Review of Reliable and Valid Noninvasive Tools for the Diagnosis of Chronic Exertional Compartment Syndrome

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Background: Currently, invasive dynamic intracompartmental pressure (ICP) measurements are considered the gold standard for diagnosis of chronic exertional compartment syndrome (CECS). During recent years, different noninvasive imaging modalities have been presented as a possible replacement for ICP measurement.

Purpose: To provide an overview of the current state of evidence and possibilities regarding noninvasive diagnostic methods for CECS.

Study Design: Scoping review; Level of evidence, 4.

Methods: The PubMed (MEDLINE) and Embase databases were searched using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Full-text articles were included if they reported on noninvasive diagnostic methods for CECS, included ≥5 patients with CECS, and were published between 1994 and 2022. Articles not written in English were excluded. Systematic reviews, letters to the editor, and case reports were not eligible for inclusion. Out of 961 articles identified in the initial search, 25 studies (N = 1257 participants) were included. Risk of bias was assessed using the Quality Assessment of Diagnostic Accuracy Studies–Comparative (QUADAS-C) tool for comparative studies and the QUADAS-2 tool for noncomparative studies. Narrative synthesis was used to present results.

Results: The level of evidence for the 25 studies ranged from 2 to 4. Four studies were classified as having a low risk of bias, 21 studies were classified as being at risk of bias. The following noninvasive diagnostic tools for CECS were reported: magnetic resonance imaging/diffusion tensor imaging (n = 8), near-infrared spectroscopy (n = 6), electromyography (n = 4), single-photon emission computed tomography (n = 5), ultrasound (n = 2), myotonometry (n=1) and predictive clinical model (n = 1). There was insufficient evidence in the literature to support the use of any of these noninvasive diagnostic tools as a gold standard for CECS.

Conclusion: Despite the need to replace the controversial use of ICP for the diagnosis of CECS, our review indicated a lack of validity on all discussed noninvasive diagnostic tools as a replacement.

Keywords: chronic exertional compartment syndrome (CECS); diagnosis; noninvasive; sports medicine; traumatology

Chronic exertional compartment syndrome (CECS) is a common and underdiagnosed cause of exertional leg pain (ELP).[13,19] CECS may occur in all fascia surrounded muscle groups but prevails in the anterior lower leg compartment (anterior CECS; 39% of all patients with CECS).[14,62] The exact pathophysiology of CECS is unknown; however, it is widely accepted that a nonphysiologic increase of pressure within a muscle compartment causes impaired muscle perfusion.[6,12,51,53] Nearly half of patients with ELP have CECS.[11] However, there is still poor awareness of this condition among physicians, paramedics, and sports coaches, and CECS is often confused with other causes of ELP.[6,37,39]

Initially, CECS was diagnosed by exclusion.[60] Currently, dynamic intracompartmental pressure (ICP) measurements are considered gold standard for diagnosis of CECS; however, the validity of this standard has been questioned.[22,25,26,28,33,63] ICP is an invasive test that carries risks such as bleeding or infection.[8,54,63] It is an unpleasant, time-consuming procedure, with patients sometimes undergoing multiple punctures for several compartment readings. Technical aspects of ICP measurements such as accuracy of catheter placement and occurrence of catheter dislodgement are unclear. One study reported that only 38% of catheters were placed accurately in deep posterior CECS.[63] Performing correct ICP readings is technically demanding and requires a learning curve. Moreover, the time interval between end of exercise and the postexercise pressure measurement may vary widely.

Ideally, the diagnosis of CECS is made using a noninvasive technique, which is accurate, patient-friendly, reproducible, and free of interobserver variability.[58,61] During

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recent years, different noninvasive imaging modalities have been presented as a possible replacements for ICP measurement. The first diagnostic modality, which was proposed over 20 years ago was magnetic resonance imaging (MRI); evidence regarding its validity was conflicting.[56] In recent years, the range of possibilities has expanded due to the development of new diagnostic tools and imaging.

Possible noninvasive diagnostic tools for CECS may be divided into 2 categories based on the model proposed by Walters et al[58]: (1) tools that measure mechanical surrogates of ICP and (2) tools that measure primarily indices of tissue perfusion. Myotonometry (MYO) and ultrasound (US) belong to the first category. MYO records the oscillation frequency of a muscle (MYO_{freq}) reflecting its elastic properties, as well as logarithmic decrement of decay (MYO_{dec}), reflecting its viscous properties.[24] Gershuni et al[19] showed that anterior compartment muscle depth as an indicator of volume changes can be measured by using the method of Martinson and Stokes[30] to estimate the cross-sectional area of a muscle group on US.[20] Single-photon emission computed tomography (SPECT), which makes use of intravenously injected radioactive isotopes (thallium-201, technetium-99 m),[15,23,32,50] near-infrared spectroscopy (NIRS), which measures changes in tissue oxygenation (StO_2),[55] and functional MRI techniques such as T1- and T2-weighted imaging as well as arterial spin labeling,[55,56] which reflect tissue and blood water content, belong to the second category. Diffusion tensor imaging is a type of MRI that provides quantitative markers of tissue microstructure such as mean diffusivity and may be used to detect muscle damage.[46,47] Changes in electromyography (EMG) frequency or amplitude may reflect nerve dysfunction, which develops as a result of elevated ICP due to inhibition of local vascular flow, followed by transient nerve ischaemia in CECS.[40,65]

Recently, 2 different predictive clinical models have been proposed to diagnose CECS. de Bruijn et al[11] presented a model incorporating age, gender, history of lower leg pathology, bilateral symptoms, types of sports (running and skating), and a painful/tensed compartment during sports as independent predictors of CECS. Fouasson-Chailloux et al[18] presented a predictive model that associated muscle hardness (odds ratio [OR], 2.18; $P < .001$) and muscle hernia after exercise (OR, 1.44; $P < .001$) with CECS.

With many new studies available regarding the use of noninvasive modalities in CECS, an overview of the current state of evidence is lacking. This is necessary to take the next step in either the development or implementation of new noninvasive diagnostic tools for use in the clinic, to ensure better patient care and a reliable clinical diagnosis before treatment is initiated. Therefore, the purpose of this review was to provide an overview of the current state of evidence. We hypothesized that some of these new tools may be as reliable as ICP to diagnose CECS.

METHODS

Literature Search

This review was conducted according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.[35] The PubMed (MEDLINE) and Embase database were searched on August 16, 2022, using a stepped strategy (Appendix Table A1). Using a thesaurus and Medical Subject Headings terms, synonyms for the terms "diagnosis" and "chronic exertional compartment syndrome" were identified and used in the first 2 steps.

The following inclusion criteria were applied: subject of the article was lower extremity CECS, the article mentioned noninvasive diagnostic methods, minimal number of patients with CECS was ≥ 5. Only articles written in English and published between 1994 and 2022 were included in this review. Reports such as unpublished manuscripts, letters to the editor, or commentaries and conference abstracts were not eligible for inclusion.

After setting of limits and removal of duplicates, the databases provided 961 articles. After screening of titles and abstracts, 95 potential articles were identified. Next, a full-text screening of these 95 articles was performed by 2 independent reviewers (A.M.K. and M.W.), with any disagreements between the reviewers resolved by consensus. Ultimately, 25 studies met all inclusion criteria and were included in this review.[§] The PRISMA flowchart of this study is presented in Figure 1.

Data Collection

All included articles were read line-by-line independently by the first author (A.M.K.) and senior author (M.W.) to extract relevant data. All relevant data were tabulated in an Excel spreadsheet (Microsoft) by the first author and consecutively extracted and checked separately and independently by the senior author. From each study, the following data were extracted: name of first author, year of publication, setting, demographic data, number of participants, lower leg compartments involved, details regarding the diagnostic modality, and study outcomes or conclusions. Questions regarding data interpretation were solved based on consensus with the senior author. Level of evidence was

[§]References 1, 5, 7, 15, 16, 21, 23, 24, 27, 31, 32, 38, 39, 41, 46, 47, 50, 52, 54–57, 59, 65, 66.

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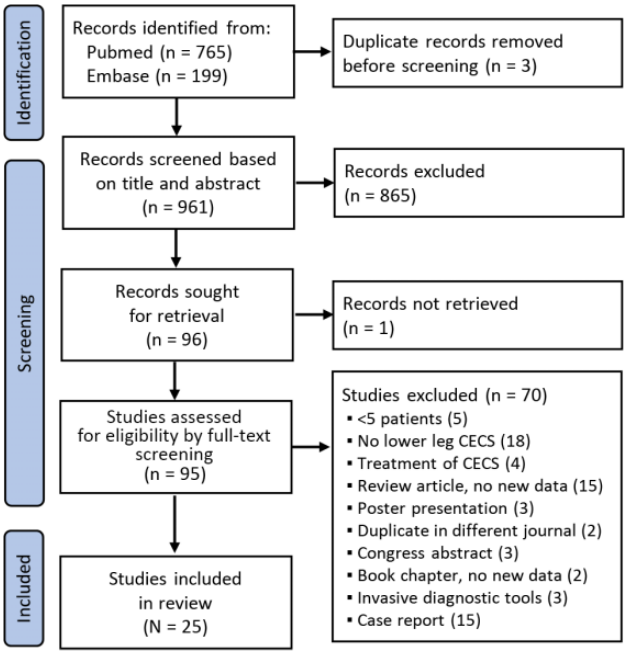

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart of study selection. CECS, chronic exertional compartment syndrome.

reported for each study following the guidelines presented by Shekelle et al.[45] Quality of evidence was assessed and reported as recommended by the Quality Assessment of Diagnostic Accuracy Studies–Comparative (QUADAS-C) tool for comparative studies and the QUADAS-2 tool for noncomparative studies. The QUADAS tool is used to assess risk of bias and concerns regarding applicability and consists of 4 key domains: (1) patient selection, (2) index test, (3) reference standard, and (4) flow and timing.[12,64]

Statistical Analysis

The primary outcome measure of this study was the validity of noninvasive diagnostic tools for CECS as expressed by sensitivity and specificity of the noninvasive diagnostic tool compared with the gold standard, ICP. As described by the *British Medical Journal*, a test was considered useful when sensitivity + specificity was $\geq$1.5 and not useful if sensitivity + specificity was $<$1.5.[34] The secondary outcome measure was the presence or absence of correlation between findings on the noninvasive diagnostic tool compared with changes in ICP in absence of a reported sensitivity or specificity.

Qualitative Data Analysis

A narrative evidence synthesis was performed, which included a tabulation of results to facilitate comparison between studies. We identified and discussed patterns as well as similarities and differences between study outcomes regarding the same diagnostic tool and the cutoff values that were used to obtain these outcomes.

RESULTS

Literature Search

The 25 included studies were on the following topics: MRI (n = 8),[1,16,27,39,46,47,54,56] NIRS (n = 6),[21,31,38,54,55,66] EMG (n = 4),[7,24,41,65] SPECT (n = 5),[15,23,32,50,52] US (n = 2),[5,59] MYO (n = 1),[24] and predictive clinical model (n = 1).[57]

Study Characteristics

The included studies had levels of evidence ranging from 2 to 4 (level 2, n = 9; level 3, n = 8; level 4, n = 8). Publication years ranged from 1994 to 2022, with data analysis performed between 1991 and 2017. In total, these studies included 1257 participants. Sample size varied from 6 to 201 participants. The mean age of participants ranged from 20.5 to 45.8 years.

Single-Photon Emission Computed Tomography

Four studies described a standardized protocol to obtain SPECT images.[15,23,32,52] Patients were subjected to graded exercise depending on which activity is known to cause the symptoms, until typical symptoms were reproduced. The isotope was injected subsequently and exercise was continued for 1 to 2 minutes to allow tracer distribution. Imaging was performed after 5 minutes and also after a variable delay of several hours.[15,23,32,50]

Hayes et al[23] first reported that TI-201 SPECT may localize anterior and lateral or posterior ischemic regions in patients with CECS. The study population consisted of 14 patients with ELP, of which 6 had another diagnosis (periostitis, nerve root compression, tibial stress fracture) and 6 had undergone previous compartment releases with recurrent symptoms. Diagnostic accuracy of SPECT for anterior CECS and cutoff values could not be derived.

Takebayashi et al[49] described 9 athletes with clinically diagnosed CECS, in some athletes in $>$1 location (anterior or lateral CECS, n = 1; anterior CECS, n = 3; lateral CECS, n = 3; deep posterior CECS, n = 4). In all patients, compartment pressures were measured in the operating room just before fasciotomy, using the Pedowitz criteria. SPECT images were obtained pre- and postfasciotomy and compared with those of healthy volunteers. Postoperative SPECT demonstrated improved isotope uptake in all compartments after fasciotomy. The average isotope uptake in healthy volunteers was 75% (anterior), 69% (lateral), 72% (superficial posterior), and 68% (deep posterior), where 100% was considered the maximum possible isotope uptake in a standard reference area. Contrary to this, ischemic compartments in patients with CECS had a mean isotope uptake ranging from 25% to 48%. The lower limits of normal for the percentage uptake were estimated to be approximately 60% (anterior) and 50% (other lower leg compartments). Qualitative analysis confirmed these quantitative results in all patients with CECS. Diagnostic accuracy of SPECT for CECS and cutoff values could not be extracted from this study.[50]

Edwards et al[15] studied Tc-99 m SPECT compared with ICP (n = 20) and fasciotomy. Out of 10 patients who

TABLE 1
Summary of Current Literature on NIRS and CECS[a]

First Author (Year)	LOE	Reference Standard	Study Population	Type of Compartment	Cutoff Value	Sensitivity/ Specificity, %	Conclusion[b]
Mohler (1997)[31]	4	ICP (Pedowitz)	10 CECS, 10 healthy controls	ANT	NR	NR	+/-
van den Brand (2004)[55]	3	Fasciotomy	Military population: 10 CECS, 8 healthy controls	ANT	NIRS: ■ Peak exercise deoxygenation: >55% ■ ICP: ≥35 mm Hg	■ Peak exercise StO_2: 95/63 ■ ICP: 90/63	+
van den Brand (2005)[54]	2	Fasciotomy	Military population: 42 CECS	ANT	NIRS: ■ Peak exercise StO_2: ≤50% ■ ΔStO_2: ≥35% ■ ICP: ≥35 mm Hg	■ Peak exercise StO_2: 78/67 ■ ΔStO_2: 85/67 ■ ICP: 77/83	+
Zhang (2012)[66]	2	History, clinical examination; if inconclusive, ICP (Pedowitz)	47 CECS, 129 other ELP	ANT	NIRS: ■ 90% reoxygenation time: >30 s	60/45	–
Rennerfelt (2016)[38]	2	History, clinical examination, and ICP (Pedowitz)	87 CECS, 72 other ELP	ANT	NIRS: ■ Peak exercise StO_2: ≤8% ■ ΔStO_2: ≥35% ■ 90% reoxygenation time: >30 s	■ Peak exercise StO_2: 34/43 ■ ΔStO_2: 94/20 ■ 90% reoxygenation time: 38/50	–
Gustafsson (2017)[21]	3	ICP (Pedowitz)	9 diabetic CECS, 11 nondiabetic CECS, 10 diabetic controls, 10 healthy controls	ANT	NR	NR	+/-

[a]ANT, anterior; CECS, chronic exertional compartment syndrome; ELP, exertional leg pain; ICP, intracompartmental pressure; LOE, level of evidence; NIRS, near = infrared spectroscopy; NR, not reported; StO_2, tissue (muscle) oxygen saturation.
[b]+, NIRS can be used as a diagnostic tool for CECS; -, NIRS cannot be used as a diagnostic tool for CECS; +/-, further research is required.

exhibited ischaemia on SPECT, 8 had elevated compartment pressures indicative of CECS or were free of symptoms postfasciotomy. Compared with treatment outcomes, sensitivity and specificity of Tc-99 m SPECT were found to be 80% and 97%, respectively.[15]

Trease et al[51] compared TI-201 SPECT with ICP measurement in 34 participants with ELP. Out of 34 participants, 25 were diagnosed with anterior CECS using the Pedowitz criteria. No difference in perfusion was found between patients with a positive or negative ICP measurement. The authors suggested no diagnostic role for TI-201 SPECT imaging in CECS.[52]

In 2006, Oturai et al[32] studied the diagnostic value of Tc-99 m SPECT in 14 patients, only to find similar results to the ones presented by Trease et al[52]; there was no correlation between increased ICP and muscle hypoperfusion. Sensitivity and specificity of Tc-99 m SPECT compared with ICP measurement were found to be 50% and 63%, respectively.

All the above-mentioned studies were small, nonblinded case-control studies of poor design with a maximum level of evidence of 3.

Near-Infrared Spectroscopy

The exact technique of obtaining NIRS values was specified in 5 studies.[21,31,38,55,66] A probe was placed on the skin parallel to the tibialis anterior muscle fibers at the middle one-third of the lower leg and connected to a spectroscope that analyzes data input and displays StO_2%.[40,44,55] StO_2 values are measured continuously before, during, and after exercise and also postoperatively if fasciotomy is performed.[21,31,38,55,66]

Sensitivity and specificity of NIRS has been studied only for anterior CECS. Devices used were a continuous dual wavelength NIRS spectrometer (Run-Man CWS-2000; NIM)[31,66] and an InSpectra tissue spectrometer (Hutchinson Technology Inc).[21,38,54,55]

The results of studies regarding the diagnostic value of NIRS for diagnosis of lower leg CECS are presented in Table 1. All studies were small-to-moderate size nonblinded case-control studies, with a highest level of evidence of 2.

In summary, based on the findings presented in Table 1, there is limited evidence that measurement of peak exercise deoxygenation may be of diagnostic value to detect the

presence of CECS diagnosed by absence of complaints after fasciotomy.

Surface Electromyography

Only the study by Rowdon et al[41] described the exact technique of obtaining EMG measurements in detail. A recording surface electrode is placed over the extensor digitorum longus and a reference electrode is placed distally over the extensor digitorum tendon. The stimulation point is situated about 9 cm proximal to the recording electrode, near the fibular head. Stimulation is performed pre- and immediately postexercise, after which the recording electrode registers response amplitudes and latencies. From these data, conduction velocities are calculated.[41]

Devices that were used were bipolar Ag/AgCI electrodes combined with a ME3000P Muscle Tester unit with a 2 MB SRAM-card (Mega Electronics Ltd)[24], a standard electromyograph (Nicolet Viking)[41] and bipolar surface electrodes (Blue Sensor, Medicotest)combined with a computerized data acquisition system (Pentium III PC with 12 bits DAQ board and LabVIEW software; National Instruments Corp).[65]

Burnham et al[7] found no impairment of nerve function correlated with increased postexercise ICP; however, deep peroneal nerve motor waveform amplitude was significantly lower in compartments with high ICP (CECS).

Rowdon et al[40] studied the conduction over the tibialis anterior muscle in 10 patients with anterior CECS and found no significant difference between pre- and postexercise conduction velocity in the CECS and control group. CECS group did have a significantly greater pre-exercise amplitude. This amplitude did not change significantly postexercise, contrary to the control group, which showed a postexercise increase in amplitude referred to as "postexercise potentiation."

Korhonen et al[24] investigated the relationship between EMG and ICP signals during rest as well as loading periods in the dorsal forearm and anterior compartment of the lower leg and found a significant correlation and linear relationship between them.

Zhang et al[65] studied EMG signals compared with ICP in 14 patients who fulfilled criteria of CECS (Rorabeck et al[40]), of which 13 had a silent EMG postexercise. Two patients were suspected of CECS based on postexercise ICP; however, after finding a positive EMG signal, they were asked to relax the leg muscles and ICP decreased immediately; therefore, they were confirmed as not having CECS. In the control group, 19 of 21 patients had a silent EMG signal caused by other diagnoses (periostalgia, medial tibial syndrome, peroneal tunnel syndrome, painful fascial defect).

Myotonometry

Korhonen et al[24] studied a population of 26 patients with dorsolateral forearm or anterior CECS and found that MYO_{freq} correlated positively and significantly with ICP at rest and during loading periods. MYO_{dec} values upon maximal voluntary contraction differed significantly between patients with increased ICP and those with normal ICP. No data on sensitivity or specificity of MYO as a diagnostic tool for CECS were reported.

Magnetic Resonance Imaging

The results of studies regarding the diagnostic value of MRI for diagnosis of lower leg CECS are presented in Table 2. Devices that were used for diffusion tensor imaging were the TIM verio T3/TIM trio T3 scanner (Siemens)[47] and the MAGNETOM Verio 3-T scanner (Siemens Healthcare) with a unilateral 15-channel knee coil.[46]

All studies were small-to-medium sized, with a highest level of evidence of 2. In summary, there is limited evidence of low-to-medium quality that a baseline to exercise intensity ratio of >1.54 is indicative of the presence of CECS.[27,39]

Ultrasound

Devices used were 2 B mode US scanners: a portable Aloka SSD-900 with a 7.5-MHz linear probe (KCL) and a Dynamic Imaging Diasus with a 5- to 10-MHz linear probe (Headley Court)[5] and a Toshiba US machine with a 5- to 7.5-MHz linear-array transducer.[59]

Birtles et al[5] found a significant difference in mean ratio of maximal voluntary contraction to anterior tibial muscle group cross-sectional area between patients with CECS and healthy controls. Furthermore, they found an excellent between-scan (intraclass correlation coefficient, 0.95-0.99) and between-day (intraclass correlation coefficient, 0.96) reliability for this method.

Wassermann and Oschman[59] conducted a retrospective trial in which they found that all patients who were complaint-free postfasciotomy or after nonoperative treatment were identified as having CECS on US (by measuring pre- and postexercise depth dimension of the symptomatic compartment). No data on sensitivity or specificity of US were reported.

Predictive Clinical Model

Vignaud et al[57] studied the diagnostic accuracy of 2 predictive diagnostic models in 201 patients suspected of CECS[11,18] and found an accuracy of 86%, sensitivity of 75%, and specificity of 98% for the model by Fouasson-Chailloux et al[18] and an accuracy of 80% with a sensitivity of 82% and specificity of 78% for a threshold of 5.56 in the model by de Bruijn.[10] The study was classified as having a low risk of bias.

Assessment of Study Quality

An assessment of quality using the QUADAS-2/QUADAS-C tool is presented in Figure 2. All eligible studies were included in this review, irrespective of their quality. Based on the QUADAS criteria, 4 studies were classified as being of "low risk of bias" and 21 studies were classified as being "at risk of bias."

TABLE 2
Summary of Current Literature on MRI and Chronic Compartment Syndrome[a]

First Author (Year)	LOE	Imaging	Reference Standard	Study Population	Type of Compartment	Exercise Protocol	MRI Protocol	Results	Cutoff Value	Sensitivity/ Specificity, %	Conclusion[b]
Eskelin (1998)[16]	3	MRI	ICP (>40 mm Hg)	Military population: 6 CECS, 7 other ELP, 4 healthy controls	ANT	Treadmill, 5 min, horizontal, 10 km/h	Pre- and postexercise	Change in normalized signal intensity on MRI correlated with change in ICP	NR	NR	+
Verleisdonk (2001)[56]	3	MRI	Fasciotomy	21 CECS, 12 healthy controls	ANT	Treadmill, 10 min, 6.5 km/h	Pre- and postexercise, 5 min postexercise	Statistically significant increase in T2-weighted signal intensity in CECS patients	NR	NR	+/-
van den Brand (2005)[54]	2	MRI	Fasciotomy	Military population: 42 CECS, 3 other ELP	ANT	Treadmill until symptoms, 5° slope, 10 km/h	Pre- and postexercise		■ Posterior compartment ratio increase >10% postexercise ■ Posterior compartment ratio increase >5% postexercise	■ Ratio >10%: 40/100 ■ Ratio >5%: 53/83	-
Litwiller (2007)[27]	3	MRI	ICP (NR) or fasciotomy	14 CECS, 28 other ELP, 8 healthy controls	ANT	Isometric dorsi-/ plantarflexion until symptoms	Pre- and postexercise		Baseline-to-postexercise intensity ratio >1.54	96/90	+
Andreisek (2009)[1]	3	MRI	ICP (Pedowitz)	9 CECS, 10 healthy controls	ANT	Isometric plantarflexion	Pre- and postexercise	No statistically significant change in T2* relaxation times or arterial spin labeling signal in CECS patients	NR	NR	-
Ringler (2013)[39]	2	MRI	ICP (Pedowitz) or fasciotomy	23 CECS, 12 other ELP	ANT	Isometric dorsi-/ plantarflexion, until symptoms	Pre-, during, and postexercise		Baseline-to-postexercise intensity ratio >1.54	96/87	+
Sigmund (2013)[47]	4	DTI	MRI (>20% increased T2w signal intensity)	14 CECS, 8 healthy volunteers	ANT, L, DP	Treadmill, 10 min or until symptoms, individual pace and resistance	Pre- and postexercise	Significant increase of diffusivity on DTI in CECS patients	NR	NR	+/-
Sigmund (2014)[46]	4	DTI	NR	CECS, healthy volunteers	ANT, L, DP	Treadmill, 10 min or until symptoms, individual pace and resistance	Pre- and postexercise	Significant exercise response in diffusivity and apparent permeability metrics on DTI in CECS patients	NR	NR	+/-

[a]ANT, anterior compartment; CECS, chronic exertional compartment syndrome; DP, deep posterior compartment; DTI, diffusion tensor imaging; ELP, exertional leg pain; ICP, intracompartmental pressure; L, lateral compartment; LOE, level of evidence; MRI, magnetic resonance imaging; NR, not reported; T2w, T2-weighted.
[b]+, MRI/DTI can be used as a diagnostic tool for CECS; -, MRI/DTI cannot be used as a diagnostic tool for CECS; +/-, further research is required.

DISCUSSION

In this review, we selected 25 studies which discussed possible noninvasive diagnostic tools for CECS. Both MRI and NIRS had shown promising results for diagnosis of CECS; however, this review found limited evidence that measurement of peak exercise deoxygenation with NIRS may be of diagnostic value to detect the presence of CECS diagnosed by absence of complaints after fasciotomy. Furthermore, there was limited evidence that a baseline-to-exercise intensity ratio of >1.54 on MRI is indicative of the presence of CECS.

Only 4 studies were classified as low risk of bias. Therefore we can draw the following conclusions based on the best available evidence: SPECT is not an accurate diagnostic tool for CECS compared with ICP (sensitivity 50%, specificity 63),[32,50] NIRS is a promising diagnostic tool for CECS compared with ICP when a cutoff value of $\Delta StO_2 \geq 35\%$ is used (sensitivity 85%, specificity 67%),[54] and there are currently no predictive clinical models that can replace ICP measurement as a diagnostic tool for CECS.[57]

This review was written for the benefit of patients with CECS. Diagnosis of CECS by ICP measurement is burdensome, time-consuming, and not without risk. Fasciotomy

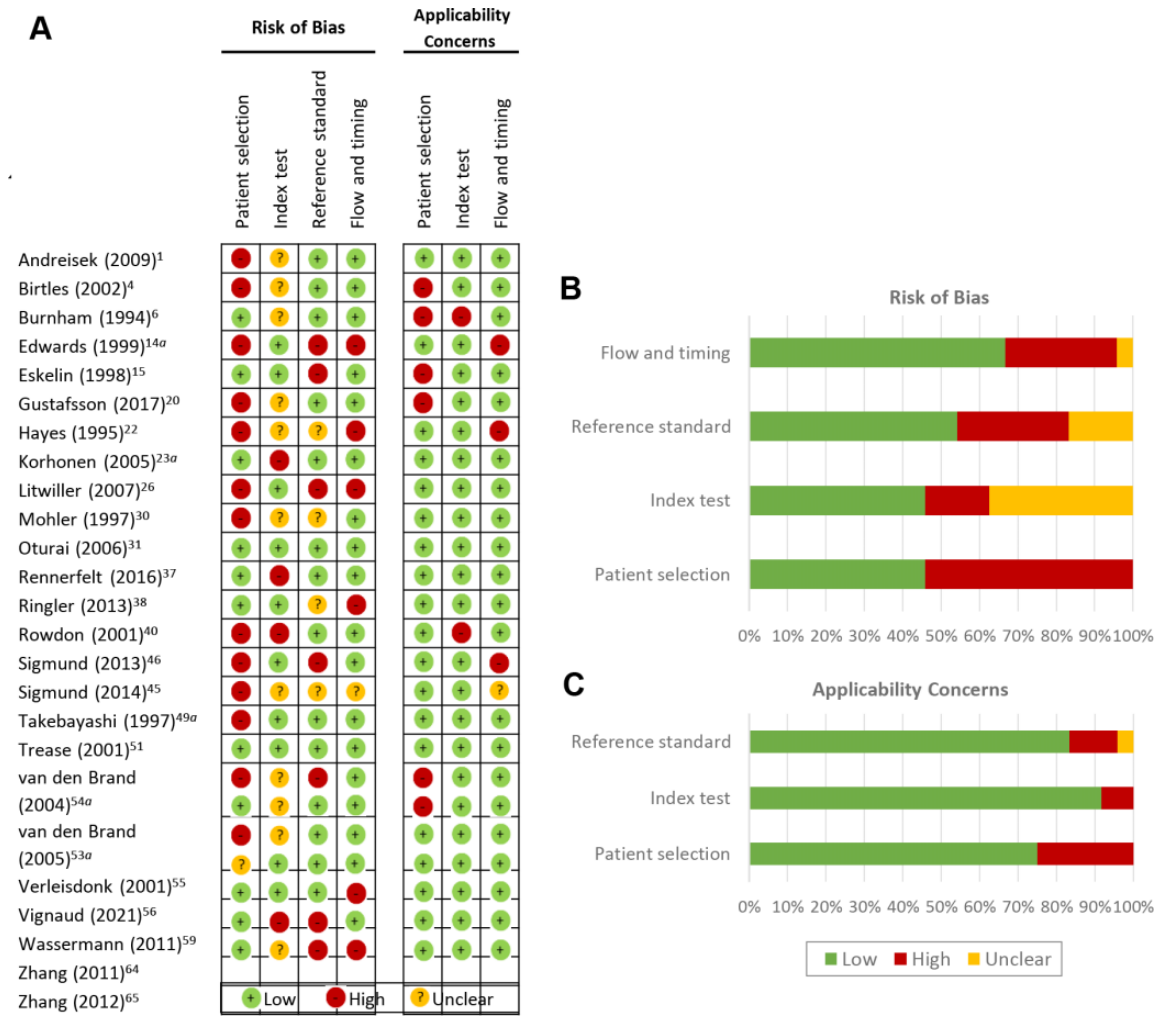

Figure 2. Quality assessment using the Quality Assessment of Diagnostic Accuracy Studies–Comparative (QUADAS-C; for comparative studies) or the QUADAS-2 (for noncomparative studies) tools: (A) by study, (B) according to risk of bias criteria, and (C) according to applicability concerns. [a]Comparative study.

should not be performed without a reliable clinical diagnosis to prevent overtreatment. Therefore, we strived to summarize the available clinical evidence and the quality of this evidence to provide a base to take the next step in CECS diagnostics in the clinic in the near future.

It is debatable whether ICP actually can serve as gold standard for diagnosis of CECS. Therefore, conclusions from the above-mentioned studies have to be drawn with caution. Diagnostic ICP criteria are based on generally weak studies.[2,51] Criteria suggested by Pedowitz et al,[33] Puranen and Alavaikko,[36] Styf and Körner,[49] or Aweid et al[3] still lack validity. Their use harbors the risk of a false diagnosis. Besides this, recent studies suggest gender-related pressure differences,[25] compartment-specific pressure differences,[26] and pressure differences between military and civilian patients.[28] These findings raise more doubts regarding the diagnostic reliability of ICP measurement.[63] Furthermore, the most accurate ICP measurement catheters on the market are very costly and have not been tested in a large population of patients with CECS.

If one looks at the feared counterpart of CECS, acute compartment syndrome, an increasing number of studies on noninvasive diagnostics have been published in the past decade.[29,42,43] Sellei et al[42,43] presented an interesting overview of different noninvasive diagnostics for acute compartment syndrome. Studies were categorized as studies on measurement of surrogates of decreased perfusion pressure (infrared imaging, pulse oximetry, laser Doppler flowmetry, contrast enhanced US or NIRS) and studies on surrogates of increased ICP (imaging, tissue hardness measurement, pulsed phase locked loop US, shear wave elastography, or compressibility). Some of the above-mentioned diagnostic modalities have not yet been tested as a diagnostic tool for CECS and therefore deserve further exploration in this field.

The most efficient way to diagnose CECS would be during a visit to the outpatient clinic. Most diagnostic modalities that are discussed in this review require at least 1 additional hospital visit. The exceptions to this are US, MYO, and quantitative muscle hardness (QMH). In recent

years, handheld US has been investigated as a possible diagnostic tool for many musculoskeletal disorders, showing promising results.[17] In a similar fashion, a portable handheld myotonometer has shown high reliability and validity for measurement of muscle tone in larger as well as smaller muscles in the body.[9] Neither of these devices need to be connected to a computer to read off results, making them easy to use in everyday clinical practice. A predictive clinical model would be most practical in the outpatient clinic. However, the currently available models are not accurate enough to replace ICP for diagnosis of CECS and aid mainly in the estimation of the risk to develop CECS.[57]

Based on our review, we recommend that a typical clinical diagnosis, combined with both increased compartment pressures and favorable clinical results after treatment, should serve as a confirmation of a truly treated CECS. More high-quality research into the reliability of novel noninvasive diagnostic tools in a large population of patients with CECS compared with healthy controls should be conducted in the near future to strive to replace ICP measurements as a diagnostic tool for CECS.

Limitations

This study has certain limitations. Data from articles that were not available on PubMed (MEDLINE) or Embase could have been missed, although the search performed was comprehensive. The limited available data for this review were heterogeneous and results were reported in different manners, due to which statistical analysis was not possible. Results from patients with all types of lower leg CECS were compared. Deep posterior CECS was not analyzed separately, even though the deep posterior compartment of the lower leg is located deeper than the anterior and lateral compartments and may differ in pressure. This review did not include pilot studies on healthy individuals or case reports. Therefore we lack reports on recent studies of novel noninvasive diagnostic tools, such as shear wave elastography.[4] Anwander et al showed that measurement of the anterior compartment compressibility ratio by compression sonography had high intraobserver and interobserver reliability.[2] Steinberg et al[48] showed significant differences in QMH measurement upon externally increased pressure of the superficial and deep posterior and anterior compartment. In 2011, Steinberg et al showed that QMH could predict an ICP >45 mm Hg in the anterior tibial compartment with 97% sensitivity and 74% specificity.[48] These results warrant more research into these novel diagnostic tools in the near future. It was not possible to carry out a meta-analysis due to heterogeneity among the included studies in reference standard due to ICP with varying cutoff values and fasciotomy as well as heterogeneity among the included studies in regard to cutoff value of the researched noninvasive diagnostic modality.

CONCLUSION

Despite the need to replace the controversial use of ICP measurements as the gold standard for diagnosis of CECS, our review indicated a lack of validity on all discussed noninvasive diagnostic tools as a replacement.

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APPENDIX

APPENDIX TABLE A1
Steps Used for the Literature Search

Step	Keywords/MESH terms	No. of Records	
		PubMed	Embase
1	Diagnosis OR diagnosing OR identification OR detection OR confirmation OR verification	13,638,974	
2	Chronic exertional compartment syndrome OR chronic exertional compartment syndromes OR chronic exertional compartment syndrome OR chronic compartment syndrome OR exertional compartment syndrome OR exertional leg pain	1839	
3	#1 AND #2	1346	
4	Limit to: English, humans, period 1995-2021, full-text available	765	199