Chronic (Exertional) Compartment Syndrome of the Legs Diagnosed with Thallous Chloride Scintigraphy

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Over the past 4 yr, we obtained ^{201}Tl lower leg scans on 14 patients with suspected chronic exertional compartment syndrome. Qualitative assessment of the images revealed that 12 scans showed reversible compartment ischemia. Retrospective quantitation confirmed redistribution in seven of nine patients. Seven patients had surgery with partial or complete resolution of their symptoms.

Key Words: thallium-201; exertional compartment pressure syndrome

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Lower leg pain is a common problem in athletes and other physically active individuals. The usual causes (*1–4*) are stress fracture, medial tibial stress syndrome (MTS) and chronic (exertional) compartment syndrome (CPS). Stress fracture and MTS are readily diagnosed by bone scintigraphy. The diagnosis of CPS, which may accompany lower leg stress injuries, may be more difficult to confirm (*5–7*).

The lower leg is divided into four muscle compartments: anterior, lateral, superficial posterior and deep posterior (Fig. 1). CPS may be defined as a condition in which tissue pressure within a closed space (compartment) bounded by bone or fascia is increased during exercise (*2,3*). This elevation in pressure reduces local blood flow, causing ischemia which results in pain and neuromuscular dysfunction, usually improved by rest. Chronic elevation of compartment pressure causes thickening of the compartment fascia, which further exacerbates the condition, resulting in the need for surgery in most cases for relief of symptoms (*1,7*).

CPS may be suspected on history and clinical examination and is usually confirmed by direct measurement of intracompartmental pressure (*2,4,5*). Compartment pressure measurements are invasive and often painful and may be normal despite typical clinical features (*8*). An alternative noninvasive method for confirming the diagnosis of CPS would be helpful.

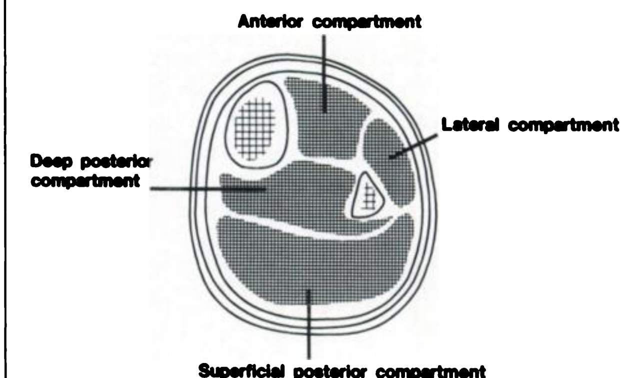

FIGURE 1. Cross-section of the right midcalf shows the four main compartments.

Thallium-201 has been used for many years to assess myocardial perfusion and has also been used as a noninvasive means of investigating peripheral vascular disease (*9–12*). This study presents the clinical data and findings of ^{201}Tl scintigraphy for 14 patients who were investigated for CPS and the distribution of lower leg ^{201}Tl uptake in three controls.

METHODS

Patients

All patients (7 men, 7 women; age 17–40 yr; mean age 30 yr) were referred between 1991 and 1994 for ^{201}Tl leg scintigraphy by sports medicine practitioners and/or orthopedic specialists (Table 1). All patients were fully assessed clinically for diagnosis of CPS and other possible causes of leg pain. Bone scintigraphy was performed in four patients with three scans showing periostitis and one study revealing bilateral tibial stress fractures (3 mo before ^{201}Tl scan). One patient had symptoms of nerve root compression and lumbar spine MRI demonstrated disc lesions at L4-L5 and L5-S1. Six patients had previously undergone compartment releases and presented with recurrent symptoms post-surgery. Compartment pressure measurements were obtained in eight patients. The controls (2 men, aged 35 yr; 1 woman, aged 40 yr) were nonsmokers with false-positive exercise-stress electro-

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TABLE 1
Patient Data

Patient no.	Age (yr)	Sex	Sport	History	Compartment pressure
1	22	F	Sprinter	2 yr diffuse bilateral calf pain; bone scan bilateral tibial stress fractures	DPC CP raised bilaterally
2	52	F	Walker	4 yr diffuse bilateral calf pain; previous AC/LC releases	DPC CP borderline elevated
3	40	F	Walker	4 yr bilateral calf pain; varicose veins	Not obtained
4	17	F	Dancer	1 yr bilateral diffuse calf pain; "shin splints" on bone scan	Left AC CP borderline elevated
5	23	M	Basketball player	1 yr bilateral anterior and posterior calf pain	Not obtained
6	19	M	Football player	2 yr chronic diffuse bilateral calf pain; AC/LC/PC fasciotomies 1 to 2 yr ago	Not obtained
7	26	M	Cyclist	Chronic anterior and posterior calf pain; previous posterior fasciotomies	Not obtained
8	32	M	Triathlete	2 yr low back and left leg pain	Not obtained
9	19	F	Hockey player	Chronic lateral and lower posterior calf pain bilaterally; AC/PC releases 1 yr ago	Left LC CP elevated right LC CP normal
10	31	M	Walker	1 yr anterolateral calf pain on walking; L > R; bone scan "shin splints"	Stryker method borderline elevated left AC post exercise
11	38	M	PE teacher	Chronic posterolateral calf pain with jogging; Ex sprinter; L > R	Not done (refused)
12	39	F	Aerobics teacher	Recurrent lower ant/lat calf pain; bilat L > R; bilat AC release 6/12 yr previously	Whitesides method 30 mm left AC CP at rest
13	40	M	Diver	Recurrent deep posterior calf pain; L > R bilateral posterior compartment releases 1 yr ago	Right DPC CP normal
14	25	F	Tennis coach	Chronic diffuse bilateral calf pain for 10 yr; maximal laterally; bone scan "shin splints"	Right DPC CP elevated at 35 mm at rest

AC = anterior compartment; CP = compartment pressure measurement; DPC = deep posterior compartment; LC = lateral compartment.

cardiographs who had a low probability of coronary artery disease and normal cardiac ^{201}Tl studies (Table 2).

Exercise Protocol

Patients fasted for 4 hr before exercising. On the study day, patients performed the exercise that was known to cause the lower leg symptoms, i.e., jogging, walking (treadmill), cycling (bicycle ergometer). When typical symptoms had been reproduced, 100 MBq ^{201}Tl were injected and exercise was continued for 1 min to allow tracer distribution at stress.

Data Acquisition

Imaging was commenced 5 min postinjection and repeated after a 4-hr delay. The patient was imaged supine using a digital gamma camera. Energy windows were set to 20% around the 74 and 135 keV peaks and low-energy, all-purpose, parallel-hole collimation was used. Anterior and posterior planar images were collected for 5 min on a 128 × 128 word matrix. SPECT imaging was then performed for 32 views of 40 sec/view through a 360° elliptical orbit. SPECT images were collected on a 64 × 64 word matrix. Acquisition of delayed images was carefully aligned to the stress dataset by the technologist.

SPECT Reconstruction

SPECT data were reconstructed by filtered backprojection using a Ramp-Hanning filter with a 0.7 cutoff frequency. Transaxial and coronal cross-sections were obtained in 25 mm slices (4 pixel thickness). Transaxial slices were reconstructed across the whole field of view to obtain 16 slices from knee to ankle. Coronal slices were produced in four slices from anterior to posterior and each leg was sliced individually from lateral to medial in four sagittal slices. Stress and delayed datasets were aligned by the technologist for reconstruction and display.

Qualitative Analysis

The images were manually normalized by intensity manipulation and copied to film using a linear grey scale. These images were assessed qualitatively by two nuclear medicine physicians.

Quantitative Analysis

Quantitative analysis was performed retrospectively in nine patients and three controls. Horizontal activity profile curves were produced for each of the four coronal slices and further subdivided into upper, middle and lower thirds across the field of view. The upper and lower limits of the regions of interest were matched for exercise and rest by the operator. The profile curves were zeroed to remove negative values. Percent change in activity between exercise and rest was determined by defining each leg separately on the curves and calculating the area under the curve. Curves from the first and second, and from the third and fourth coronal frames were added to divide the leg into anterior and posterior regions. The major contribution to uptake in the anterior region was from the anterior and lateral compartments, which were not separated further for quantitation. The posterior region contained mainly the deep and superficial posterior compartments which were also not quantitated separately.

Redistribution was defined as a qualitative or quantitative in-

TABLE 2
Clinical Results

Patient no.	^{201}Tl qualitative* Right	Left	^{201}Tl quantitative† Rt ant / Rt post	Rt total	Lt ant / Lt post	Lt total	Surgery and/or follow-up
1	AC+	AC+	10		18		Bilateral
	PC+	PC+		14		17	AC/PC
			17		17		releases improved
2	PC+	PC+	−11		−6		Bilateral
				−11		−15	SPC/DPC releases;
			−11		−22		mild improvement
3	Normal	Normal	N/A		N/A		Sclerotherapy
							varicose veins
4	AC+	AC+	N/A		N/A		Surgery not performed
5	PC+	PC+	−33		−52		Surgery not performed
				−24		−20	
			−16		−3		
6	PC+	PC+	N/A		N/A	j	Bilateral PC releases improved
7	AC+	AC+	22		27		Surgery not performed
	PC+	PC+		29		30	
			34		32		
8	Normal	AC+	N/A		N/A		Surgery; left SPC/DPC mild
		PC+					improvement; MRI disc
							lesions L4/5, L5/S1
9	LC+	LC+	N/A		N/A		LC/PC releases bilaterally improved
	PC+						
10	AC+	AC+	25		32		AC/PC releases bilaterally improved
	LC+	LC+		31		33	
			39		33		
11	AC+	AC+	16		19		Surgery not performed
	PC+	PC+		20		16	
			23		15		
12	AC+	AC+	29		32		Bilateral AC releases; recent
	LC+	LC+		19		21	surgery no follow-up
			8		10		
13	AC+	AC++	23		31		Surgery not decided
	PC+	PC++		17		28	
			13		26		
14	AC+	AC+	25		32		Awaiting surgery
				26		34	
			26		35		
Control 1	Normal	Normal	−1		−10		Normal cardiac ^{201}Tl
				−12		−9	
			−21		−9		
Control 2	Normal	Normal	−20		−19		Normal cardiac ^{201}Tl
				−9		−10	
			−3		−5		
Control 3	Normal	Normal	−15		−7		Normal cardiac ^{201}Tl
				−23		−7	
			−31		−6		

*Qualitative assessment of ^{201}Tl scan: + = redistribution.

†Quantitation of ^{201}Tl scans expressed as the percent change in activity between stress and delay for anterior (Ant), posterior (Post) and whole (Tot) calf (anterior plus posterior).

AC = anterior compartment; LC = lateral compartment; PC = superficial and deep posterior; compartments; NA = not available.

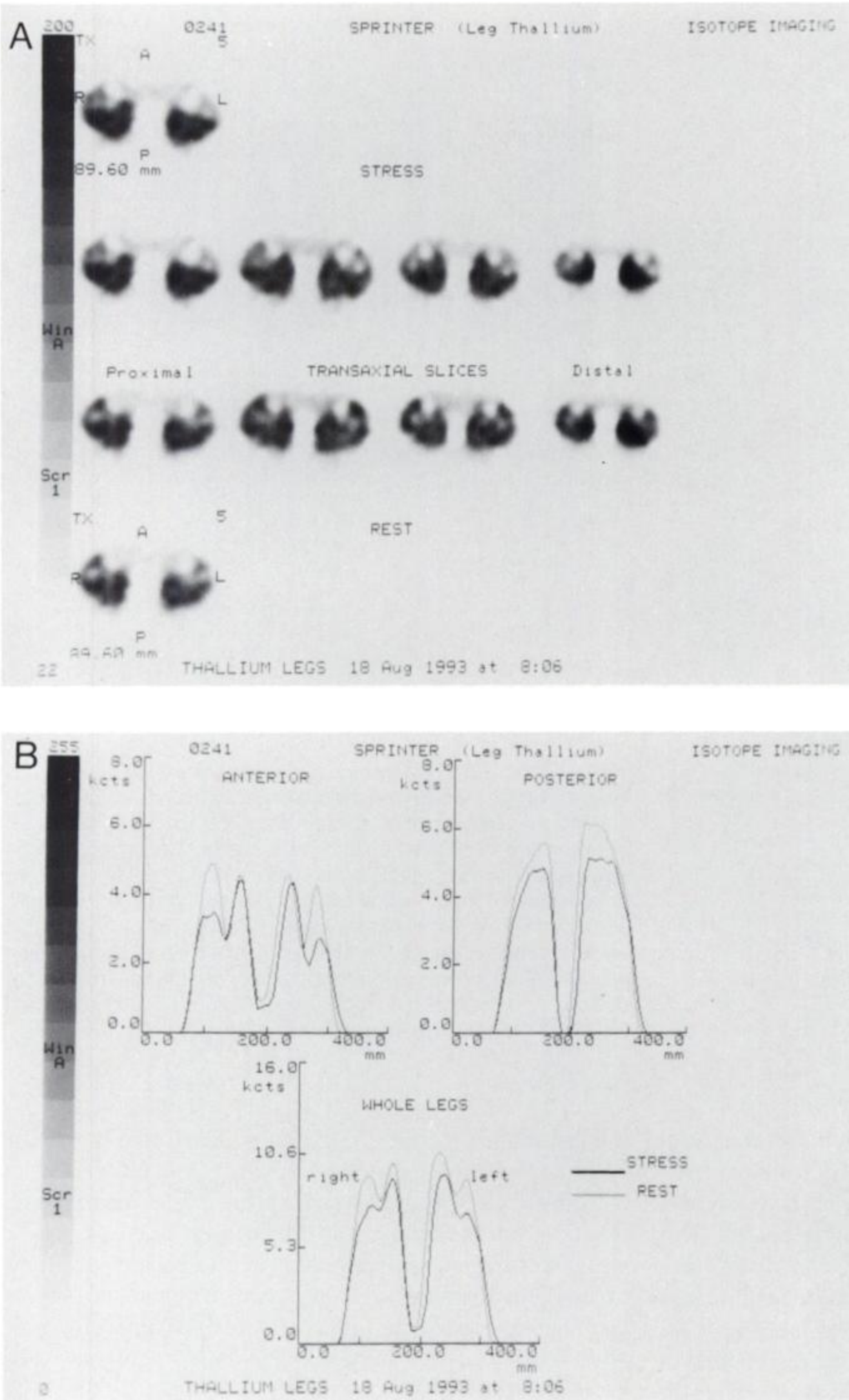


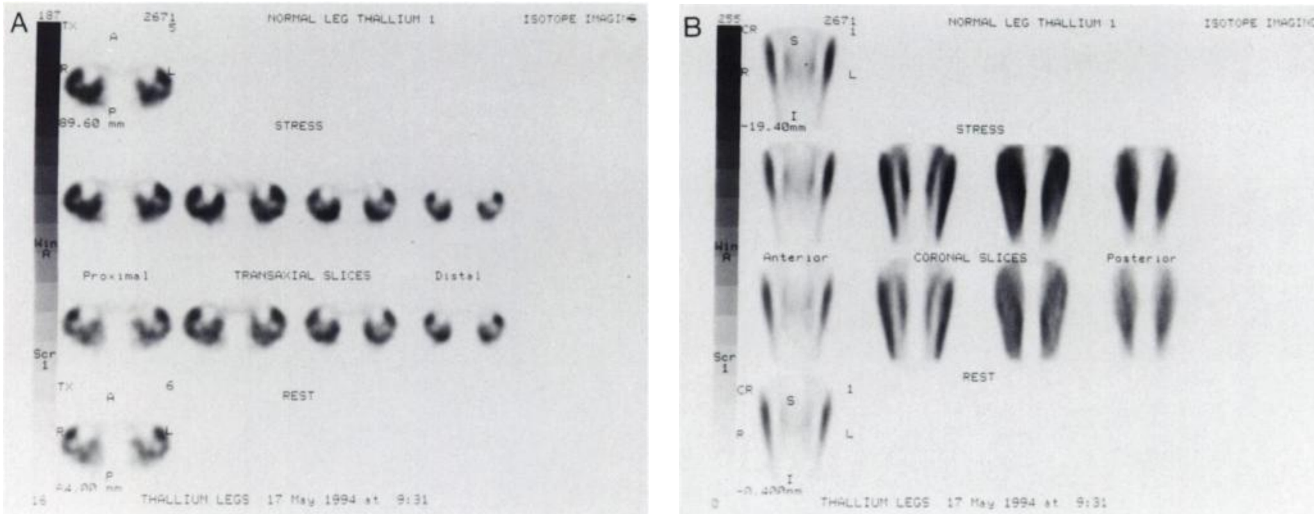
FIGURE 2. Patient 1, a 22-yr-old female sprinter with diffuse bilateral calf muscle pain. (A) Selected transaxial SPECT slices of the calves, superior to inferior. Upper row: stress; lower row: 4-hr delay. (B) Stress and delayed count profile curves for the anterior, posterior and whole (anterior plus posterior) midcalf. Qualitative and quantitative assessment of the ^{201}Tl scan shows reversible ischemia in the anterior and posterior compartments.

crease in uptake or counts relative to the stress image. Washout was defined as a qualitative or quantitative reduction in uptake or counts compared to the stress image.

Quantitative data are shown in Table 2. Activity curves from the middle third of the calf were selected for display in Figures 2 and 3.

RESULTS

Reversible compartment ischemia was qualitatively defined in 13 patients (Table 2). Quantitation was performed retrospectively in nine of these patients and confirmed reperfusion in seven. In two patients who qualitatively showed reperfusion, quantitation indicated variable washout, suggesting false-positive results. The controls showed uniform uptake and variable washout by qualitative and quantitative analysis. Bone scintigraphy done prior to ^{201}Tl leg scans was positive in all of the four studies (three periostitis, one bilateral stress fracture). Thallium leg scans were positive by qualitative assessment in all four of these patients. Quantitative results were available in three of the



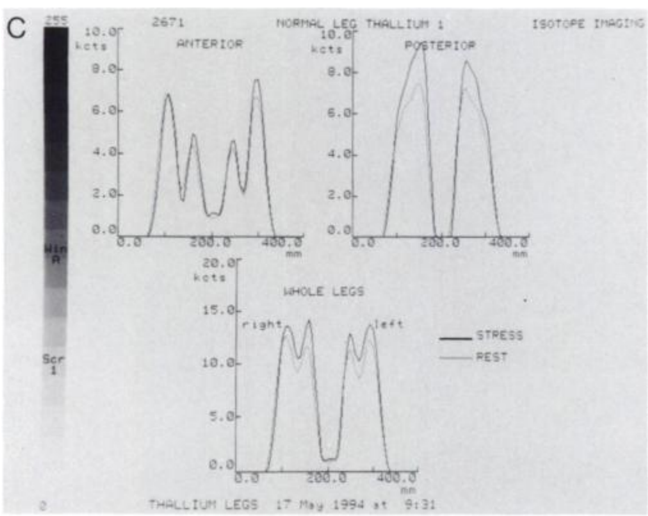


FIGURE 3. Control subject, a 35-yr-old nonsmoking man with no leg symptoms. (A) Selected transaxial SPECT slices of the calves, superior to inferior. Upper row: stress; lower row: 4-hr delay. (B) Selected coronal slices, anterior to posterior. Upper row: stress; lower row: 4-hr delay. (C) Stress and delayed count profile curves for the anterior, posterior and whole (anterior plus posterior) mid calf. These images show homogenous muscle uptake of ^{201}Tl in the immediate poststress and delayed images, with the tibia appearing as a large photopenic defect anteromedially and the fibula as a small photopenic defect posterolaterally. Quantitation (Table 2) confirmed washout in the delayed images.

four patients and confirmed redistribution in all three. Previous surgery for CPS had been performed in six patients. Thallium scans were positive qualitatively in all six patients and positive quantitatively in five. The one patient with qualitative but not quantitative demonstration of CPS (Patient 2) had repeat surgery with mild improvement. Quantitative analysis suggests that this study was false-positive.

Compartment pressure measurements were obtained in eight patients. Pressure measurements were elevated in four patients, borderline in three and normal in one. All four patients with elevated compartment pressure had positive ^{201}Tl scans, qualitatively, which were confirmed by quantitative analysis in three. Quantitative analysis was not available for one of these patients.

For the three patients who were borderline, qualitative assessment showed reversible compartment ischemia. Quantitation was available for two patients and showed reversible ischemia in one and washout in the other (Patient 2). Patient 13 had a normal compartment pressure measurement. The pressure measurement had been performed in the right leg, whereas quantitative and qualitative assessment of the ^{201}Tl scan indicated that the major reversible change was in the left leg.

Compartment surgery was performed in seven patients, five of whom had previous compartment releases. There was definite clinical improvement in four patients and mild improvement postoperatively in two. One patient had recently undergone surgery and no follow-up data were available. Of these seven surgical patients, all had shown reversible ischemia by qualitative assessment of the ^{201}Tl scans. Retrospective quantitation was available in four of these patients, which confirmed redistribution in three patients. In Patient 2, retrospective quantitative analysis suggested washout rather than redistribution (false-positive). This patient had only mild improvement postoperatively. Mild improvement was also seen in Patient 8, who had a positive ^{201}Tl scan by qualitative and quantitative analysis; MRI revealed lower lumbar disc lesions.

DISCUSSION

An overlap of problems may occur with patients having various features of CPS, stress fracture and/or periostitis.

The presence of tibial stress syndrome should not exclude assessment for CPS (*1,2*). The four patients in this study with positive bone scans also demonstrated reversible perfusion defects on their ^{201}Tl scans. Because CPS may be associated with other stress-related conditions, further diagnostic testing is often required to confirm the presumptive diagnosis of CPS. Presently, the diagnosis of CPS is usually confirmed by direct measurement of compartment pressure. Many techniques are available (*13*) and there is no uniform agreement regarding the optimal method or diagnostic criteria to determine this measurement. The insertion of needles into the calf muscle may be painful and may, on occasion, impair the athlete's ability to exercise for dynamic pressure measurement. Only one compartment can be studied at a time dynamically, whereas multiple compartments may be involved in CPS (*3,7*), each of which would require individual invasive testing for confirmation of CPS. Many of the patients in this study showed reversible ischemia both anteriorly and posteriorly on ^{201}Tl images, which supports the observation that multiple compartments are often involved in CPS.

Compartment pressure measurements may also be normal in the presence of typical symptoms of CPS (*8*). These considerations indicate the need for a reliable noninvasive test to complement clinical assessment and compartment pressure measurements to diagnose CPS.

We have shown that ^{201}Tl may be used to investigate patients with suspected CPS. Thallium-201 can localize ischemia to anterior or posterior regions of the calf. Thallium-201 also demonstrates the pathophysiology of CPS, i.e., that exercise-related elevation of intracompartmental pressure results in a reduction in local muscle blood flow and that reperfusion occurs during the resting phase. Quantitative assessment of the ^{201}Tl images improves the accuracy of the scan; qualitative assessment may be misleading when multiple compartments are involved or when variable washout occurs.

In this study, ^{201}Tl demonstrated reversible ischemia in the four patients with typical symptoms of CPS and elevated compartment pressure measurements. In contrast, the control subjects showed uniform uptake in the early images and washout in the delayed images.

The findings on ^{201}Tl were variable in the three patients with borderline elevated compartment pressure measurements. One of these patients (Patient 2) who proceeded to surgery experienced only mild improvement postoperatively. Retrospective quantitation of the ^{201}Tl scan showed washout indicating that the qualitative interpretation was incorrect. This patient probably did not have CPS. Surgery was not performed in the second case (Patient 4) who was shown to have reversible ischemia anteriorly by qualitative assessment of the scan. Quantitation was not available in this case, and the final diagnosis remains uncertain. Surgery was performed in the third case (Patient 10) who was shown to have reversible ischemia by qualitative and quantitative assessment. He showed definite improvement postoperatively making a diagnosis of CPS with only borderline elevated compartment pressure most likely.

Compartment pressure measurement was normal in one case. The ^{201}Tl scan showed that the maximal reversible change was anterior and posterior in the left calf, whereas direct measurement of pressure had been performed in the right calf. Repeat pressure testing of the left calf would be required to confirm or exclude the diagnosis of CPS. To date, this repeat measurement has not been performed.

Technetium-99m-sestamibi, a more recently available myocardial perfusion agent, has also been used to assess CPS with conflicting results (*14,15*). The study by Amendola et al. concluded that the pathophysiology of exertional compartment syndrome was not related to ischemia (*14*). Our cases demonstrate that local blood flow is reduced when exercise produces symptoms and that reperfusion occurs with rest. This would indicate that ischemia accompanies symptoms and is consistent with current concepts regarding the pathophysiology of CPS (*2,3,5,7*).

Recent studies have also showed that ^{99m}Tc-sestamibi, in contrast to ^{201}Tl, may underestimate the extent of a perfusion defect in patients with severe myocardial hypoperfusion (*16*). Technetium 99m-sestamibi does not redistribute and requires two sets of injections on alternate days for a complete study. For reasons of convenience, cost and possibly greater sensitivity, ^{201}Tl may be the preferred radiopharmaceutical for investigation of CPS.

MRI has also been evaluated as a noninvasive method for diagnosis of CPS. In the study by Amendola et al. (*14*), no statistically significant change could be demonstrated postexercise, and the authors concluded that the practical value of MRI in the diagnosis of CPS was unclear and that MRI was not indicated in the routine assessment of CPS.

Nonoperative treatment for CPS is unsuccessful in 100% of patients (7) and surgical treatment by fasciotomy is successful in 60% to 100% of patients (*2*). Relapses may be attributed to insufficient fasciotomy or fasciectomy. Of interest, six of the patients in this study had previously undergone surgery for CPS and had relapsed. This would suggest that surgery had either been incomplete or had been performed on the wrong compartments, supporting the need for more reliable diagnostic testing in CPS before surgery is undertaken.

These preliminary data are encouraging and would indicate the potential use of ^{201}Tl in the investigation of CPS. Thallium-201 can demonstrate the pathophysiology of CPS, i.e., that elevated pressure reduces local blood flow in the calves resulting in ischemia. A large population of cases and controls will need to be studied fully to evaluate the role of ^{201}Tl in the diagnosis of CPS.

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