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# Systematic Review of Innovative Diagnostic Tests for Chronic Exertional Compartment Syndrome

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Authors

**Ewan D. Ritchie[1], Sanne Vogels[1, 2], Thijs T. C. F. van Dongen[1, 3], Boudewijn L. S. Borger van der Burg[1], Marc R. M. Scheltinga[4], Wes O. Zimmermann[5, 6], Rigo Hoencamp[1, 3, 7, 8]**

Affiliations

1 Department of Surgery, Alrijne Hospital Location Leiderdorp, Leiderdorp, Netherlands
2 Department of Trauma Surgery, Erasmus Medical Center, Rotterdam, Netherlands
3 Defence Healthcare Organization, Ministry of Defense, Utrecht, Netherlands
4 Department of Surgery, Máxima Medical Centre, Veldhoven, Netherlands
5 Department of Sports Medicine, Royal Netherlands Army, Utrecht, Netherlands
6 Department of Military and Emergency Medicine, Uniformed Services University of the Health Sciences, Bethesda, United States
7 Department of Surgery, Leiden University Medical Center, Leiden, Netherlands
8 Trauma Research Unit, Department of Trauma Surgery, Erasmus Medical Center, Rotterdam, Netherlands

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Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

Correspondence

Sanne Vogels
Alrijne Hospital Location Leiderdorp, Surgery Department,
Simon Smitweg 1
2353 GA Leiderdorp
Netherlands
Tel.: +31 071 582 8282
s.vogels@erasmusmc.nl

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## ABSTRACT

The diagnosis chronic exertional compartment syndrome is traditionally linked to elevated intracompartmental pressures, although uncertainty regarding this diagnostic instrument is increasing. The aim of current review was to evaluate literature for alternative diagnostic tests. A search in line with PRISMA criteria was conducted. Studies evaluating diagnostic tests for chronic exertional compartment syndrome other than intracompartmental pressure measurements were included. Bias and quality of studies were evaluated using the Oxford Levels of Evidence and the QUADAS-2 instrument. A total of 28 studies met study criteria (MRI n = 8, SPECT n = 6, NIRS n = 4, MRI and NIRS together n = 1, miscellaneous modalities n = 9). Promising results were reported for MRI (n = 4), NIRS (n = 4) and SPECT (n = 3). These imaging techniques rely on detecting changes of signal intensity in manually selected regions of interest in the muscle compartments of the leg. Yet, diagnostic tools and protocols were diverse. Moreover, five studies explored alternative modalities serving as an adjunct, rather than replacing pressure measurements. Future research is warranted as clinical and methodological heterogeneity were present and high quality validation studies were absent. Further optimization of specific key criteria based on a patient's history, physical examination and symptom provocation may potentially render intracompartmental pressure measurement redundant.

**ABBREVIATIONS**

| | |
|---|---|
| ERLP | exercise-related leg pain |
| ICP | intracompartmental pressure |
| ICPM | intracompartmental pressure measurement |
| MRI | magnetic resonance imaging |
| NIRS | near infrared spectroscopy |
| SPECT | single photon emission computed tomography |

# Introduction

Chronic exertional compartment syndrome (CECS) is a condition characterized by a sensation of predictable pain and tightness upon performing repetitive physical activity. CECS is one of the causes of exercise-related leg pain (ERLP) in active individuals, athletes and military service members [1, 2]. Symptoms are thought to result from elevated intracompartmental pressure (ICP) secondary to muscular expansion within a relatively noncompliant fascia, though the exact pathophysiological mechanism is unknown [3]. Muscle compartments of both the upper and lower extremities can be affected, with involvement of one of the four leg compartments being most commonly reported. Symptoms may become disabling, particularly as they may emerge sooner each time after covering a specific distance [4].

The presence of CECS is suspected on the basis of a characteristic history and a painful muscle palpation immediately after provocative exertion. The diagnosis is more likely once too high ICPs are demonstrated by invasive needle or catheter manometry. This diagnostic technique allows for measurement of ICPs before, during and after provocative exercise, with the 1 minute post-exercise value probably being most indicative [5]. Commonly applied ICP cut-off values were proposed by Pedowitz [6] (resting ICP > 15 mmHg; ICP one minute after exercise > 30 mmHg; ICP five minutes after exercise > 20 mmHg). However, consensus regarding these threshold values and a standardized test protocol are currently lacking [5, 7]. In addition, ICP patterns during exercise were shown to be complex, with ICP values greatly exceeding Pedowitz criteria in selected participants without symptoms [8]. Any correlation between exertional pain and ICP is even further challenging the assumption that CECS is solely a problem of rising pressures [1, 9]. Moreover, the invasive character of an ICP measurement (ICPM) with risk of pain, hematoma, nerve damage or infection is considered a disadvantage.

Alternatives for the commonly applied ICPM are currently not widely integrated in the diagnostic work-up of CECS. A first suggestion for alternative diagnostic testing was proposed in 1982 as alterations in Korotkoff sounds were thought to reflect an elevated ICP [10]. Styf et al. [11] combined ICPM with the measurement of nerve conduction velocity by using electromyography (EMG), whereas Reneman [12] explored a combination with phlebography. In subsequent decades, alternative strategies focused on magnetic resonance imaging (MRI), single-photon emission computed tomography (SPECT), near-infrared spectroscopy (NIRS), or several forms of ultrasonography [7, 13, 14]. However, an overview of the available evidence for the use of these alternatives in CECS management is currently lacking, and thus ICPM remains the universally used diagnostic test irrespective of its disadvantages.

Considering these limitations of ICPM, the aim of this systematic review is to evaluate the currently available literature regarding methods other than ICPM to diagnose CECS. Results of this review may stimulate the development of more accurate and less invasive diagnostic techniques for CECS.

# Materials and Methods

## Search strategy

The search strategy and systematic analysis were performed according to the PRISMA statement methodology and registered prospectively in PROSPERO (CRD42019142928) [15]. A search was conducted in PubMed, EMBASE, Web of Science, Cochrane, CENTRAL, and Emcare using key words “chronic exertional compartment syndrome”, “anterior compartment”, “posterior compartment”, “peroneal compartment”, “exertional leg pain”, “medial tibial pain”, “overuse injuries”, and “diagnosis”. All related MeSH terms, synonyms and plurals were entered (supplementary **table 1**). Studies published between January 1st of 1970 and May 1st 2021 were eligible. In addition, relevant publications identified outside this strategy were added manually, based upon subjective expert opinions of this group of authors.

## Inclusion criteria

Clinical studies published in English, or fully translated into English, reporting on a minimum of five human participants who were likely suffering from leg CECS were considered. Studies were included if the diagnosis of CECS was based on a clinical examination (history of pain and tightness; physical examination of tenderness on palpation) and suggestive images of MRI scans, SPECT scans, NIRS or other diagnostic modalities different from ICPM. Studies comparing the results of these alternative diagnostic tools to ICPM were also included.

## Exclusion criteria

Studies concerning acute compartment syndrome, compartment syndrome secondary to a condition other than repetitive physical activity (like running or marching), or a compartment syndrome in body parts other than the leg were excluded. Reports with focus on combinations of CECS with Medial Tibial Stress Syndrome (MTSS) or Popliteal Artery Entrapment Syndrome in an affected individual patient were not considered. Reviews, case reports, letters, expert opinions and narrative articles were excluded. If two articles were reporting on an identical cohort, the smallest study was excluded.

## Data analysis

Study design, patient demographics, applied diagnostic test(s), and comparator groups of included studies were entered into an Excel spreadsheet (Microsoft, Redmond, Washington, 2010) by two researchers (SV and ER) independently. Studies reporting on comparable diagnostic modalities were grouped together. Subsequently, the presence of clinical and/or methodological heterogeneity was evaluated qualitatively. Results of studies with comparable designs were pooled and tested for statistical heterogeneity.

## Assessing the quality of evidence

Levels of evidence were assigned to the included studies, according to the Oxford 2011 Levels of Evidence [16]. Potential bias and quality of studies was evaluated according to the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) instrument [17]. The risk of bias was assessed in 4 different domains (patient selection, index test, reference standard and flow and timing of the study), whereas applicability concerns were assessed using 3 domains (patient selection, index test and reference standard). The judgement of bias was done by the two researchers independently, using the signaling questions presented in the QUADAS-2 instrument. Discrepancies between reviewers were resolved by discussion or by consultation of the senior author (RH).

# Results

## Study selection

A total of 3,621 studies were identified (▶ **Fig. 1**). Following duplicate removal and screening of title and abstract, 196 articles were assessed for eligibility. Of these, 87 reports covered a diagnostic modality. As ICPM was studied in 59 of these, 28 studies met inclusion criteria.

## Study characteristics

A total of 2,980 participants (CECS patients n = 1,404, ERLP patients n = 1,483, healthy controls n = 93; ▶ **Table 1**) were studied in these 28 reports. The evaluated alternative diagnostic tests were MRI (n = 8), NIRS (n = 4), MRI and NIRS together (n = 1) or SPECT scans (n = 6; ▶ **Fig. 1**, Supplementary **Table 2**–**4**). The nine remaining studies reported on a miscellaneous group of modalities, including EMG (n = 2) and nerve conduction (n = 2; supplementary **Table 5**). Most studies (n = 24) were published before 2015 (range 1982 to 2018). After data extraction, the presence of clinical and methodological heterogeneity was deemed highly likely. The variety in study designs and test protocols hampered the performance of data pooling and sensitivity analysis.

## Magnetic resonance imaging (MRI, n = 9)

Eight of the nine studies evaluating MRI as a suitable diagnostic test for CECS (Supplementary **Table 2**) used ICPM as reference [18–25]. Exercise protocols provoking symptomatology varied from performing dorsi- or plantar flexion against resistance [19, 22, 23] to the use of a treadmill [18, 20, 24–26]. Images were obtained either before and after exercise [18–20, 24–26] or during isometric contraction of the lower leg muscles [22, 23]. One study reported on images at rest in clinically symptomatic patients [21]. All studies used similar MRI processing protocols, by analyzing changes in signal intensity for specific regions of interest.

Four studies suggested promising results for T1-weighted [18], T2-weighted [20, 25] or diffusion tensor imaging [26] scans. Two additional studies showed that a 1.54 ratio of signal difference in T2-weighted scans obtained in rest and during isometric contraction was considered an appropriate cut-off point for abnormally elevated ICPs [22, 23]. Sensitivity and specificity were 96 % and 88 %, respectively.

On the contrary, two studies using T2-weighted scans failed to correctly identify patients with CECS [19, 24]. The ninth study not using an exercise protocol concluded that MRI was only suitable as adjunct to ICPM, in order to exclude bone abnormalities [21].

## Near infrared spectroscopy (NIRS, n = 5)

Five studies exploring the applicability of NIRS used ICPM as reference standard (Supplementary **Table 3**) [24, 27–30]. Studies (n = 2) with the Runman probe (NIM inc., Philadelphia) used dorsi- or plantar flexion against resistance for provocation of symptoms [27, 29], whereas studies (n = 3) with the InSpectra Tissue Spectrometer (Hutchinson Technology inc., Hutchinson, Minnesota) used a treadmill [24, 28, 30]. Position of both probe types was at the middle third portion of the tibialis anterior muscle. Relative changes in oxygenation were measured continuously before, during and after exercise in all 5 studies.

Reports with the Runman probe indicated that reoxygenation of muscles after exercise in patients with CECS required more time compared to other ERLP patients and control participants [27, 29]. Both studies concluded that NIRS is a useful noninvasive adjunct tool for evaluation of CECS of the anterior compartment.

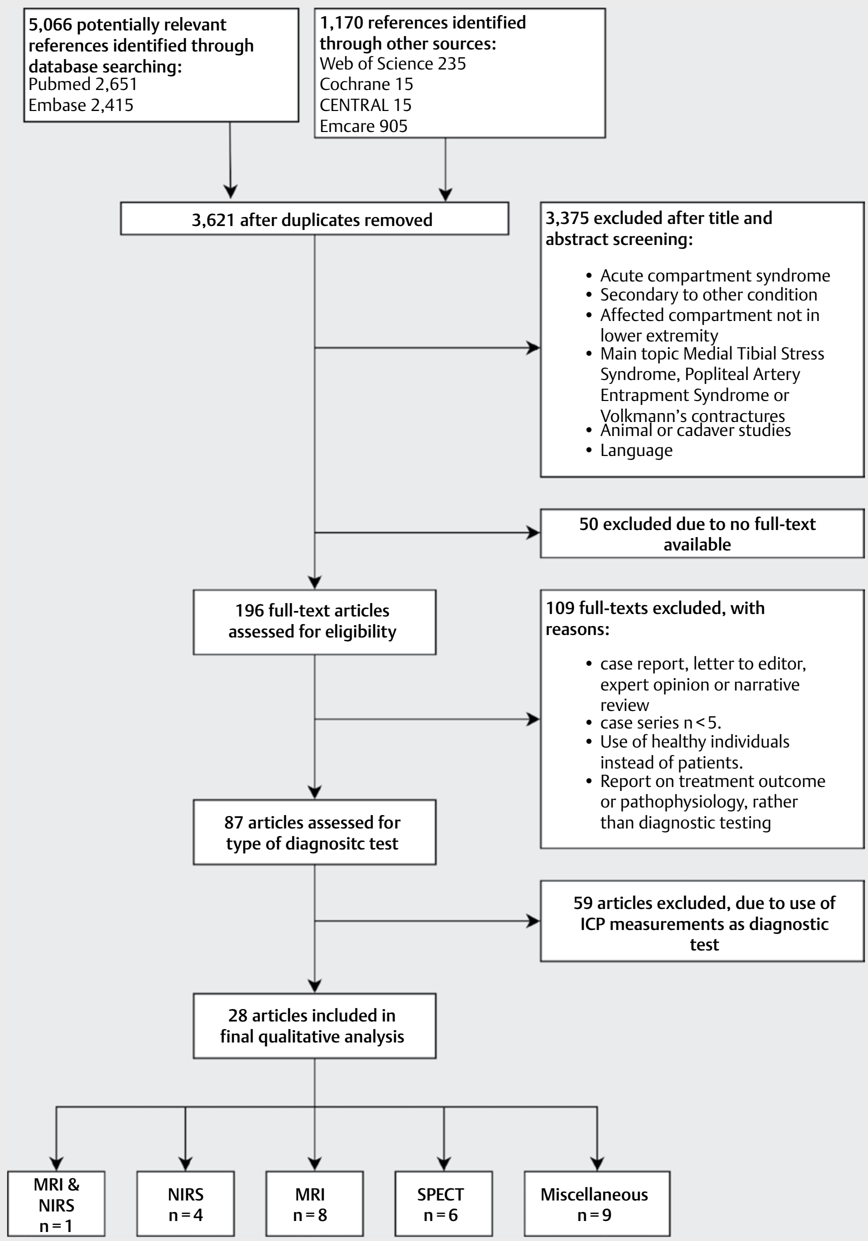
These findings could not be confirmed in a recent study by Rennerfelt et al. [28] with the InSpectra Tissue Spectrometer. Sensitivity and specificity ranged from 1–38 % and 1–50 %, respectively, when analyzing various indicator thresholds during and after exercise in CECS and ERLP patients (e. g. peak-exercise deoxygenation and reoxygenation time). A 94 % sensitivity was found for the percentage change between peak-exercise and baseline oxygenation, although specificity was just 20 %. The authors therefore concluded that NIRS could not accurately distinguish CECS from other types of ERLP.

Two other studies also using this InSpectra probe suggested that NIRS and ICPM were equally effective in distinguishing patients with CECS from healthy volunteers [30] or other ERLP patients [24]. They based their conclusions on substantial differences during exercise, but could not confirm the prolonged recovery time after exercise. The authors reported that NIRS could serve as a noninvasive and user-friendly equivalent to ICPM.

## Single-photon emission computed tomography (SPECT, n = 6)

The usability of SPECT scans for CECS was researched in six studies with ICPM as a reference standard (Supplementary **Table 4**) [31–36]. Scans were obtained before and after treadmill exercise in three studies, whereas two other studies only obtained scans after exercise. The sixth study did not use an exercise protocol and did not further specify timing of the scan. All studies used different dosages of analogues of either Technetium or Thallium.

The two studies investigating two different types of Technetium used comparable protocols as scans were obtained and analyzed for isotope uptake after exercise and in rest, whereas participants served as their own control [32, 33]. Edwards et al. [32] found a 80 % sensitivity and a 97 % specificity for distinguishing CECS from ERLP, using their protocol. In contrast, Oturai et al. [33] reported that SPECT had a mere 50 % sensitivity and a 63 % specificity, indicating that this technique was not useful for diagnosing CECS.




▶ **Fig. 1** Flow chart of selected studies.

A study using Thallium also evaluated participants after exercise and in rest, but compared patients with CECS to healthy controls [36]. These results showed that CECS was characterized by a redistribution pattern of the isotope, rather than a washout (as was the case in controls). These preliminary data were found to be promising.

Two other studies using a Thallium injection only obtained scans after exercise [34, 35]. The first study found evident ischemic compartments in legs of patients with CECS, when comparing perfusion patterns to healthy volunteers [34]. Perfusion signals clearly improved after surgical treatment. However, a subsequent study using unaffected compartments as control could not confirm these findings, suggesting a limited diagnostic role for SPECT [35].

## Miscellaneous alternative diagnostic procedures

Among the nine remaining studies, two studies reported promising results regarding a noninvasive diagnostic test (Supplementary **Table 5**) [10, 37]. These two studies showed that laser doppler flow has a different time course in CECS [37], and that Korotkoff sounds were more persistent in the tibialis anterior artery in CECS [10]. Subsequent studies confirming these findings were not identified using our search strategy.

▶ **Table 1** Summary of Studies (n = 28)

| Author | Year | Study design | Level of evidence | Study population (n) | | | | Male/ female | μ age in years (range) | Affected compart-ments | μ duration of symptoms in months (range) | Diagnostic test | | | | Compared to ICP manom-etry? |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | CECS pa-tients | ERLP pa-tients | Con-trols | Civil or mili-tary? | | | | | Civil or mili-tary? | MRI | NIRS | SPECT | |
| Abraham et al. [37] | 1998 | P | 4 | 6 | – | 7 | C | – | – | – | – | N | N | N | Y | Y |
| Allen et al. [31] | 1995 | R | 4 | 28 | 32 | – | C | 40/20 | 29 (-) | A, DP | – | N | N | Y | N | Y |
| Amendola et al. [18] | 1990 | P | 3 | 5 | 15 | 5 | C | 14/11 | – (15–59) | A, L, DP, SP | – | Y | N | N | N | Y |
| Andreisek et al. [19] | 2009 | P | 4 | 9 | – | 10 | C | 11/8 | – (20–47) | A | – | Y | N | N | N | Y |
| Burnham et al. [43] | 1994 | P | 4 | 6 | – | – | C | 4/2 | 27 (23–34) | A, L, DP | 35 (2–132) | N | N | N | Y | Y |
| de Bruijn et al. [38] | 2018 | R | 4 | 698 | 713 | – | C | 633/778 | – (12–90) | A, L, DP | – (1–360) | N | N | N | Y | Y |
| Edwards et al. [32] | 1999 | R | 4 | 11 | 7 | – | C | – | – | A, L, DP, SP | – | N | N | Y | N | Y |
| Eskelin et al. . [20] | 1998 | R | 4 | 6 | 7 | 4 | M | 17/0 | – (18–30) | A | – | Y | N | N | N | Y |
| Fouasson-chailloux et al. [39] | 2018 | R | 4 | 96 | 29 | – | C | 94/41 | – | A, L, DP | – | N | N | N | Y | Y |
| Hayes et al. [36] | 1995 | P | 4 | 5 | 9 | 3 | C | 9/8 | – (17–40) | A, L, DP | – | N | N | Y | N | Y |
| Kiuru et al. [51] | 2003 | R | 4 | 14 | 10 | – | M | 23/1 | – (18–23) | A | 3 (1–13) | Y | N | N | N | Y |
| Korhonen et al. [40] | 2005 | P | 4 | 11 | 6 | – | C | – | – | A | – | N | N | N | Y | Y |
| Litwiller et al. [22] | 2007 | P | 4 | 14 | 28 | 8 | C | – | – | – | – | Y | N | N | N | Y |
| Mohler et al. [27] | 1997 | P | 3 | 10 | 8 | 10 | C | – | – | A | – | N | Y | N | N | Y |
| Oturai et al. [33] | 2006 | P | 4 | 6 | 8 | – | C | 12/2 | – (21–57) | A, DP, SP | – | N | N | Y | N | Y |
| Rennerfelt et al. [28] | 2016 | P | 3 | 87 | 72 | – | C | 76/83 | – (14–67) | A | – | N | Y | N | N | Y |
| Rennerfelt et al. [41] | 2018 | P | 4 | 168 | 309 | – | C | 258/219 | – (15–70) | A | – | N | N | N | Y | Y |
| Ringler et al. [52] | 2013 | P | 3 | 23 | 53 | – | C | 29/47 | 30 (10–76) | A | – | Y | N | N | N | Y |
| Rowdon et al. [44] | 2001 | P | 3 | 10 | – | 10 | C | 14/6 | – (14–40) | A | – | N | N | N | Y | Y |
| Sigmund et al. [26] | 2013 | P | 3 | 14 | – | 8 | C | 12/10 | – (15–44) | A, L, DP, SP | – | Y | N | N | N | N |
| Takebayashi et al. [34] | 1997 | R | 4 | 9 | – | 8 | C | 11/6 | – (18–28) | A, L, DP, SP | – | N | N | Y | N | Y |
| Trease et al. [35] | 2001 | P | 3 | 25 | 9 | – | C | 20/14 | 29 (18–55) | A, DP | – | N | N | Y | N | Y |
| van den Brand et al. [24] | 2005 | P | 3 | 42 | 3 | – | M | – | – | A | – | Y | Y | N | N | Y |
| van den Brand et al. [30] | 2004 | P | 3 | 10 | – | 8 | C + M | 15/3 | – | A | – | N | Y | N | N | Y |
| Verleisdonk et al. [25] | 2001 | P | 3 | 21 | – | 12 | C | 24/9 | – (18–35) | A | – | Y | N | N | N | Y |
| Willey et al. [10] | 1982 | P | 4 | 7 | 15 | – | C | 17/5 | – (16–30) | A | – | N | N | N | Y | N |
| Zhang et al. [42] | 2011 | P | 3 | 16 | 21 | – | C | 24/13 | 33 (16–56) | A | – | N | N | N | Y | Y |
| Zhang et al. [29] | 2012 | P | 3 | 47 | 129 | – | C | 73/103 | 34 (14–76) | A | 71 (3–360) | N | Y | N | N | Y |

A = anterior compartment, C = civil, DP = deep posterior compartment, L = lateral compartment, M = military, N = no, P = prospective, R = retrospective, SP = superficial posterior compartment, Y = yes.

Five studies suggested that various alternative modalities potentially served as an adjunct to ICPM, rather than replacing it [38–42]. Patients with CECS were demonstrated to have distinct EMG patterns, that could differentiate between elevated ICP's due to either volumetric load or concomitant contraction of the muscle [40, 42]. This approach could potentially prevent a false positive diagnosis in a CECS patient. Three questionnaire studies focusing on patient characteristics provided tools for more accurate selection of patients with an indication for ICPM, so useless and potentially harmful procedures can be prevented [38, 39, 41].

Nerve conduction studies did not contribute to a diagnosis of CECS, neither as a stand-alone modality, nor as an adjunct [43, 44].

### Risk of bias and quality of evidence

The overall quality of included studies was low whereas structured validation studies were lacking (▶ **Table 1**, ▶ **Table 2**). For instance, the majority of studies (93 %) used ICPM as reference standard with various cut-off values (e. g. Pedowitz (n = 11), > 35 mmHg 1 min after exercise (n = 4), > 40 mmHg 1 min after exercise (n = 4), other cut-off value (n = 2)). Five studies (5/26, 19 %) did not even define their used cut-off value for ICPM. Two studies did not incorporate a reference standard in their study protocol. Concerns regarding applicability of patient selection were raised in studies with populations only consisting of military service members, thereby possibly hampering extrapolation of findings to civil populations. Furthermore, sample sizes were often small with a limited number of controls.

## Discussion

The current overview mainly identifies conflicting evidence regarding the diagnostic ability of alternative diagnostic tests for diagnosing CECS in a leg. Promising results were reported in half of the included studies (14/28), although diagnostic modalities and protocols were diverse. Validation studies confirming these promising results were not performed. Currently, a large gap of knowledge is present with respect to an easy-to-use and reliable non-invasive alternative for the commonly used ICPM for CECS.

▶ **Table 2** Analysis of quality scores using the QUADAS-2 instrument [17]

| Author | Risk of bias | | | | Applicabilityconcerns | | |
|---|---|---|---|---|---|---|---|
| | Patient selection | Index test | Reference standard | Flow and timing | Patient selection | Index test | Reference standard |
| Abraham et al. [37] | ● | ○ | ○ | ○ | ● | ○ | ○ |
| Allen et al. [31] | ● | ● | ○ | ● | ● | ● | ○ |
| Amendola et al. [18] | ○ | ○ | ● | ● | ○ | ○ | ● |
| Andreisek et al. [19] | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Burnham et al. [43] | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| de Bruijn et al. [38] | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Edwards et al. [32] | ○ | ○ | ● | ○ | ○ | ○ | ● |
| Eskelin et al. [20] | ○ | ○ | ○ | ○ | ● | ○ | ○ |
| Fouasson-chailloux et al. [39] | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Hayes et al. [36] | ○ | ○ | ● | ○ | ○ | ○ | ● |
| Kiuru et al. [51] | ○ | ● | ○ | ● | ○ | ● | ○ |
| Korhonen et al. [40] | ● | ○ | ○ | ○ | ● | ○ | ○ |
| Litwiller et al. [22] | ○ | ○ | ● | ○ | ○ | ○ | ● |
| Mohler et al. [27] | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Oturai et al. [33] | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Rennerfelt et al. [28] | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Rennerfelt et al. [41] | ○ | ○ | ● | ○ | ○ | ○ | ● |
| Ringler et al. [52] | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Rowdon et al. [44] | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Sigmund et al. [26] | ○ | ○ | ● | ○ | ○ | ○ | ● |
| Takebayashi et al. [34] | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Trease et al. [35] | ○ | ● | ○ | ○ | ○ | ● | ○ |
| van den Brand et al. [24] | ○ | ○ | ○ | ○ | ● | ○ | ○ |
| van den Brand et al. [30] | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Verleisdonk et al. [25] | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Willey et al. [10] | ○ | ● | ● | ○ | ○ | ● | ● |
| Zhang et al. [42] | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Zhang et al. [29] | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

● = high; ○ = low

This is the first study that provides an extensive literature overview on alternative diagnostic tests in CECS. Today's focus in literature is on the reliability and accuracy of ICPM [5, 7], although several critical discussions regarding alternative tests are available [7, 45]. Although clear recommendations were provided by Roberts et al. [5] and Aweid et al. [7], a universally accepted standardized protocol and/or cut-off value for ICPM in CECS remain yet to be defined. As the value of ICPM is increasingly questioned, shifting perspective from the invasive ICPM to alternative testing modalities for CECS is indicated. Another aspect underlining this urgent need is the unexpected restricted availability of needle equipment throughout Europe (▶ **Table. 3**).

Potentially promising results were provided by MRI (n = 4), NIRS (n = 4) and SPECT (n = 3), techniques that all focused on detecting changes in signal intensity in manually selected regions of interest of the leg muscle compartments. Using this strategy, high levels of sensitivity (96 %) and specificity (88 %) were found using T2 weighted MRI scans at rest and during isometric contraction. In addition, good test characteristics (sensitivity 80 %, specificity 97 %) were also found for SPECT scans using Technetium obtained at rest and following peak-exercise. As for NIRS, an impressive sensitivity (94 %) was found when observing the percentage-change between peak-exercise and baseline oxygenation, but the specificity of this indicator was a dismal 20 %. Nevertheless, focusing on changes in signal intensity should be part of the future study protocols in CECS.

Remarkably, 86 % of the included studies are more than five years old. In addition, just seven reports (25 %) were published after the appearance of two systematic reviews questioning the validity and reliability of ICPM [5, 7]. These findings raise the question whether any new or modern imaging and diagnostic techniques are currently considered at all for CECS. This is possibly explained by the obscureness of the exact etiology of CECS as well as the ongoing doubt regarding ICP as the reliable diagnostic modality of CECS. If one considers CECS as the consequence of locally induced ischemia, NIRS might be a useful adjunct. Interestingly, second or third generation NIRS probes (other than the Runman and/or InSpectra probe) are successfully introduced in various other fields of medicine [46]. Moreover, if aberrant tissue perfusion plays a role in the pathogenetic mechanism of CECS, near-infrared fluorescence with indocyanine green could be of importance. This technique was recently found to be of value in the management of peripheral arterial disease and therefore of interest for forthcoming research projects in our research group [47].

Apart from exploring novel technical developments, further finetuning of simple or already available diagnostic strategies should not be overlooked. For example, two studies stipulated the potential use of ultrasonography reflecting levels of ICPs [14, 48]. In addition, predictive models such as nomograms or evaluation of specific pain profiles after symptom provocation might have value as an easy-to-use and noninvasive alternative to ICPM [1, 38, 49]. By identifying key criteria, the use of additional invasive diagnostic tests might even become unnecessary. Such an approach was proposed by the American College of Rheumatology regarding diagnostic criteria for giant cell temporal arteritis [50]. A first attempt at the formulation of such criteria is currently being pursued using a modified Delphi questionnaire with an international study group.

▶ **Table. 3**

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|---|
| Although beyond the scope of this review, there is a current shortage of available specific indwelling catheters for ICPM. For almost two years we have experienced an unexpected restriction of needle equipment throughout Europe, as sales of the indwelling Slit catheters and side-port needles by Stryker (Kalamazoo, MI) were permanently discontinued. This brand of catheters and needles was commonly used, often with locally established (brand specific) cut-off points. As a consequence, a number of clinicians changed from Stryker to less familiar ICPM needle systems, without knowing how comparable these different needle (static) ICPM systems are. These uncertainties would have been less urgent if alternatives had been studied more extensively. |

Several limitations of the presented findings must be addressed, the most prominent being the lack of uniformity amongst applied test protocols and diagnostic modalities. Resulting in serious clinical and methodological heterogeneity. Moreover, the limited number of controls and small study populations further hamper comparison of individual study outcomes. The absence of large and well-structured trials impedes formulation of clear guidelines for subsequent research. Nevertheless, the current overview clearly illustrates the direction of future studies, particularly as the gold diagnostic standard of CECS is still lacking.

## Conclusion

The measurement of ICP to confirm CECS is associated with serious limitations, whereas alternative diagnostic tests are currently not available. The present review found that approximately half of the studies evaluating alternative diagnostic tests for CECS, including MRI, NIRS and SPECT reported encouraging results. However, these studies are of low quality with serious clinical and methodological heterogeneity and therefore not opportune for clinical practice. Validation studies with univocal endpoints and standardized protocols are required to determine superiority amongst alternative diagnostic test for CECS. At the same time, with further optimization of diagnostic criteria based on a patient's history, physical examination and symptom provocation, diagnostic testing with ICPM might become obsolete. The current overview will stimulate further development of more accurate and less invasive diagnostic testing of patients with CECS.

## Practical Implications

- The current overview provides an impetus and window of opportunity for future research in the field of diagnostic testing for patients suffering from chronic exertional compartment syndrome.
- Promising results were reported in half of the included studies, although no structured validation studies were encountered.
- The possibility of comparing individual outcomes was hampered by the lack of uniformity amongst applied test

protocols and diagnostic modalities, the limited number of controls, and the small study populations.

- Further optimization of diagnostic criteria based on a patient's history, physical examination and symptom provocation has the potential to make diagnostic testing with intracompartmental pressure measurement obsolete.

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### Conflict of Interest

The authors declare that they have no conflict of interest.

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