A prospective blinded evaluation of exercise thallium-201 SPET in patients with suspected chronic exertional compartment syndrome of the leg

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Abstract. This study compared the quantitative and qualitative results of leg thallium-201 single-photon emission tomography (SPET) imaging in patients with and without raised intracompartmental pressure associated with exercise-related leg pain. The purpose of this study was to clarify the aetiology of chronic exertional compartment syndrome (CECS), and to investigate the diagnostic applications of ^{201}Tl SPET in CECS. Thirty-four study participants underwent compartment pressure testing (CPT) between March and August 2000. There were 25 positive CPT results (patient group), and nine negative CPT results (control group). All 34 participants underwent scintigraphy. Quantitative and qualitative assessments were performed for the anterolateral and deep posterior compartments of the lower leg. There was no significant difference in either quantitative or qualitative assessments of perfusion between those compartments with and those without CECS. In contrast, a marked effect of exercise type upon compartment perfusion pattern was noted. Results of this study indicate that there is no compartment perfusion deficit in those patients with raised intracompartmental pressure associated with CECS, and suggest a non-ischaemic basis for the pain associated with CECS. They also suggest no role for exercise perfusion scintigraphy in the diagnosis of this syndrome.

Keywords: Chronic exertional compartment syndrome – Diagnosis – Muscle – Sports medicine – Thallium-201

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Introduction

Exercise-related lower leg pain is a common symptom in the exercising public [1, 2, 3, 4]. Despite its prevalence, this entity is poorly understood, and frequently misdiagnosed. One of the most common causes of lower leg pain is chronic exertional compartment syndrome (CECS). In the sports medicine community, CECS of the lower leg is of major importance due to its prevalence among athletes and its debilitating nature.

The aetiology of CECS is incompletely understood, but it is widely thought that abnormal increases in intramuscular pressure during exercise impair local perfusion, thereby resulting in tissue ischaemia and pain [4, 5, 6, 7, 8]. Thallium-201 single-photon emission tomography (SPET) scan, commonly used to detect myocardial ischaemia, has been used to investigate a small number of CECS patients [9, 10]. Results suggested that the pain of compartment syndrome was associated with reduced perfusion to affected compartments during exercise. These studies provided the impetus for this investigation.

Patients presenting with CECS complain of cramping, burning or aching pain and a sensation of fullness or tightness in and around the affected compartment(s) with exercise [11, 12, 13, 14, 15, 16, 17, 18, 19]. Clinically it is difficult to differentiate CECS from other causes of exercise-induced lower leg pain [20, 21]. Therefore, a definitive diagnosis is made on the basis of measurements of intracompartmental pressure.

Compartment pressure testing (CPT) involves the insertion of a catheter into the muscle compartment, after which the patient is required to exercise with the catheter in place. Pressures vary depending on the technique used for measurement, the timing of measurement in relation to exercise, the position of adjacent joints and the depth to which the catheter is inserted [4, 16, 22, 23, 24]. In addition, the measurement of intracompartmental pressure is invasive and is associated with pain and the risk

of neurovascular injury. With the risks and discomfort associated with the CPT, investigation into alternative diagnostic methods was warranted.

The purpose of this study was to correlate the results of a series of ^{201}Tl SPET scans with the compartment pressure test, to determine its ability to diagnose compartment syndrome and to establish the association of ischaemia with the pain of the syndrome.

Materials and methods

Patients

Patients were prospectively recruited from two local sports medicine centres between March and August 2000. Patients were invited to participate if they were between 18 and 55 years of age, if they presented with an exercise-related pain in any of the muscle groups below the knee associated with a sensation of fullness or tightness in and around the symptomatic muscle compartment(s), and if physical examination revealed that the symptomatic muscle compartment(s) were firm or tight to palpation following exercise. Any patient who had undergone previous decompressive surgery for CECS was excluded because of the unknown consequences of previous surgery within the same compartment.

There were 20 male and 14 female participants. The mean age of the study group was 29 years (range 18–55). There were 12 patients with anterior compartment symptomatology, 12 with posterior compartment symptomatology, and ten with both anterior and posterior compartment symptoms. Participants typically developed their symptoms from running (10, 29%), or walking (8, 24%). Other sports which produced the symptoms in individual patients included Australian Rules football (7), triathlon (3), soccer (2) and cricket (1). There were three members of the armed forces who reported marching as the most aggravating activity they performed.

The study protocol was approved by the Alfred Hospital Human Research Ethics Committee prior to initiation of the study. All subjects provided witnessed and written informed consent.

Compartment pressure testing procedure

Four medical practitioners at the sports medicine centres performed the compartment pressure tests, using a standard testing protocol. For each subject, only the most symptomatic leg was studied in order to reduce post-test disability for the patient. A Stryker intracompartmental pressure monitor system was used in conjunction with an indwelling slit catheter, quick pressure monitor set and 150 cm extension tubing (Stryker Instruments, Kalamazoo, Mich.). Following insertion of the catheter, patients were required to perform compartment-specific exercises to induce their pain. The exact form and duration of exercise used to produce symptoms at the time of pressure measurements for each patient were recorded and used in conjunction with subsequent ^{201}Tl SPET imaging. This was done in an attempt to ensure that pressure and scintigraphic measurements were obtained under comparable and clinically relevant physiological conditions. For the diagnosis of CECS in this study, a pre-exercise resting pressure of >15 mmHg, or a 1-min resting post-exercise pressure greater than 30 mmHg, or a 5-min resting post-exercise pressure of >20 mmHg was considered to be indicative of CECS. Participants were then divided into two groups on the basis of CPT results. Those participants with a negative CPT were classified as "normal", while those with a positive CPT were subsequently considered as the "patient" study group. None of the "normal" patients were identified to have any vascular pathology.

Thallous chloride scintigraphy

Thallous chloride scintigraphy (^{201}Tl SPET imaging) was performed in the Nuclear Medicine Department of the Alfred Hospital, Melbourne, Australia. Following insertion of an intravenous line, participants performed their exercise protocol as established at the time of their CPT. The participants were then injected with ^{201}Tl chloride (0.8 MBq/kg of body weight, capped at 80 MBq) intravenously and exercise was continued for 2 min to allow tracer distribution at stress. SPET images were obtained at 5 min and 180 min (stress and redistribution images) with the patient in the supine position.

Image acquisition

Images were acquired on an Optima NXAC Gamma Camera System (General Electric Medical Systems, Milwaukee). A dual-head 90° gamma camera, with a small rectangular field of view (337 mm×183 mm) and 6.5 mm NaI crystal thickness, was used to acquire 32 views over 360° with step-and-shoot methodology for 40 s per stop through a circular orbit. The images were collected on a 64×64 matrix. A low-energy, high-resolution parallel-hole collimator (1.4 mm hexagonal, 31.5 mm length, 0.2 mm septal thickness) was used to optimise spatial resolution and minimise scattered ^{201}Tl photons in the acquired image. The Optima NXAC gamma camera used dual-window acquisition, peaked at 72 keV using a 30% window and at 167 keV using a 20% window, to optimise the detection of the main photon emissions of ^{201}Tl. The same image duration and sequence were used for redistribution images 3 h later.

Image reconstruction

An independent senior scientist encoded all images prior to review. All reconstruction and analyses were performed blinded. Generation of initial transaxial images was performed with a General Electric Genie-based, standardised "SPET Protocol." Ramp back projection and a Butterworth prefilter (power 7, cut-off 0.31) was used to generate transaxial images with the reconstruction limits set at maximum. Angles and limits of oblique images were defined, and new transaxial limits were set to 22 slices using coronal and sagittal views. Reconstruction width for transaxial and oblique images was set at 6 mm per slice. The reconstruction field of view included both legs.

Interpretation of ^{201}Tl SPET images

Quantitative analysis. A specially created "LEG SPET" protocol was used to generate and display 11 slices at 12 mm per slice in a proximal to distal format. The image was then panned left or right, for right or left leg processing respectively. An initial, anterolateral region of interest (ROI) was drawn on the middle slice (slice 6). The image was subsequently displayed in dual colour scales with the upper threshold set to the maximum pixel count from the ini-

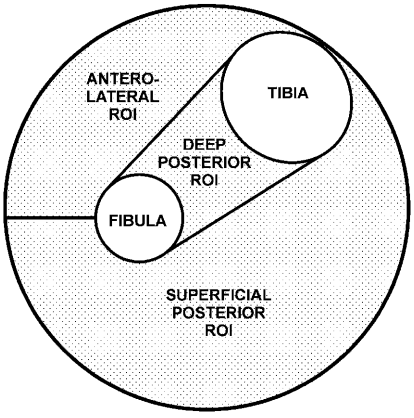

Fig. 1. Anatomical borders used to demarcate the three regions of interest for the right leg

tial ROI. Slice six was displayed using a GE_COLOR scale and the other slices were displayed in linear grey scale to assist in the identification and definition of anatomical landmarks for the ROI (Fig. 1). The final, anterolateral ROI was then drawn around the 30% threshold colour contour (blue/green colour border) on slice 6. This process was then repeated for the superficial and deep posterior ROIs. The ROIs were moved on the proximal and distal slices to a position of "best fit", allowing for slight anatomical changes between slices. Curves of the mean percentage of maximum leg uptake (mean leg slice counts per pixel/maximum count for any pixel in that leg) for each of the compartments were generated, as was a table displaying the mean pixel counts per slice for each ROI. The procedure was then repeated for the other leg.

To allow comparison of different patients, the mean pixel count for each compartment, in each slice of leg, was expressed as a percentage of the maximum pixel count for that leg (mean pixel ratio). Two data sets (two patients with confirmed CECS of the anterior compartment) were unable to be processed, as the data were lost.

Reliability of quantitative analysis. Intra-observer reliability of the chief investigator was established by reconstructing a random sample of 40 patient scans, approximately half stress and half redistribution, on two occasions separated by a 2-week interval. The sample was equivalent to 80 leg scans, which was 60% of a maximum of 132 leg scans that could be analysed. Mean pixel counts were calculated on slices 3, 6 and 9 for each compartment within each leg. This gave a total of 240 slice data sets used to assess the reproducibility of both the actual drawing of the ROIs for the three compartments and the realignment of the ROIs at proximal and distal ends of the leg.

Inter-observer reliability was assessed by comparison with an experienced nuclear medicine technologist (J.R.). The technologist reconstructed a sample of 90 leg scans independently from the principal investigator. This represented two-thirds of the scans performed. Data were compared for slices 3, 6 and 9, for each compartment, within each leg, for a total of 270 slice data sets.

Qualitative analysis. Qualitative analysis was performed independently by three nuclear medicine physicians (M.J.K., A.B. and A.T.). The physicians interpreted the images in a blinded manner without knowledge of any patient information or of any other observer's opinion. Images were displayed for analysis on a Sony 21-inch, high-resolution monitor. Stress and redistribution images were displayed side by side, in 256 linear grey scale. Physicians were instructed to read all 11 slices of both the stress and the redistribution images for each compartment, in one leg, prior to moving onto the next compartment. A five-point scoring system was used to assess each of the stress and the redistribution images. Each compartment on stress imaging was graded as either very hypoperfused (1), moderately hypoperfused (2), mildly hypoperfused (3), equally perfused (4) or hyperperfused (5) in relation to the other compartments within the same leg. Redistribution images for each compartment were graded to have either markedly redistributed (1), moderately redistributed (2), mildly redistributed (3), remained unchanged (4) or to have undergone reverse redistribution (5) relative to the stress images. Scans were deemed to be positive for a compartment perfusion deficit if they had a summed stress and redistribution score of less than or equal to 5. Each physician scored each of the compartments in both legs for all patients. Where there was disagreement between the opinions of the first two physicians, the opinion of the independent blinded third physician was used. Thus the final result was taken as the one where two or more of the three assessors were in agreement.

Following all quantitative analyses and review of images, the scan identities were decoded and participants were allocated to either the control or the patient group depending on their CPT result. Cross-referencing with pressure study results then allowed determination of the pathological compartment(s) for each patient. Subsequent analysis was confined to those compartments with a confirmed pressure study result, whether abnormal or normal (anterior and deep posterior compartments only were measured).

Statistical methods

Interval data were examined for normality using visual inspection of the data, values for kurtosis and skewness and by conducting Shapiro Wilks tests. Parametric tests were then employed for data analysis. Where data were ordinal or failed to meet the assumptions of normality and homogeneity of variance, non-parametric tests were employed. Two-tailed level of significance was set at α=0.05. Statistical tests for the primary analyses are detailed below.

Comparisons of mean pixel ratio for stress and redistribution in the 11 slices between patients (+ve CPT) and controls (–ve CPT) were made using mixed 2×11 analysis of variance (ANOVA). In these ANOVA, slice was the repeated measure while group was a between-subject factor. Given the small numbers, the anterolateral and deep posterior groups were combined for these analyses. For qualitative ^{201}Tl scores, comparisons between patients and controls for scores greater than or less than 5 were made using chi square.

Results

Compartment pressure testing

Of the 34 participants, 25 (74%) had a positive CPT, and nine (26%) had a negative CPT. Subject characteristics for the patient (+ve CPT) and control (–ve CPT) groups are displayed in Table 1. Pressure values obtained from the group during CPT are demonstrated in Fig. 2.

Table 1. Subject characteristics in patient and control groups

	Positive CPT (25 pts)	Negative CPT (9 pts)
Male to female ratio	16:9	5:4
Age (yrs), mean (SD)	28.2 (9.2)	30.8 (9.1)
Symptoms, unilateral:bilateral	3:22	2:7
Involved compartments, anterior:deep posterior	12:13	3:6

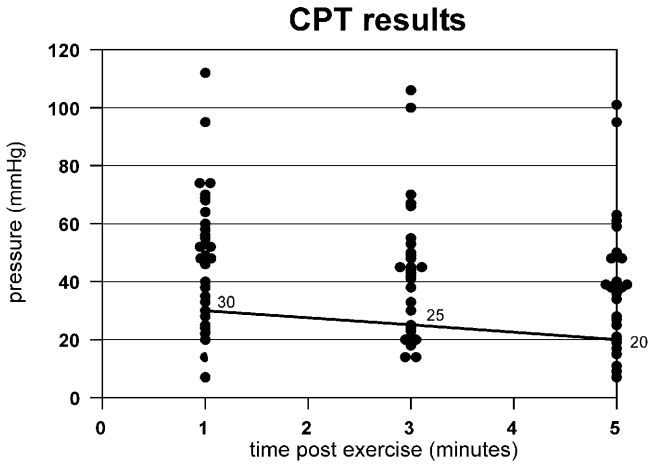

Fig. 2. Pressure value results for each patient obtained during CPT, at 1, 3 and 5 min post exercise. The *thick black line* illustrates the diagnostic cut-off pressures for CECS; patients above the line were considered positive for CECS, while those below the line were considered negative for CECS

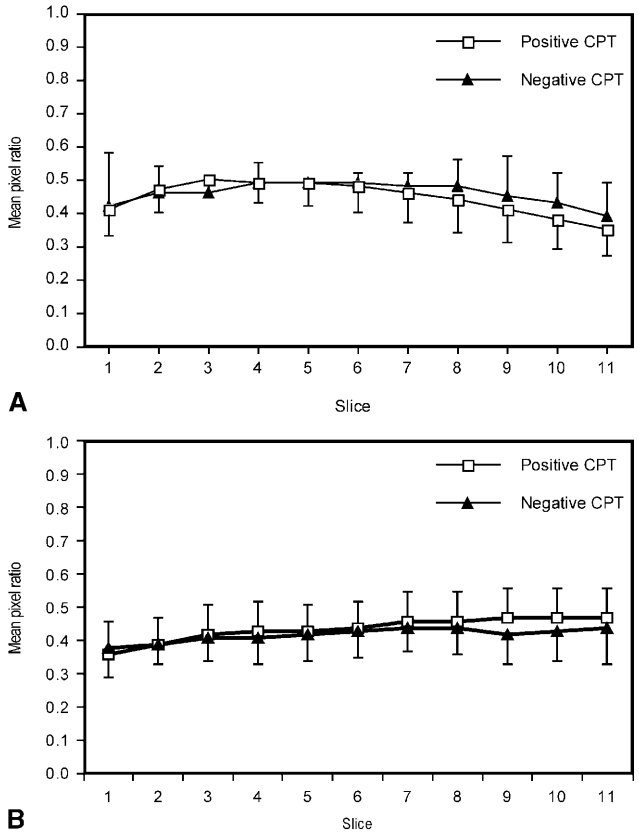

Fig. 3A, B. Quantitative analysis of the mean (SD) pixel ratios, by compartment. **A** Anterior stress images, by slice. **B** Deep posterior stress images, by slice

^{201}Tl SPET imaging comparison

Quantitative analysis. Quantitative analysis was performed on the anterolateral and deep posterior ROIs in all 11 slices within the CPT leg. There was no significant difference in the pixel ratio at any slice comparing the positive and negative CPT groups in either ROI (interaction term not significant, group main effect [anterolateral: F (1,30)=1.35, P=0.25] [deep posterior: F (1,30)= 1.30, P=0.67]). The mean and standard deviation for the pixel ratio in the stress images are displayed in Figs. 3A (anterior compartment) and 3B (posterior compartment).

Intra-observer reliability for quantitative analysis. A correlation co-efficient was calculated for each slice. High r values indicated excellent reproducibility for slices in both the anterior (r range 0.93–0.98) and the deep posterior compartments (r range 0.85–0.97) across the six slices examined (Table 2). A slight but statistically significant difference between the mean pixel count of readings 1 and 2 for both compartments was demonstrated.

Inter-observer reliability for quantitative analysis. Correlation co-efficients demonstrated very high r values indicating excellent reproducibility, with 11 of 12 compartments slices analysed having an r value >0.90, and five of 12 slices having an r value of >0.97. There was, however, a slight but statistically significant difference between the mean pixel count of the principal investigator and the experienced nuclear medicine technologist, in both compartments (Table 3).

Qualitative analysis. On qualitative analysis one patient was deemed to have a perfusion deficit consistent with CECS (score of ≤5). The remaining 33 patient stress and redistribution images were considered normal. Chi square analysis revealed that there was no significant difference between CPT groups for qualitative scores less than or equal to and scores greater than 5 in the anterolateral compartment. In the deep posterior compartment, statistical analysis could not be performed, as there were no patients with scores of less than 5 to suggest an ischaemic compartment.

Table 2. Intra-observer reliability of quantitative analysis performed by the principal investigator

	Reading 1	Reading 2	*r* value (right leg)			*r* value (left leg)		
	Mean (SD)	Mean (SD)	Slice 3	Slice 6	Slice 9	Slice 3	Slice 6	Slice 9
Anterolateral compartment (*n*=240)	77.5 (23.5)	78.7 (20.7)*	0.96	0.97	0.97	0.94	0.98	0.93
Deep posterior compartment (*n*=240)	66.0 (14.8)	63.9 (14.3)**	0.88	0.92	0.85	0.95	0.97	0.95

Paired *t* tests: **t*(240)=–2.06, *P*=0.04; ***t*(240)=5.93, *P*<0.0001

Table 3. Inter-observer reliability of quantitative analysis

	Reading 1	Reading 2	*r* value (right leg)			*r* value (left leg)		
	Mean (SD)	Mean (SD)	Slice 3	Slice 6	Slice 9	Slice 3	Slice 6	Slice 9
Anterolateral compartment (*n*=270)	76.8 (24.0)	73.1 (23.3)*	0.98	0.98	0.98	0.97	0.98	0.92
Deep posterior compartment (*n*=270)	64.0 (14.8)	68.4 (16.8)**	0.92	0.94	0.82	0.90	0.96	0.91

Paired *t* tests: **t*(270)=8.06, *P*<0.0001 ***t*(270)=–8.49, *P*<0.0001

Qualitative analysis in patients with symptoms in more than one compartment

Qualitative scoring was based on a comparison of one compartment with another within the same leg. In patients with symptoms and raised intracompartmental pressure in collateral compartments within the same leg, perfusion may have been universally decreased. It is therefore possible that decreased perfusion within the compartments of these patients was comparatively underscored. To further assess the qualitative scores obtained, the patient group was divided into three groups: those with isolated anterior symptoms, those with isolated posterior symptoms and those with both anterior and posterior symptomatology. There was no significant difference in the anterior or posterior qualitative scoring in the stress images between those patients who had an isolated compartment with CECS and those with more than one compartment involved. This means that scoring in one compartment was not biased by the presence of symptoms or by confounding changes in muscle perfusion in another compartment within the same leg.

Investigation of possible confounding "exercise effect" when compartment-specific exercise was performed

An "exercise effect" was investigated quantitatively and qualitatively to determine whether perfusion was dependent on the specific type of exercise performed.

Quantitative comparison. Patients within this study performed three different types of exercise. To determine whether and which exercise type might influence perfusion, participants were subdivided into three specific exercise groups: (a) participants who had performed resisted dorsiflexion [for patients with anterior compartment symptoms only (*n*=6)], (b) participants who had only walked or ran [for anterior and/or posterior compartment symptoms (*n*=10)]; and (c) participants who had performed hops, jumps or calf raises [for posterior compartment symptoms only (*n*=18)]. A pixel ratio (anterior pixel count/posterior pixel count) at slice 3 was calculated for each of the patients in the exercise subgroups. The mean pixel ratio for those patients who performed resisted dorsiflexion (*n*=6) was 2.2±1.0, which was much higher than the values of 1.3±0.5 and 1.2±0.3 for patient exercise subgroups groups (b) and (c) respectively (*P*<0.001). These results are illustrated in Figs. 4A–D, which contrast the stress images and mean pixel ratio graphs of a patient who performed resisted dorsiflexion and a patient who performed non-compartment-specific exercises, both with anterior CECS.

Because this exercise effect was confined to participants who performed resisted dorsiflexion (*n*=6), the comparison of perfusion between patients with positive and negative CPT was re-analysed quantitatively without these six patients. Results confirmed the earlier findings of no difference in perfusion between the patients (+ve CPT) and controls (–ve CPT).

Qualitative comparison. Following the results of quantitative comparison, the qualitative results of each nuclear medicine physician (NMP) were compared with the exercise protocol for each patient, and are shown in Table 4.

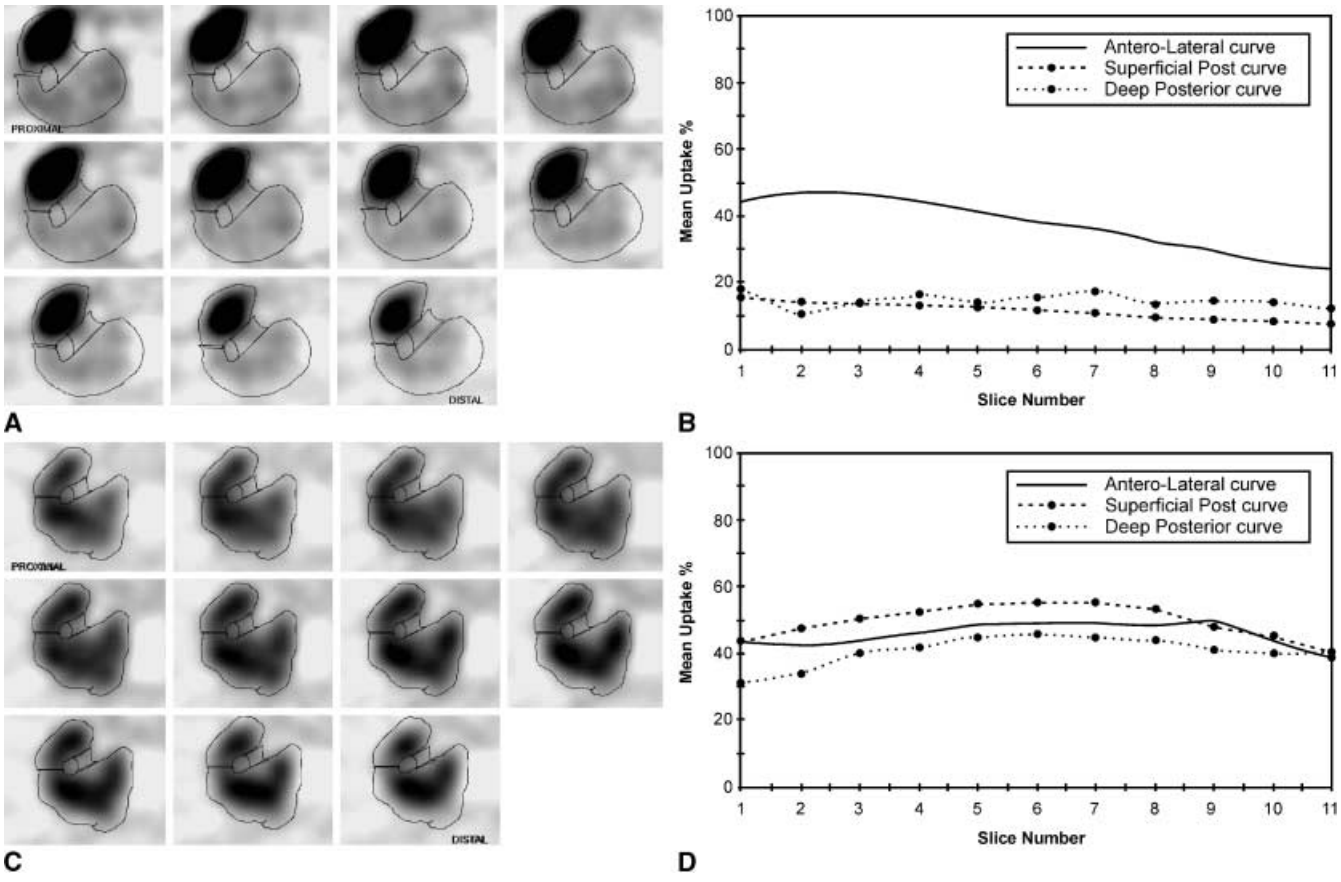

Fig. 4A–D. Comparative perfusion in patients who performed different exercises. **A** Slices 1–11 in a patient with anterior CECS who performed resisted dorsiflexion exercises. **B** Anterior compartment and posterior compartment mean pixel ratio curves from a patient with anterior CECS who performed resisted dorsiflexion exercises. **C** Slices 1–11 in a patient with anterior CECS who performed non-compartment-specific exercises. **D** Anterior compartment and posterior compartment mean pixel ratio curves from a patient with anterior CECS who performed non-compartment-specific exercises

All three NMPs scored the anterolateral compartment as hyperperfused (stress score=5) on stress image analysis in the same five of six patients who performed resisted dorsiflexion. These results demonstrate that an exercise effect was also seen on qualitative analysis. This exercise effect in these five patients was independent of the patient's CPT result, with three anterior CECS positive patients (see Fig. 4A) and two anterior CECS negative patients exhibiting the effect. Re-analysis of those patients who performed posterior compartment- or non-compartment-specific exercises demonstrated that there was no significant difference in qualitative scoring between those patients with positive and those with negative CPT results (see Fig. 4C). Thus, there remained no significant difference in perfusion between those patients with positive and those with negative CPT results, when exercise type was removed as a confounding factor.

Discussion

This study measured the relative muscular compartment perfusion of participants with exercise-induced lower leg pain using ^{201}Tl SPET. The results of this study demonstrated that there was no difference in relative perfusion between those compartments with and those without CECS.

The results of this study suggest that muscle ischaemia may not be present in CECS. The results are con-

Table 4. Qualitative stress scores for the anterolateral compartment in those patients who performed resisted dorsiflexion exercises

Exercise performed	NMP 1		NMP 2		NMP 3	
	Stress score 5	Stress score <5	Stress score 5	Stress score <5	Stress score 5	Stress score <5
Resisted dorsiflexion	5	5	5	10	5	7
Other exercise	1	23	1	18	1	21

cordant with those of Balduini et al. [21], who used phosphorus-31 nuclear magnetic resonance spectroscopy (^{31}P NMR) and demonstrated ischaemia only in those patients in whom intracompartmental pressure was greater than systolic blood pressure (>160 mmHg). No participant in this study recorded CPT values >110 mmHg, and so the ability of ^{201}Tl SPET to validate the results of Balduini et al. [21] cannot be established. The non-ischaemic findings of this study are also supported by studies published by Amendola et al. [25] using magnetic resonance imaging, who concluded that the pathophysiology of CECS did not appear to be related to ischaemia.

If the pain of CECS is not attributable to ischaemia, as the results of this study suggest, by what mechanism does the pain associated with the syndrome arise? Humphries [26] suggests three possible alternative mechanisms of pain in CECS. The first is excessive fascial stretch leading to stimulation of sensory fibres within the fascia, and to pain, a theory also put forward by Rorabeck et al. [27] and Schepsis et al. [28]. The theory of fascial stretch receptor-mediated pain is supported by the high success rates of fascial release (fasciotomy) as a treatment for CECS. The second theory proposed by Humphries is intramuscular pressure receptor-mediated pain, while the third is that metabolic by-products might act as a pain mediator in CECS [26]. In light of the results of this study, all three theories warrant further investigation.

Despite the findings of this study it is still possible that some of the pain associated with CECS is attributable to ischaemia, as widely suggested in the literature [4, 5, 6, 7, 8, 9, 10, 29]. It is possible that the pain associated with CECS may be due to an imbalance between oxygen supply and demand, rather than to an absolute reduction in perfusion. This prospective blind study has demonstrated that no perfusion deficit exists in those patients with CECS, but could not examine the oxygen extraction at the intramuscular level. Near infrared spectroscopy (NIRS) has been used to investigate CECS in two small studies [6, 30], where it demonstrated greater relative post-exercise deoxygenation, as well as delayed reoxygenation following exercise, in those patients with CECS when compared to those without. These studies demonstrated that there was greater oxygen extraction in patients with CECS in the initial 30 s of exercise, in comparison to the CECS-negative controls. Mohler et al. [6] concluded that early differences in oxygen saturation between patients and controls resulted from increased extraction of oxygen from the intracompartmental circulation. It is possible that the increased deoxygenation demonstrated by these studies illustrates a perfusion/demand mismatch that did not involve an absolute reduction in muscle perfusion.

The results of this study contrast with two earlier studies using ^{201}Tl SPET imaging [9, 10] and two technetium-99m sestamibi studies [7, 31] which suggested a possible role for exercise compartment perfusion scintigraphy in diagnosing CECS. It is possible that the negative results of our study could be related to a number of significant differences between our study and the earlier studies. These differences include: (a) our larger group of patients with pressure measurements, (b) our use of symptomatic rather than asymptomatic controls, (c) the fact that our patients performed identical exercise before both pressure measurements and scintigraphy, and (d) the blinded and reproducible techniques that were used in our study.

In comparison to earlier studies, this study had a larger subject group, with 25 patients with confirmed CECS, and nine symptomatic controls with confirmed intracompartmental pressure study results. Earlier studies obtained pressure measurements in smaller numbers of patients, who may not necessarily have been representative of the CECS population. Hayes et al. [10] examined 14 patients and three controls, but pressure measurements were obtained in only eight subjects, only four of whom had CECS. Takebayashi et al. [9] examined nine patients with CPT-confirmed CECS, and eight (asymptomatic) controls; compartment pressures were increased in six of the nine compartments qualitatively assessed to be ischaemic.

The symptomatic controls used in this study produced lower mean pressure values than the asymptomatic controls used by Takebayashi et al. [9], and provided a more realistic control group to evaluate the diagnostic accuracy of scintigraphy. One of the aims of this study was to assess the diagnostic potential of ^{201}Tl SPET imaging in CECS. To be of value as a CECS diagnostic method, the ^{201}Tl SPET scans need to be able to differentiate between those symptomatic patients with and those without raised intracompartmental pressure. The results of this study suggest that this is not possible.

It was felt in our study that the patient needed to perform the identical type and amount of exercise prior to both CPT and ^{201}Tl SPET, so that comparison of the results would be most meaningful. In establishing an exercise protocol for each patient, it was thus possible to ensure that the perfusion, as determined by the ^{201}Tl SPET scan, was assessed under comparable conditions to the pressures obtained during CPT, as well as correlating with the development of the patient's symptoms. This did not apply to earlier studies. In the study published by Takebayashi et al. [9], CPT measurements were obtained in surgery following 1 min of isometric foot dorsiflexion. In contrast, prior to ^{201}Tl SPET imaging, patients were required to run on a flat treadmill at 5 km/h, a different exercise altogether, that could have resulted in different levels of compartment perfusion.

This study performed prospective independent and blinded qualitative and quantitative analysis. As no measurements of inter-observer and intra-observer variability were performed in previous studies, intra- and inter-observer reliability of the quantitative analysis was a focus of this study, and showed excellent correlation and reproducibility.

In conclusion: This study was unable to reproduce the results of early smaller studies using ^{201}Tl SPET imaging, which had suggested a diagnostic role for ^{201}Tl SPET imaging in CECS. The results of this study are in accordance with the results of studies using ^{31}P NMR spectroscopy, NMR and NIRS. The results obtained during this study do not support the currently favoured theories associating ischaemia with CECS. The major findings of this study were that there was no difference between the perfusion of those patients with a positive CPT result and those patients with a negative CPT result, and that muscle compartment ^{201}Tl uptake was primarily determined by the type and amount of exercise performed by an individual. This is a finding consistent with the known physiological increase in muscle perfusion that occurs with exercise.

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