduct a longitudinal study using the same cohort. As per the above response, this is now underway. The following has been added to the methods section: Detailed comparison of PT an CON subjects has previously reported. [27]

Results:

- Page 10, Line 11: Should the total PT number be 20 rather than 13?
  This has been amended in the text – thank you.
- Include a separate section that outlines results for the study’s second objective (correlation of IMCP’s to function and symptom improvement).
- The objective is to compare responders to non-responders.

Discussion:

- Please include a more complete discussion of the study’s limitations – see comments above in Methods.
- Why do the authors think the PTSURG-NR group had higher IMCP than controls in all phases? Discuss hypotheses (could these have been incomplete releases?).

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In considering possible alternative reasons for failure to respond to fasciotomy, work published by Mathis et al since the completion of this study looking at swine models suggests that the length of incision of the fascia correlates to the subsequent post-operative IMCP (J E Mathis et al. "Effect of Lower Extremity Fasciotomy Length on Intracompartmental Pressure in an Animal Model of Compartment Syndrome: the Importance of Achieving a Minimum of 90% Fascial Release," Am J Sports Med, October 31, 2014. doi:10.1177/0363546514554601). We consider this to be an important insight from this study requiring further study to clarify. This is something we are trying to address in future treatment pathways. Animal studies have shown that post-operative IMCP can be related to the length of fasciotomy. It is likely that this is what is observed in this data.

- Why do the authors think so many PT subjects were able to complete the entire protocol? Does this mean IMCP didn't necessarily correlate with pain?
- IMCP-vs-pain correlation is not made here. Pain has much inter-individual variability. We have previously reported the importance of pain in CECS classification. Further evidence can be taken from the responders-vs-non-responders comparison. It is possible that IMCP levels are not perfectly correlated with pain due to other factors.
- Comment on the NR. Do you think it was because they had incomplete releases? Why did they have?

As above response.

- Page 15, Line 15: Authors state that there was a significantly lower IMCP in PT SURG-R compared to NR during Phase 2, but in Results section and according to Table 2, this was a nonsignificant finding. Which is correct?
- Phase 2 is recognised as the most valuable diagnostic time point with the greatest discriminating potential in CECS. [27] The lower IMCP in PT SURG-R compared to PT SURG-NR observed (although not significant in this relatively small sample), both of which would fall below the suggested diagnostic cut-off of 105mmHg. Before final submission, please make sure to correct all punctuation errors (several comma's omitted).
- Amendments to grammar and punctuation have been made.

Reviewer: 2

Comments to Author
This cohort study of CECS (anterior compartment) is welcomed as the relationship between symptoms; IMCP and treatment are far from clear. Whilst the testing methodology is clearly described I found the paper difficult to follow. Specifically:

- The follow-up time post fasciotomy is significantly variable: 6-60 months
- This is a limitation due to the study design as per response to reviewer 1.
- The way the results are presented are difficult to interpret: ? use a flow diagram to help understand to differences within the post-fasciotomy groups: 12 asymptomatic; 8 with symptoms. Only 7 of 13 PT cases were able to complete the exercise challenge; but n=20?
- Amended as per the response to reviewer 1
- Discussion Line 39: adjust language: "on a par with"
- This has been changed to: comparable
- Methods: Allocation of groups: it would be useful to know the symptoms of the post-fasciotomy group (all of whom were returned to 'normal duties')
- Data relating to level of post-operative functional level or level of duties returned to was not collected for this study. We have not suggested all post-operative cases were returned to 'normal duties'. The definition of 'normal duties' is a broad concept as all post-operative cases were in ongoing military service and being gainfully employed. The degree of restriction on completing all 'role' elements also varies by branch, trade, rank and role. It is therefore difficult to control for all of these factors and how meaningful conclusions hence we have taken a symptom and function based approach to the allocation of group membership as most members personnel are required to complete some form of ambulant functional testing. Data relating to return to duties has been previously described by Waterman but we consider is similarly confounded and acknowledged by the authors.
- P14 Lines 20-36: please explain why post-fasciotomy IMCP might be lower irrespective of symptoms and reaction to exercise protocol. ? Suggests symptoms are not related to IMCP?
- It is not clear whether symptoms have reduced (to a small degree) compared to pre-operatively in PT SURG-NR as this is unpaired data.
- Discussion p15 Lines 3-5: “intrinsic role of IMCP in CECS” – please elaborate
We believe that finding further advances the evidence for the intrinsic role of IMCP as the key driver of symptoms as well as diagnostic and treatment target in CECS.
- Consider including JSSM 2018 paper De Brujin: Risk factors for CECS with potentially helpful risk nomogram
- Please reconsider the conclusion, as I am not convinced that your data backs up the conclusions you have drawn.
- We disagree with this point – this is the first study to examine the effects of fasciotomy on IMCP using newly described and more accurate IMCP criteria than previously available and supports the role of fasciotomy in reducing IMCP.