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Review

The validity of the diagnostic criteria used in chronic exertional compartment syndrome: A systematic review

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Chronic exertional compartment syndrome (CECS) of the lower limb is part of a group of overuse lower limb injuries with common presenting features. It is commonly diagnosed by the measurement of raised intramuscular pressures in the lower limb. The pathophysiology of the condition is poorly understood, and the criteria used to make the diagnosis are based on small sample sizes of symptomatic patients. We carried out a systematic review to compare intramuscular pressures in the anterior compartment of healthy subjects with commonly used criteria for CECS. Thirty-eight studies were included. With the exception of relaxation pressure, the current criteria for diagnosing CECS, considered to be the gold standard, overlap the range found in normal healthy subjects. Several studies reported mean pressures that would prompt a positive diagnosis for CECS, despite none of the subjects reporting any symptoms. The intramuscular pressure at all time points has also shown to vary in relation to a number of other factors other than the presence of CECS. Taken together, these data have major implications on the ability to use these published criteria for diagnosis and question the underlying pathophysiology. Clinicians are recommended to use protocol-specific upper confidence limits to guide the diagnosis following a failed conservative management.

Overuse lower limb injuries are common both in initial military training and in endurance sports (Riddell, 1989; Cowan et al., 1996; Yates & White, 2004). Up to 20% of all runners sustain a lower limb injury each year (Marti, 1984), and rates of 20–40% are reported in military personnel (Pullinger, 1999 personal communication; Rauh et al., 2006). Diagnoses include shin splints, medial tibial stress syndrome, anterior knee pain, Achilles tendinopathy, iliotibial band syndrome, stress fractures, and chronic exertional compartment syndrome (CECS). Many of these diagnoses are made on history and examination without invasive investigation, but this is not the case in CECS, which cannot be diagnosed on magnetic resonance imaging (MRI) investigation or history alone.

CECS is an overuse condition presenting as pain in the lower limb, associated with the muscles contained within the myofascial compartments of the shank. The anterior compartment of the lower leg, containing tibialis anterior, extensor digitorum longus, extensor hallucis longus, and peroneus tertius, is reported as being affected most often (Reneman, 1975). Although this is not exclusive with the deep posterior compartment of the lower leg, the erector spinae, the extensor compartment of the forearm and the adductor compartment of the foot all reported with compartment type symptoms and elevated intramuscular pressure (IMP) in the literature (Rydholm et al., 1983; Styf, 1987; Gielen et al., 2009; Padhiar et al., 2009).

The pathophysiology of CECS is unknown. It is commonly defined as a condition where abnormally high IMP during exercise impedes local blood flow impairing neuromuscular function of the tissue within a compartment (Styf et al., 1987; Zhang et al., 2011). There is limited evidence that this results in cellular damage (Edmundsson et al., 2010). Although it is unclear why there is an increase in pressure, there is evidence from studies using near-infrared spectroscopy that those with increased IMP have decreased oxygenation in comparison to controls (Mohler et al., 1997; van den Brand et al., 2005). Fascial collagen structure has shown to be amenable to local effects in myofibroblast proliferation in the rat, but to date, no fascial integrity study has been performed in those diagnosed with this condition. A variety of theories have been postulated as to why raised intracompartmental pressure is seen including muscle hypertrophy or reduced compartment volume due to a decreased fascial compliance (Turnipseed et al., 1995),

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abnormally increased fluid content in the compartment or shorter periods of muscle relaxation. This highlights the question as to whether the rise in pressure is a cause or consequence of the syndrome, or whether indeed, the syndrome does not represent purely muscular overload.

The currently accepted gold standard diagnostic technique for CECS is IMP measurement. This originates from the diagnosis of acute compartment syndrome, which is a direct result of tissue hypoxia and subsequent fluid extravasation and compartmental pressure rise and tissue necrosis if left untreated. IMP measurement is commonly performed using a slit indwelling catheter inserted into the muscle belly of the compartment to be tested under local anesthetic. Various parameters and cutoff points of IMP have been proposed as useful criteria in diagnosing the condition including resting IMP, either mean, peak, or relaxation (in between contractions) IMP during exercise and postexercise IMP (Styf et al., 1987; Pedowitz et al., 1990). Critical values for diagnosing CECS have been proposed using pre (e.g. ≥15 mmHg; Pedowitz et al., 1990), during (e.g. ≥50 mmHg; Puranen & Alavaikko, 1981), relaxation (e.g. ≥35–50 mmHg; Styf, 1988), and 1 (e.g. ≥30 mmHg; Styf, 1988; Pedowitz et al., 1990) or 5 (e.g. ≥20 mmHg; Pedowitz et al., 1990) min postexercise.

A number of other noninvasive diagnostic methods have been considered including ultrasound (Lynch et al., 2009), near-infrared spectroscopy (van den Brand et al., 2004), MRI (Theodosopoulos et al., 2004), and measurements of blood flow using nuclear techniques (Zhang & Styf, 2004).

The majority of studies used to form the basis of the criteria for diagnosis did not include healthy controls for comparison. The criteria were developed in studies with serious methodological limitations. Perhaps the most widely used criteria are those set by Pedowitz et al. (1990). The main strength of this study is the large sample size ($n = 159$). However, this study has several significant flaws when compared with the quality assessment of diagnostic accuracy studies methodology checklist for studies of diagnostic test accuracy (Whiting et al., 2003). The main limitation is that a valid comparison group was not used: the reference test and the index test were not independent (they were in fact the same test). Groups of symptomatic individuals that failed to meet preset IMP cutoff points (that were changed during the study) were compared with those that IMP is above the cutoff point. As such, the groups were already preselected to have differences in IMP. Limitations of other studies include the comparison of symptomatic and asymptomatic limbs in the same subjects (Styf et al., 1987) and comparison with only very small numbers of healthy controls (Puranen & Alavaikko, 1981). A study that measures pressures in a large number of asymptomatic and symptomatic subjects is required to define thresholds (preferably with the aid of receiver operating characteristic curves).

The usual outcome of a diagnosis being confirmed with raised IMPs is an invasive surgical procedure of fasciotomy or fasciectomy to “release” the compartment. Long-term follow-up studies are few, but Slimmon et al. (2002) demonstrate potential causes of operative failure as incorrect diagnosis, or failure to address multiple compartments in the leg simultaneously.

The objective of this study was to carry out a systematic review of IMP before, during, and after exercise in the tibialis anterior in healthy subjects and to compare with the diagnostic criteria commonly in use for CECS.

Materials and methods

Literature search

A literature search was performed using MEDLINE/PubMed. The search included all indexed articles appearing from 1966 to March 2010 with the key words “intramuscular pressure,” “intracompartment pressure,” “intracompartmental pressure,” “anterior compartment pressure,” or “anterior tibial compartment pressure” and their plurals. The reference lists of all relevant articles were hand searched for pertinent studies that may have been missed during the computerized search.

Inclusion criteria

All studies in English or with English translation were acquired. All studies included asymptomatic (no mention of a history of symptoms in either leg) human subjects. No interventions were used on the subjects prior to or during the testing, including interventions on the contralateral leg (baseline measures before an intervention were permitted). Observations that may be recorded during normal clinical examination (e.g. presence of shoe orthotics and catheter depth) were included.

Exclusion criteria

Papers that only reported IMP as a percentage of resting pressure were excluded.

Data handling

Data on IMP (tibialis anterior) were extracted before, during, and after exercise from included trials. Pressure was converted to mmHg when required. Data collected from the selected studies included age, measuring technique, type and duration of exercise, the number of compartments measured, and IMP at all time points reported. IMP at rest was in the supine position unless otherwise stated. In all cases, the mean was used when presented. Where individual data were presented, these were summarized to provide mean and standard deviation statistics. Median pressure was used if this was the only information available. Where only graphical information was displayed, data were measured from the graphs. Data were assumed to be unilateral unless otherwise specified. If bilateral data were reported for each leg, or if multiple measurements were made on the same subject, the data were plotted separately on the graphs.

Results

Five hundred and eighteen studies were identified of which 38 articles were included (Fig. 1). These are identified with citations in Figs 2–6. Exercise in most cases was either treadmill walking/running or ankle dorsiflexion. IMPs for cycling, skiing, and a leg press exercise

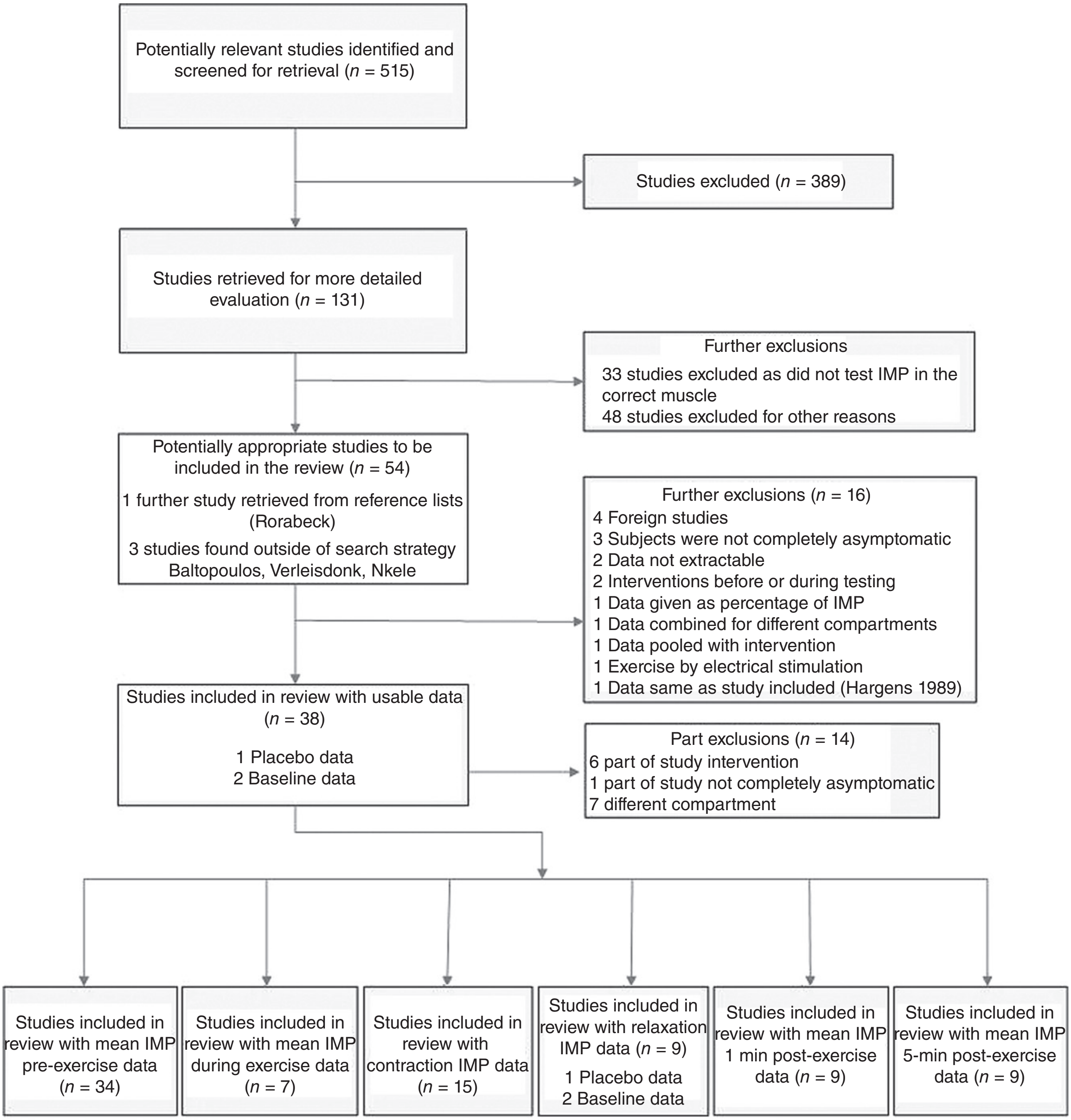

Fig. 1. A flow chart showing inclusion and exclusion of studies in the review.
IMP, intramuscular pressure.

were also reported. Typically, the duration of exercise was lower for the dorsiflexion exercise (from 10 s to 20 min) in comparison with running (1.5–120 min). Measuring techniques consisted of either a fluid filled catheter (needle, wick, or slit) or a transducer tipped catheter. The solid-state transducer intracompartment (STIC) catheter was also used that combines both these approaches (McDermott et al., 1982). The STIC catheter features a solid-state transducer with high frequency response that is inserted through the lumen of a fluid-filled catheter connected to a constant infusion system.

The lowest IMP was identified pre-exercise at rest, contraction IMP was the peak IMP, although the value of this varied depending on the type of exercise. Relaxation IMP (range 0–30 mmHg) was slightly higher than resting IMP (range 0–20 mmHg), and after exercise, these values began to return back to the resting IMP. Three studies reported IMP between 1 day and 4 days postexercise. These studies generally found a full return to pre-exercise resting IMP at these time points. Hargens et al. (1989) found the 2-day postexercise pressure to be higher after eccentric in comparison with concentric

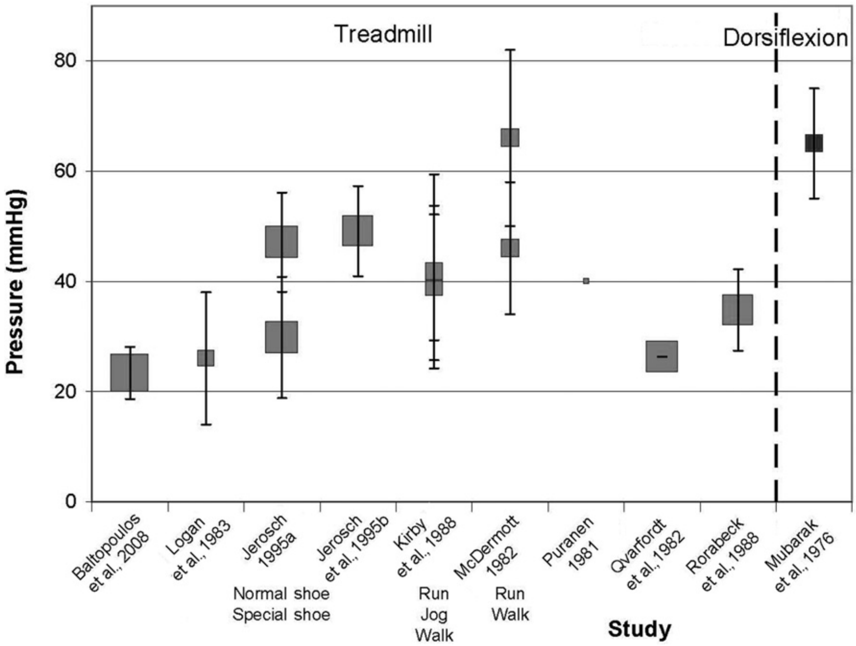

Fig. 2. Mean pressure during exercise. The center of each box represents a reported mean value, and the error bars represent one standard deviation. Box size is dependent on the sample size (range 9–48) for each reported value. Where more than one value was reported in a study, the condition is listed in order from highest to lowest mean pressure (see text below year of study). The exercise used in each study is color coded (treadmill exercise in green and dorsiflexor exercise in blue).

dorsiflexion exercise. In general, there was more variability in contraction IMP than postexercise IMPs. Standard deviations were approximately three times the values seen at rest.

Ten studies reported pressures during exercise with nine of these during running (range 5–20-min duration; Fig. 2). Mean pressure during exercise varied between 23 mmHg and 66 mmHg. Nine studies reported relaxation pressures; however, in only one of these studies, the exercise was running (Fig. 3). The mean relaxation pressure during running was almost always greater than the mean relaxation pressures reported during ankle dorsiflexion exercise.

Five (including one case study) out of 34 studies found the mean pre-exercise pressure to be higher than the Pedowitz criterion of 15 mmHg (Pedowitz et al., 1990; Fig. 4). Two out of 10 studies found the mean pressure during exercise to be above the Puranen criterion of 50 mmHg. All of the studies found mean relaxation pressure to be below the Styf criterion of greater than 35–50 mmHg. One out of 11 studies found mean postexercise pressure after 1 min to be above the Pedowitz criterion of 30 mmHg (Fig. 5). One out of 10 studies found mean postexercise pressure after 5 min to be above the Pedowitz criterion of 20 mmHg (Fig. 6).

Discussion

This study demonstrates conflicting evidence regarding the validity of IMP as a means of making a diagnosis of CECS in the anterior compartment of the shank. With the exception of relaxation pressure, many of the confidence intervals at all these time points overlap the commonly used criteria set by Puranen and Pedowitz. If a measured IMP is above the criteria, clinicians can not have confidence as to whether the subject belongs to the upper end of the distribution curve for healthy subjects or at the lower end of the curve for subjects with CECS.

Padhiar and King (1996) suggest that IMP testing for CECS should be carried out using an exercise-specific protocol to bring on the pain. However, IMPs are dependent on a number of different variables. The reason for the variability in the pressures has been investigated in several studies as detailed below. This large variability suggests that IMP criteria for diagnosing CECS can only be applied when the same measurement technique and exercise protocol to provoke symptoms is used as that was used to develop them.

The actual technique of measuring IMP introduces potential confounding variables. The depth of the catheter affects IMP at all time points (Nakhostine et al., 1993). Higher pressures (c. 15–40 mmHg more during contraction) in the tibialis anterior are found when the tip of the catheter is close to the centrally lying tendon in comparison with tips located close to the myofascia or the interosseous membrane. Sejersted et al. (1984) also demonstrated a linear relationship between depth and IMP during contraction. This relationship was not present when the muscle was relaxed. Values presented suggest that there was approximately a 30 mmHg change for every centimeter of depth in the vastus media-

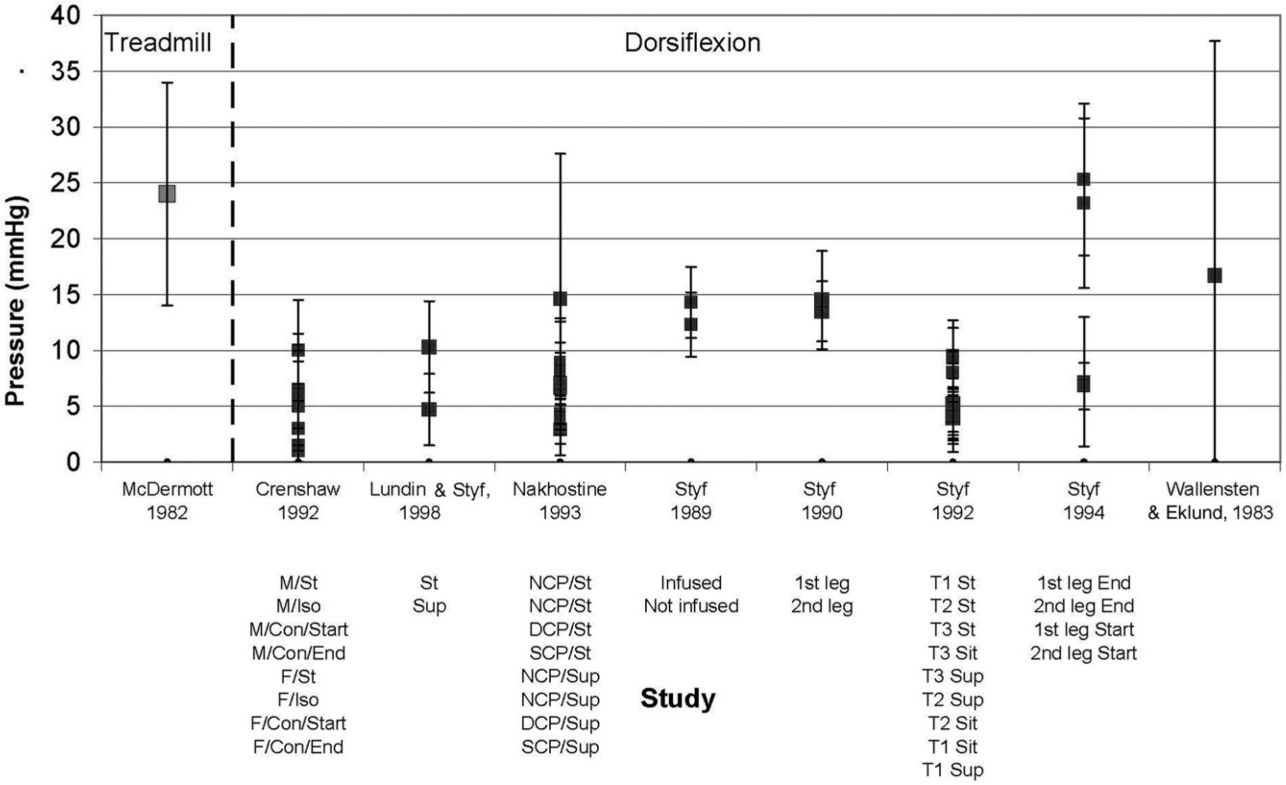

Fig. 3. Relaxation pressure during exercise. The center of each box represents a reported mean value, and the error bars represent one standard deviation. Box size is dependent on the sample size (range 5–11) for each reported value. The exercise used in each study is color coded (treadmill exercise in green and dorsiflexor exercise in blue). Where more than one value was reported in a study the condition is listed in order from highest to lowest mean pressure (see text below year of study).
M, Myopress catheter; F, fiber-optic catheter; St, standing exercise; Sup, supine exercise; Sit, sitting exercise; Iso, isometric exercise; Con, concentric exercise; Start, start of exercise; End, end of exercise; NCP, normal catheter placement; DCP, deep catheter placement; SCP, shallow catheter placement; T1,T2,T3, consecutive trials; leg [left or right; 1st or 2nd (when unspecified)].

lis muscle (at a standard force of 50% of maximal voluntary contraction). Sadamoto et al. (1983) similarly observed reductions of up to 50% lower IMP with a more superficial placement. Nine of the included studies did not report either catheter insertion distance or insertion angle. To estimate catheter depth, it is important to report both these variables. Perhaps more worryingly, seven of the studies reported a range of insertion distances. Even when studies did report distances in some cases, it was not clear whether this was overall or after puncturing the fascia. Clearly, differences in skin thickness will have an effect on relative depth. Insertion angles in the included studies ranged from 20 degrees to 45 degrees, with some changing after fascia puncture.

Gershuni et al. (1982) report a mean anterior compartment width using ultrasound (skin surface to interosseous membrane) of 29.0 mm ± 0.9 increasing by c. 2.5 mm after exercise in young adults. Although this study suggests that tibialis anterior muscle depth has low variability, subject characteristics of age, height, and weight are not reported preventing any conclusions on generalizability. In addition, the ultrasound scanner was located more distally than the usual location for pressure testing. Using simple trigonometry, for those studies that reported both insertion distance and angle, catheter depths (distance perpendicular to skin) ranged from 1 mm to 29 mm. Only four of the studies were less than 8 mm, the remaining studies ranged from 18 mm to 29 mm. Differences in pressure between these studies could at least be partly explained by catheter depth. Interestingly, Nakhostine et al. (1993) recommend, based on the results of their study, that “diagnosis of compartment syndromes should be based on pressure readings from the deep portion of a muscle.” This suggests that they believe that there is more of an issue of false negatives rather than the false positives that are apparent in this review.

Additionally, fluid-filled catheter systems can require periodic flushing with saline to maintain catheter patency (Styf & Korner, 1986). In comparison with wick catheters, slit catheters are designed to reduce the need to flush by maintaining saline-tissue fluid continuity (Shakespeare et al., 1982). Partial loss of catheter patency occurring during exercise can lead to a dampened response affecting the recorded contraction and relaxation pressure (Styf & Korner, 1986). They also

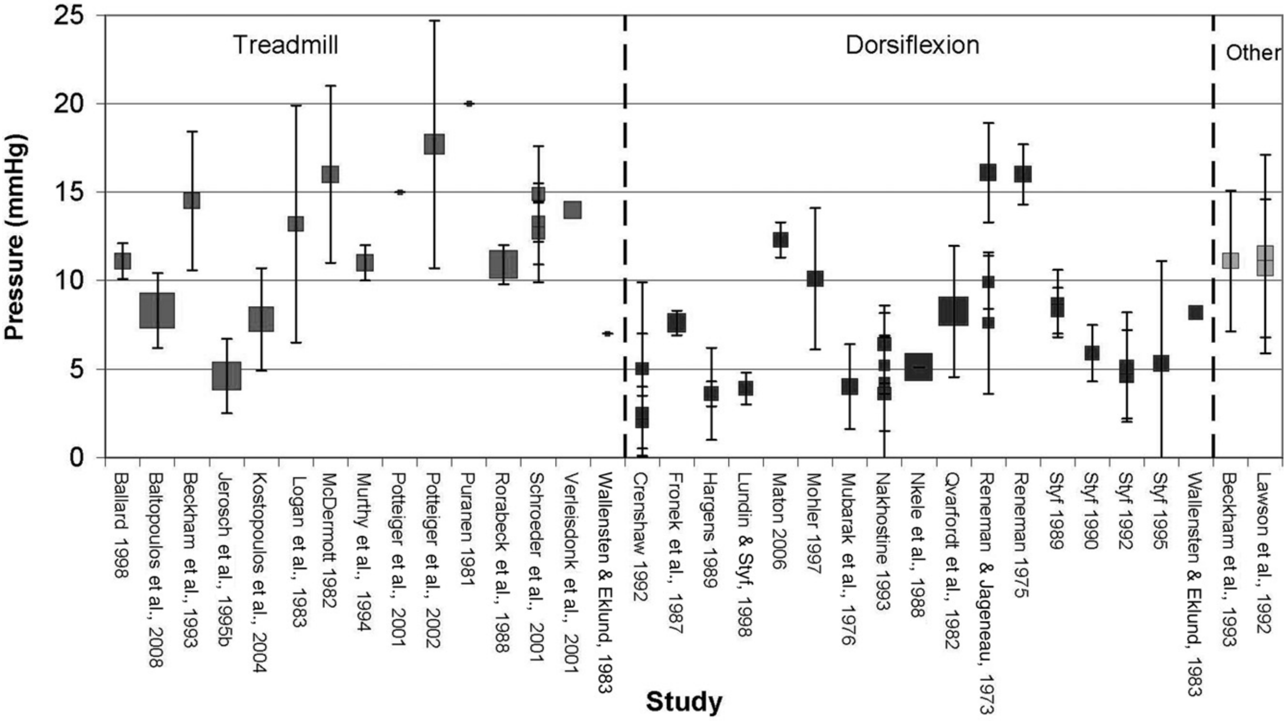

Fig. 4. Pre-exercise pressure. The center of each box represents a reported mean value, and the error bars represent one standard deviation. Box size is dependent on the sample size (range 1–48) for each reported value. The exercise used in each study is color coded (treadmill exercise in green, dorsiflexor exercise in blue, and other exercise in orange).

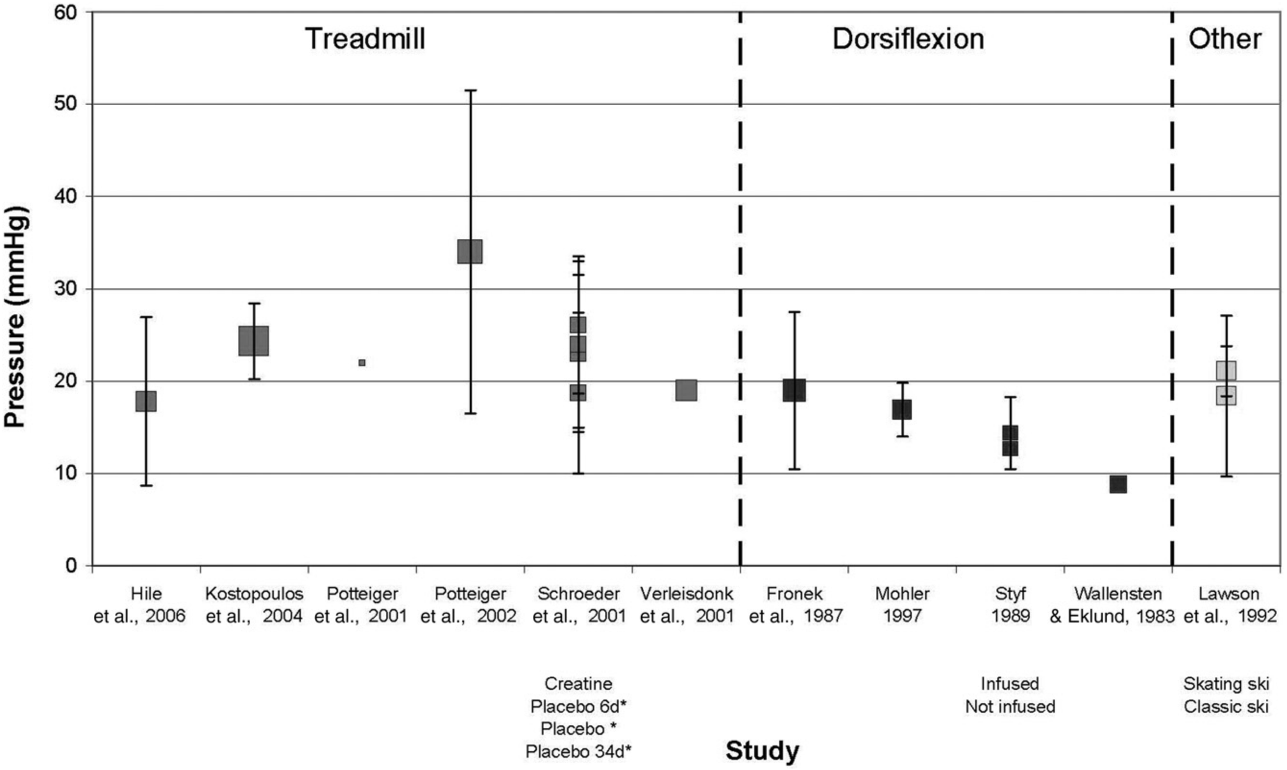

Fig. 5. Pressure 1 min after exercise. The center of each box represents a reported mean value, and the error bars represent one standard deviation. Box size is dependent on the sample size (range 6–24) for each reported value. Where more than one value was reported in a study, the condition is listed in order from highest to lowest mean pressure (see text below year of study). The exercise used in each study is color coded (treadmill exercise in green, dorsiflexor exercise in blue, and other exercise in orange).
Placebo 6d, placebo group after x days; *, different set of subjects.

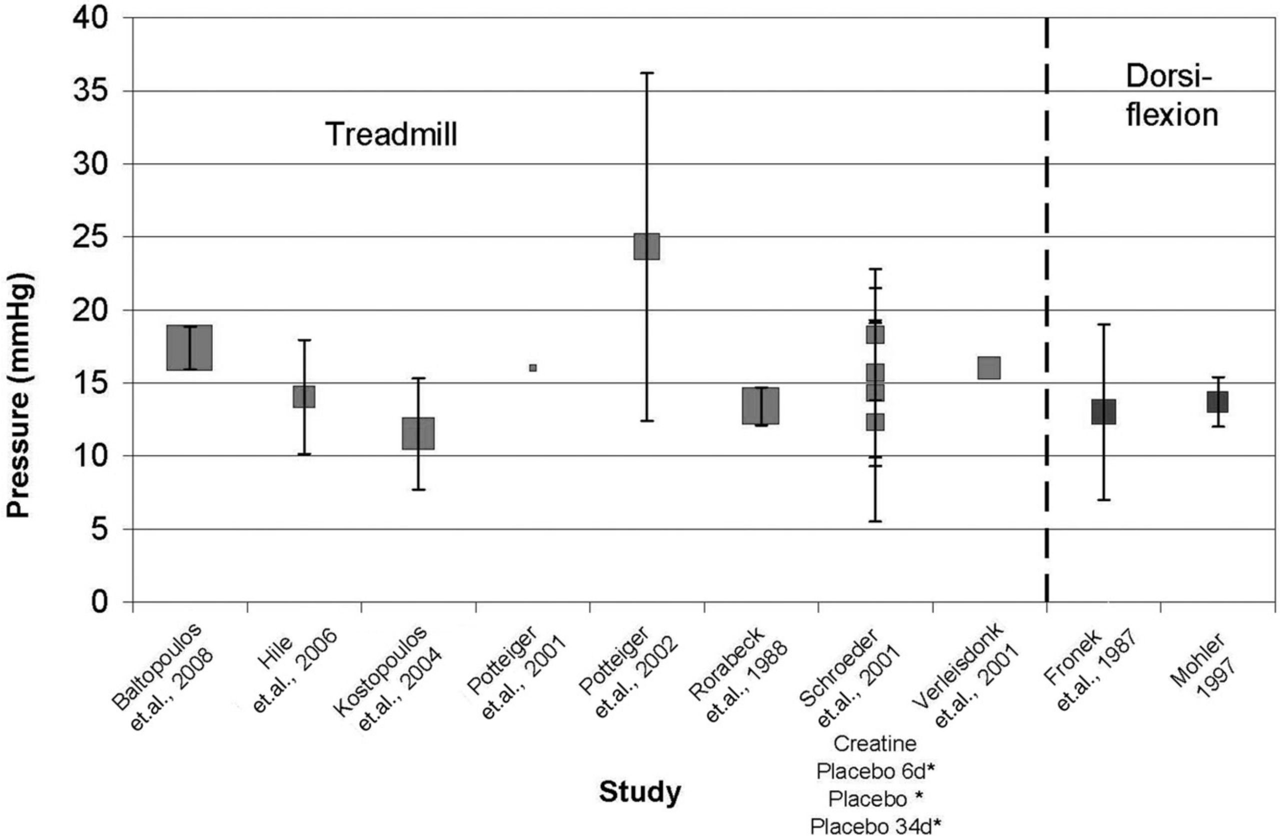

Fig. 6. Pressure 5 min after exercise. The center of each box represents a reported mean value, and the error bars represent one standard deviation. Box size is dependent on the sample size (range 7–48) for each reported value. The type of exercise used in each study is color coded (treadmill exercise in green, dorsiflexor exercise in blue, and other exercise in orange).Where more than one value was reported in a study, the condition is listed in order from highest to lowest mean pressure (see text below year of study and abbreviation list). Placebo 6d, placebo group after x days; *, different set of subjects.

report that the act of infusing fluid at a rate of 3.0 mL/h does not affect the recorded pressure at rest. Furthermore, using the Myopress catheter (Atos Medical, Horby, Sweden), there was no difference in pressure during exercise whether infusion was used or not (Styf et al., 1989).

Variability in the pre-exercise pressures is the lowest of the parameters and is only known to be affected by the variables described above. Muscle tonus could also be expected to contribute to pre-exercise pressures. All the other pressures are also dependent on the exercise. Furthermore, it is important to note that measurements using the needle and wick catheters have been found to have a poor dynamic response (McDermott et al., 1982). Therefore, measurements of contraction pressure, relaxation pressure, and mean pressure during exercise using these techniques should be viewed with caution.

Contraction pressure is highly dependent on the contraction force generated (Sadamoto et al., 1983; Sejersted et al., 1984). It has been well correlated with Electromyographic (EMG) studies (Maton et al., 2006), and as it measures the result of force generation from within the muscle, some have considered it as a better surrogate measure of muscle contraction intensity than EMG. Shoe construction (Jerosch et al., 1995a) has been demonstrated to affect contraction pressures during running. A shoe with a negative sole reduced the plantarflexion angle at heelstrike, reduced the duration of plantarflexion (eccentric action of tibialis anterior), and reduced pressure by more than 20 mmHg. Contraction pressure is therefore dependent on the type and intensity of muscle contraction (Aratow et al., 1993; Styf et al., 1995). Walking produces lower contraction pressures and mean pressures in comparison with running (McDermott et al., 1982; Ballard et al., 1998). Introducing variables such as velocity, incline, or loaded marching are likely to positively increase contraction force in response to increased load and introduce further variability, potentially introducing significant false-positive test results.

Relaxation pressure has shown to increase over the course of a 2-min dorsiflexion exercise (Styf et al., 1994). In contrast, Crenshaw et al. (1992) did not find any difference between the start and end of a 20-min dorsiflexion exercise. Three studies have demonstrated relaxation pressure to be higher during standing dorsiflexion exercise in comparison with seated or supine dorsiflexion (Crenshaw et al., 1992; Styf et al., 1992; Nakhostine et al., 1993). The results of the current review also show that relaxation pressure during the only-running protocol produces higher pressures than almost all the dorsiflexion protocols. Further, comparative studies are needed to confirm this.

By definition, the mean pressure during exercise is dependent on the contraction pressure, on the relaxation pressure, and on the length of time that the muscle is contracted and relaxed during each gait cycle (or other contraction cycle). It is therefore also dependent on any of the variables mentioned above that affect relaxation and contraction pressure. In line with the study of shoe sole geometry by Jerosch et al. (1995a), symptomatic patients changing from a rearfoot to a forefoot landing reduced the mean IMP during treadmill running (Kirby & McDermott, 1983).

If IMP is simply considered a measure of muscle contraction force and duration, a higher IMP in suspected CECS patients during running may represent over activation of the muscles of the anterior compartment; although the IMP in the tibialis anterior muscle in patients with other lower limb problems has not been tested. Mubarak et al. (1982) report IMP in the deep and superficial posterior compartments in a series of 12 patients with medial tibial stress syndrome. It is conceivable that IMP could be a risk factor for pain in the anterior compartment rather than the cause of the pain itself, given the paucity of physiological supportive evidence in the chronic condition. Raised relaxation IMP and postexercise IMP in CECS patients could be explained by a greater stress response due to greater use during running. However, this does not account for the differences seen during standardized dorsiflexion exercises. Future studies elucidating the mechanism of pain are essential in aiding our understanding of this condition.

Postexercise pressures are believed to vary for a variety of reasons. After exercise, there may still be some low-level muscle activity that may cloud the results (Zhang et al., 2011). Possible reasons for this are muscular hypertension syndrome, pain after exercise, and needle discomfort. Eccentric contractions also lead to an increased postexercise pressure response in comparison with concentric contractions (Hargens et al., 1989). During and after eccentric contractions, sarcomere structure is disordered, releasing Na^+ and increasing the pH of the interstitial fluid (Yeung et al., 2002b, 2003). This may in turn explain the increase in fluid content in the compartment and therefore raised pressure. The development of transverse-tubular vacuoles in eccentrically exercised muscles may also contribute to increased pressure (Yeung et al., 2002a).

In addition to the reasons described above, the measuring equipment has varying sensitivity and accuracy. The transducer-tipped catheters have greater sensitivity and therefore implied better accuracy. The relationship of IMP to force has recently been questioned. A study using a fiber-optic-tipped pressure sensor in a rabbit model demonstrated highly variable pressure readings during isotonic contraction (Ward et al., 2007; Winters et al., 2009). The authors believe that this variability is due to transducer movement during contraction. A new urodynamic catheter has been developed with the transducer surrounded by a small compliant fluid-filled structure (Johnson et al., 2009). It was developed to reduce errors from direct sensor movement against the tissue wall. Miniaturization of this catheter for IMP testing could provide a more reliable output and easier administration. A current solution to this problem could be to use the STIC catheter for dynamic recording of intramuscular fluid pressure as it is less susceptible to these small-tip movements. One concern is the larger diameter required that may lead to more muscle trauma/pain and conceivably altered muscle-contraction patterns. The introduction of local anesthetic to allow for indwelling catheter placement adds further potential for error both by the volume effect of the local anesthetic bolus and also by myotoxic effects of local anesthesia on normal muscle function (Yagiela et al., 1981; Irwin et al., 2002).

In conclusion, the current criteria for confirming the diagnosis of CECS, considered to be the gold standard, are flawed as described. The IMP at all the gold-standard time points has shown to be dependent on variables other than the presence or absence of CECS, and considerable overlap exists in the available literature between normal and symptomatic subjects in IMP measurement. Studies that combine dynamic IMP measurements in healthy subjects, subjects with confirmed non-CECS diagnoses (e.g. tibial stress fracture or medial tibial stress syndrome), and subjects with suspected CECS (with other conditions ruled out) are essential to determine the sensitivity and specificity of this type of testing. The current diagnostic criteria certainly cannot be applied with reliable certainty in any compartment outside that of the anterior compartment of the shank, and the authors believe that the use of current diagnostic criteria for CECS should not be used to make a diagnosis, pending prospective normative studies with varying protocols. The author's current practice is now to try first conservative biomechanical approaches (e.g. encouraging a forefoot-strike running pattern) to reduce muscle load. Failing this approach, we recommend that compartment pressure testing is carried out using a published protocol with data on asymptomatic subjects. The use of non-standard protocols is not recommended. Referral for fasciotomy should then be based on a combination of clinical signs and IMP values.

The maximum reported upper confidence limits for pre, during, relaxation, and post 1- and 5-min IMPs are 32 mmHg, 98 mmHg, 59 mmHg, 69 mmHg, and 48 mmHg, respectively. Pressures above these maximum values could certainly be considered abnormal under any circumstance. Although guaranteeing high specificity, the use of these values as cutoffs would likely have severe consequences on sensitivity. The mean (weighted to account for sample size) upper confidence limits for the five time points are 14 mmHg, 54 mmHg, 18 mmHg, 36 mmHg, and 23 mmHg, respectively. The weighted mean should provide a better representation of true population values. However, these weighted means do not take into account the differences between the studies as described above that can affect IMP. Therefore, we recommend that only the confidence limits from the studies in this review (or unpublished results on asymptomatic subjects using the investigators' own protocol) that use the chosen method of investigation should be used to guide diagnosis. Without information on the lower confidence limits from symptomatic subjects, it is not possible in this review to comment on the best diagnostic thresholds for a particular protocol that maximizes both specificity and sensitivity.

Perspectives

The present review suggests that the diagnostic gold standard for CECS is flawed. Definitive statements on the diagnostic sensitivity and specificity for each criterion acquired through IMP testing can not yet be made. It is clear from this review that clinicians need to be aware of the limitations of this type of testing and the potential to alter IMP independent of pathology. These flaws could potentially lead to false positives and subsequent fasciotomy where it is not indicated. We recommend that if clinicians carry out IMP testing, they should use a protocol with standardized catheter depth, exercise type, intensity and duration, footwear, and equipment. Furthermore, it may be wise to raise some of the diagnostic thresholds to improve test specificity at the expense of sensitivity. The studies of Jerosch and Kirby also provide potential mechanisms through a change in running biomechanics, either by coaching or with shoe/orthotic prescription, to reduce IMP to levels that may alleviate the condition. We therefore recommend that conservative treatment using the suggested mechanisms is tried prior to IMP testing and/or surgical intervention. Clearly, further research is required to improve diagnostic testing and the role of possible conservative treatment options for this condition.

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