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Oxygen Saturation Measurement of Calf Muscle During Exercise in Intermittent Claudication

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Objectives: *to evaluate the oxygen saturation of the calf muscle measured by means of spatially resolved spectroscopy (SRS) in claudicants.*
Methods: *a total of 150 legs in 84 consecutive patients with calf claudication were studied by SRS. Oxygen saturation (SmO_2) and the relative changes in oxygenated haemoglobin (HbO_2) and deoxygenated haemoglobin (Hb) of the gastrocnemius muscle were measured during a treadmill walking test (2.4 km/h, 12%, 5 min)*
Results: *exercise was associated with a decrease in HbO_2 and an increase in Hb. There was no difference in SmO_2 at rest among all groups. The decrease oxygen saturation correlated well with the severity of symptoms of IC.*
Conclusion: *muscle oxygen saturation measurement by SRS can be used clinically to provide objective information regarding the severity of IC.*

Key Words: Near-infrared spectroscopy; Peripheral vascular disease; Intermittent claudication; Ischaemia; Skeletal muscle; Exercise.

Introduction

Although the basis of intermittent claudication (IC) lies in functional ischaemia of the calf muscles during exercise, muscle oxygenation during exercise is not yet well demonstrated in patients with IC because of the lack of appropriate parameters. Recently, spatially resolved spectroscopy (SRS), based on intensity changes at multiple spacing, was introduced and its reliability has been evaluated in tissue-like phantoms[1] and in the cerebral tissue.[2] Oximeters using SRS provide not only the change in haemoglobin concentration, but also the absolute value of tissue oxygen saturation. However, to date patients with IC have not been studied.

The aim of this study was to evaluate oxygen saturation of the calf muscles measured by SRS in patients with calf claudication. In addition, the reproducibility of SRS measurements during exercise was examined.

Patients and Methods

The protocol used in this study was approved by the local ethics committee. All measurements were made after obtaining the patients' informed consent. A total of 150 legs in 84 consecutive patients who complained of calf claudication were studied from March to September 2000. There were 76 men and 8 women with a mean age of 66 (range 33–83) years. Subjects were excluded for the following reasons: venous insufficiency such as varicose veins or deep vein thrombosis, surgical procedures in the preceding 6 months, inability to complete treadmill walking for reasons other than IC such as breathlessness or palpitations, or severe cardiac or pulmonary disease. When SRS measurements were performed bilaterally and the subject stopped walking due to unilateral calf pain, only the symptomatic leg was studied, and the contralateral leg was excluded.

Spatially resolved spectroscopy

The optode of a tissue oximeter based on SRS (OM-220, Shimadzu Co., Japan) was positioned on the posterior aspect on the calf, over the medial head of the gastrocnemius muscle. The optical probe consisted of two separate detectors fixed at 2.5 and 4 cm from the emitter. The optode (distal end of the emitter and the detector) was kept at a constant distance and geometry by a rubber shell that, in turn, was firmly attached to the skin longitudinally with a bandage. This instrument has been previously tested in muscle studies.[3] Near infrared light penetrates the skin,

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subcutaneous fat and underlying muscle, and is either absorbed or scattered within the tissues. Part of the scattered light is detected by the detector. The penetration depth is estimated to be about 2 cm.[4] The influence of subcutaneous adipose tissue on near infrared light propagation in leg muscle and on the sensitivity of a near-infrared spectrophotometer has been recently investigated, and the authors concluded that near infrared light penetrates shallow regions of muscle under the skin and subcutaneous fat even when the adipose tissue thickness is 1.5 cm.[5]

The relative changes in oxygenated haemoglobin (HbO_2) and deoxygenated haemoglobin (Hb) and muscle oxygen saturation (SmO_2) were continuously measured in the standing position: (a) at rest until a stable baseline was reached (minimum 30 s); (b) during walking; and (c) during the subsequent recovery period at rest (maximum 10 min). Data were collected every second, and the average for 30 s at rest before treadmill walking and at the end of walking were taken as SmO_2 at rest and at the end of exercise, respectively.

Treadmill test with SRS measurement

After measuring ABPI at rest, the patient stood on the treadmill-walking machine (Aeromiu, Nihon-Koden Co., Japan). A standard treadmill-walking test[6] was performed, with some modification of the maximum speed and the way of raising the slope. This treadmill design began at a 0% slope with a speed of 0.8 km/h. The slope was increased gradually to 12% over 30 s, and the speed was increased by 0.8 km/h every 15 s to 2.4 km/h. Walking lasted for as long as each patient was able, with a maximum duration of 5 min. At the end of the walking test, the treadmill slope was returned to 0%.

Reproducibility of muscle oxygen saturation measurement

Another cohort of 11 patients with 22 legs (10 men and one woman with a mean age of 69 years (range 53–77)) underwent repeated SRS measurements to determine the reproducibility of SdO_2 at rest and at the end of exercise. A treadmill test with SRS measurement was performed on the same patient on two different days. The interval between the first and second tests ranged from 2 to 26 days (mean 11.2 days).

Statistics

Statistical analyses were performed with Wilcoxon rank test to compare SmO_2 at rest and at the end of exercise in each group and Fisher's protected least significant difference to compare ABPI and SmO_2 among all types of legs. Results were expressed as median with the 95% confidence interval (CI) in parentheses. A value of $p < 0.05$ was considered statistically significant. The reproducibility for SdO_2 at rest and at the end of exercise was analysed by means of the intraclass correlation coefficient (r_I).[7] According to this value, agreement was considered "almost perfect" ($r_I \geq 0.81$), "substantial" ($0.80 \geq r_I \geq 0.61$), "good" ($0.60 \geq r_I \geq 0.41$), "fair" ($0.40 \geq r_I \geq 0.21$) or "slight" ($0.20 \geq r_I$).[8] The reproducibility for ABPI at rest was also analyzed with r_I in order to compare its values with SmO_2.

Results

Categories of legs

All legs were divided into two groups according to the pattern of serial changes in haemoglobin. Normal legs were characterised by no change in HbO_2 or Hb with exercise (Fig. 1a). IC legs were characterised by a decrease of HbO_2 and an increase in Hb during exercise (Fig. 1b). IC legs were also differentiated into three groups according to the severity of IC. Legs with mild IC were able to complete the 5-min walking test without symptoms. Moderate IC legs were able to complete the test with symptoms. Severe IC legs were unable to complete the test due to severe symptoms.

SRS measurements were performed in one leg in one patient and in both legs in 83 patients who complained of bilateral claudication. In 17 of the 83 patients who had bilateral measurements, the contralateral leg was excluded according to the protocol when claudication only developed in one leg during exercise. In the remaining 66 measurements, 54 patients completed the 5-min treadmill test, while 12 patients could not finish the test. In the 54 patients with bilateral symmetrical claudication who completed the treadmill test, the combination of muscle oxygenation types in the two legs was normal–normal (5 patients), normal–mild IC (4), normal–moderate IC (6), mild IC–mild IC (16), mild IC–moderate IC (8) or moderate IC–moderate IC (15). In all 12 patients who were unable to complete the test because of equally severe pain in both legs, the combination of NIRS types in the two legs was severe IC–severe IC.

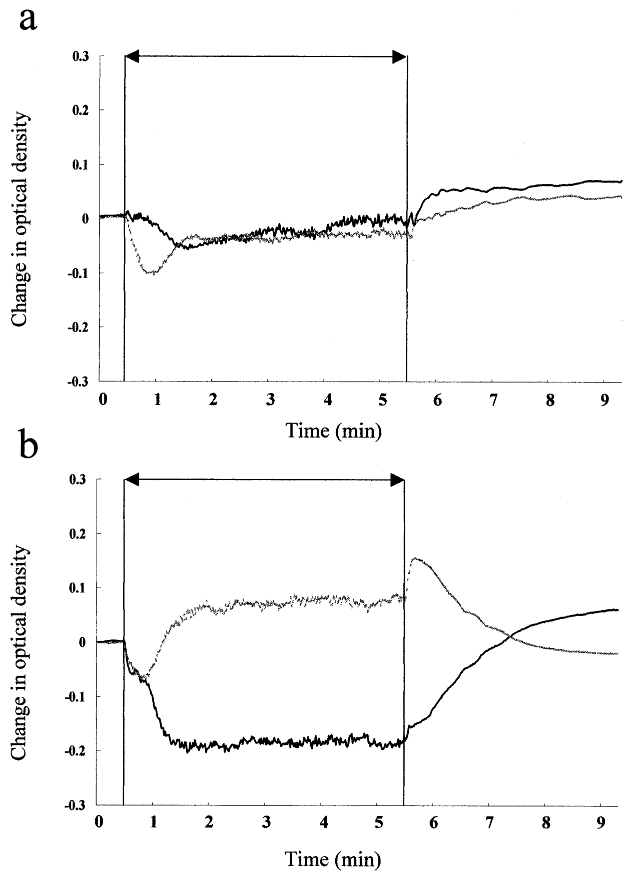

Fig. 1. (a) Typical normal leg and (b) leg with intermittent claudication tracings of oxygenated haemoglobin (solid line) and deoxygenated haemoglobin (dotted line) during a treadmill-walking test with spatially resolved spectroscopy.

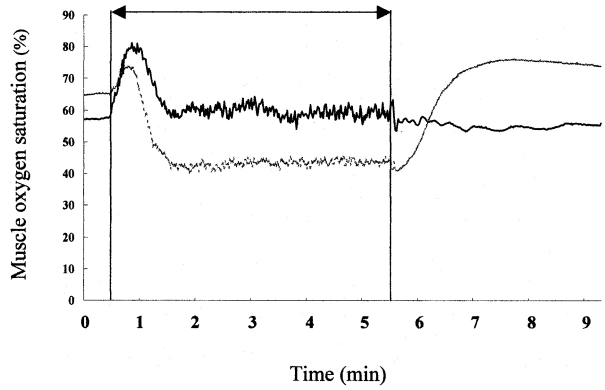

Fig. 2. Typical tracings of muscle oxygen saturation in normal leg (solid line) and leg with intermittent claudication (dotted line) during a treadmill walking test with spatially resolved spectroscopy.

Measurements for both legs were included in the analysis for patients with equal claudication, because they could not differentiate the leg that was worse.

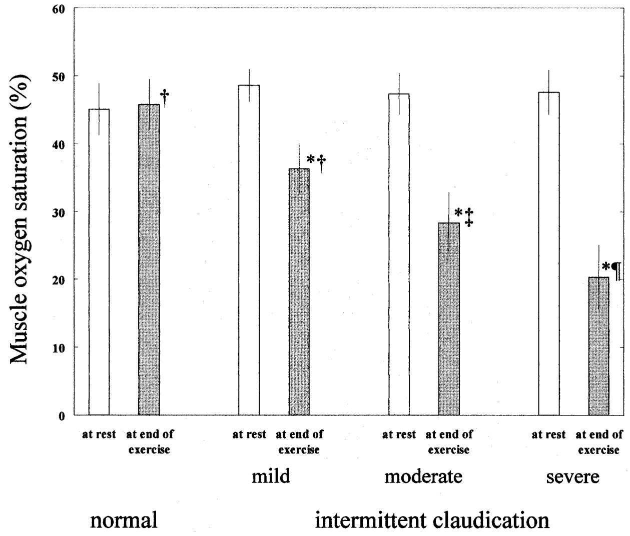

Fig. 3. Muscle oxygen saturation at rest and at the end of exercise in all types of legs (median with 95% CI). $^*p < 0.0001$ compared with muscle oxygen saturation at rest (Wilcoxon rank test). † $p < 0.01$ compared with normal leg, ‡ $p < 0.01$ compared with mild IC leg and ¶ $p < 0.01$ compared with moderate IC legs (Fisher's protected least significant difference).

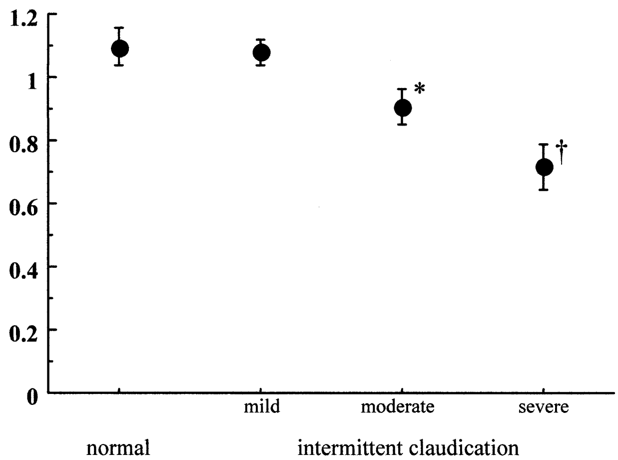

Fig. 4. Ankle brachial pressure index in all types of legs (median with 95% CI). $^*p < 0.0001$ compared with mild IC leg and † $p < 0.0001$ compared with moderate IC legs (Fisher's protected least significant difference).

Muscle oxygen saturation

The decrease in SmO_2 at the end of exercise was proportionally correlated with the severities of claudication among all IC groups, while there was no difference in SmO_2 at rest between normal and each IC group (Fig. 3). The mean ABPI at rest was significantly different between three types of IC legs, while there were no differences between normal legs and mild IC legs (Fig. 4).

Table 1. Reproducibility of muscle oxygen saturation and ankle brachial pressure index.

	First measurement Median (95% CI)	Second measurement Median (95% CI)	Intraclass correlation coefficient (95% CI)
ABPI at rest	0.73 (0.53–0.84)	0.75 (0.54–0.92)	0.94 (0.86–0.97)
SmO_2 at rest	47 (38–54)	46 (38–49)	0.88 (0.73–0.95)
SmO_2 at the end of exercise	24 (4–40)	21 (7–37)	0.93 (0.84–0.97)

ABPI = ankle brachial pressure index, SmO_2 = muscle oxygen saturation.

Reproducibility of muscle oxygen saturation measured by spatially resolved spectroscopy

Twenty-two measurements of SRS in 11 patients (10 men and one woman) were performed. All legs had IC. Table shows the results of reproducibility of ABPI at rest, and SmO_2 at rest and at the end of exercise. "Almost perfect" agreement was found for repeated measurements of ABPI at rest and SdO_2 at rest and at the end of exercise.

Discussion

Though IC is a major symptom in patients with peripheral vascular disease (PVD), the evaluation of IC is easily affected by the patient's subjective perception and attitude. Objective assessment of muscle oxygenation during exercise is absolutely necessary in the evaluation of IC, because the basis of IC lies in functional ischaemia during exercise, not in the ischaemia at rest. Cheatle *et al*.[9] had firstly reported that muscle oxygen consumption at rest is significantly decreased in PVD patients using NIRS technique. In contrast, Koojiman *et al*.[10] found no difference in muscle oxygen consumption at rest between PVD patients and normal controls and more increased muscle oxygen consumption after exercise in PVD patients. The efficacy of the measurement of muscle oxygen consumption is not certain on the evaluation of IC. Moreover, their hypothesis, that the pathlength of near-infrared lights in the PVD patients are equal to that in normal controls, is not confirmed yet. We have previously reported[11,12] that the resaturation time of muscle after exercise measured by near-infrared spectroscopy is well correlated with the severity of IC. While other papers[10,13] supported our result that the assessment of muscle resaturation after exercise is effective in evaluating IC, it has been difficult to assess the desaturation of muscle during exercise using conventional NIRS technique. Our approach in this paper is different from our previous ones[11,12]and others[9,10] in that the absolute value of muscle oxygen saturation was directly measured during walking using the newly investigated SRS oximeter. Boushel *et al*.[14] reported that oxygen saturation of calf muscle measured by the different SRS oximeter was 66% at rest. They found that muscle oxygen saturation remained unchanged from the rest level up to 5 W and significantly decreased at the higher loads than 7 W of plantar flexion exercise in the young healthy volunteers. These results support our findings that no decrease in muscle oxygen saturation in normal group because the workload of our treadmill protocol was very low. Regarding the discrepancy of the level of muscle oxygen saturation at rest between their value and ours (45–49%), the difference in population, equipment,[15] posture and exercise might explain.

Although the "mild IC" group was differentiated from the normal group only by the NIRS patterns, muscle oxygen saturation at the end of exercise was proportionally correlated with the severities of claudication among all IC groups. These results suggest that the "mild IC" group, with NIRS claudication pattern without symptoms, has a potential risk in worsening of claudication. Moreover, the findings of a significant difference in muscle oxygen saturation at the end of exercise and no difference in ABPI at rest between normal subjects without symptoms and patients with mild symptoms of claudication suggest that SRS measurement could contribute to the surveillance of peripheral vascular disease in the elderly subjects with normal ankle pressure.

The reproducibility of muscle oxygen saturation measurement, not only at rest but also during exercise, is almost equal to that of pressure measurement with Doppler at rest. These results confirm the previous reports in normal control[14] and in a small number of patients with peripheral vascular disease measured by phase modulated spectroscopy.[16] In conclusion, the decrease of muscle oxygen saturation during exercise was well correlated with the severity of symptoms of intermittent claudication. Muscle oxygen saturation measurement by spatially resolved spectroscopy could be used therapeutically to provide objective information regarding the severity of IC.

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