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Calf and non-calf hemodynamic recovery in patients with arterial claudication: implication for exercise training.

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KEYWORDS

Intermittent claudication; Calf pain; Exercise oximetry; symptoms; ischemia

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HIGHLIGHTS:

- Arterial claudication can result in calf (C) and/or non-calf (NC) ischemia.
- Transcutaneous oximetry allows simultaneous C and NC ischemia monitoring.
- Both C and NC ischemia normalize in less than 10 minutes in most patients.
- Only ischemia severity and body mass index correlate to recovery time.
- NC frequently exceeds C ischemia recovery time, in patients with claudication.

ABSTRACT:

Background: Previous studies in patients with arterial claudication have focused on calf hemodynamic recovery. We hypothesized that the duration of hemodynamic recovery with TcPO₂ at calf and non-calf levels would be shorter than 10 min. We analyzed the factors that influence the recovery time.

Methods: We monitored limb changes minus chest changes from rest (DROP) of transcutaneous oximetry on buttocks, thighs and calves, during and following a treadmill test (3.2km/h; 10% grade). We calculated the time required to reach 50% (50%RT) and 10% (90%RT) of minimal DROP value (DROP_m) from walking cessation. Regression analyses were used to determine the factors associated to 50%RT and 90%RT.

Results: Of the 132 patients studied, 18.2% reported isolated non-calf pain by history. Of the 792 recovery time values, only 3 (0.4%) and 23 (2.9%) were in excess of 10 minutes for 50%RT and for 90%RT, respectively. A weak correlation was found between each of the 792 DROP_m and 50%RT ($r=-0.270$, $p<0.001$) as well as for 90%RT ($r=-0.311$, $p<0.001$). Lowest DROP_m and BMI (but not age, sex, the use of beta-blockers, the duration of the walking period) were associated to both 50%RT and 90%RT.

Conclusion: Although recovery duration correlates significantly with the severity of ischemia of the same location, a wide discrepancy exists and the longest recovery time does not always correlate to the localization of the mores severe ischemia. Non-calf ischemia should be measured when one aims at objectifying the biological effects of exercise or the effects of treatments on recovery from exercise.

ABBREVIATIONS

- ABI Ankle to brachial systolic pressure index
- BMI Body mass index
- DROP Decrease from Rest of Oxygen Pressure
- DROPm Lowest DROP value recorded during or following exercise
- LEAD Lower extremity arterial disease
- MWT Maximum walking time
- NIRS near infrared spectrometry
- RBFi Regional blood flow impairment
- SD Standard deviation
- TcpO₂ Transcutaneous oxygen pressure
- 50%RT Time required for DROP to reach 50% of the lowest value
- 90%RT Time required for DROP to reach 10% of the lowest value

INTRODUCTION:

Lower limb pain while walking is a frequent symptom in elderly patients. In vascular medicine, vascular type claudication in patients with lower extremity artery disease (LEAD) has been defined for years as a lower limb pain or discomfort, that is absent at rest and disappears within 10 minutes when exercise is stopped¹. We previously showed that, when walking de-novo after a period of rest, patients may reproduce their symptoms earlier if hemodynamic recovery is not optimal.² This is one of the proposed explanations for the curvilinear relationship between maximal walking distance and the preceding duration of the stop that was observed on global positioning system recordings of community walking in patients with claudication². Then, determination of the duration of hemodynamic recovery could be of interest in rehabilitation programs, to define the optimal duration of recovery before the next walking. Most studies performed on hemodynamic recovery in LEAD patients have focused on calf, although non-calf ischemia is frequent, even in patients with calf-only symptoms³. We also previously showed that among patients complaining isolated calf pain a perfect concordance with symptoms on treadmill and underlying ischemia (calf pain only and calf ischemia only) was observed in only 19.5% of the cases⁴. It is possible that in some patients, in the recovery period non-calf ischemia may last longer than calf ischemia and that calf hemodynamic recovery may not be the proof that lower limb ischemia has recovered in non-calf areas, but this point has never been studied.

Transcutaneous oxygen pressure (TcPO₂) recordings allows the monitoring of lower limb regional blood flow impairment (RBFi) at the buttocks, thighs and calves levels simultaneously, in patients with claudication⁵⁻⁷. The specific interest of the technique is to provide continuous measurable values at different limb levels bilaterally and throughout the walking and recovery periods

We hypothesized that: 1/ The duration of hemodynamic recovery with TcPO₂ would be shorter than 10 min, consistently with the duration of pain in the definition of arterial claudication; 2/ Recovery time would be proportional to the severity of exercise-induced ischemia and/or duration of walking. 3/ The recovery duration at the calf would exceed the duration of recovery at non-calf levels specifically in patients complaining calf claudication. 4/ Ischemia and recovery time would be higher at the calf than non-calf localizations, specifically in patients with calf-claudication by history; 5/ We analyzed the factors that influence the recovery time.

MATERIAL AND METHODS

Study population:

We used exercise TcPO₂ as a routine among all patients referred to our laboratory for exercise-induced claudication of suspected arterial origin⁵⁻⁸. At arrival, all subjects had to fill a questionnaire about their age, gender, ongoing treatment, past history, presence or absence of significant history (active smoking, diabetes mellitus, hypercholesterolemia, arterial hypertension, lower limb vascular surgery). Patients also self-completed the Edinburgh claudication questionnaire. While patients were admitted to the test room, the time required to

walk 10 meters in the corridor at usual speed was recorded to estimate their ability to walk on treadmill at the goal speed. Stature and weight were recorded to calculate body mass index (BMI: kg/m²). When not available in the recent patient file, ankle to brachial index (ABI) on each leg was measured as the ratio of the highest systolic blood pressure in each ankle from the right and left posterior tibial or dorsalis pedis arteries, divided by the highest brachial systolic blood pressure. The lowest of the two legs ABI was recorded for each patient. An ABI < 0.90 was considered positive results for the presence of stenoses on the arterial tree toward the ankle. Missing or non-compressible values were encoded negative.

Exercise tests.

Patients that were able to walk 10 m in less than 15 sec were proposed a standard treadmill procedure consisting in a transmission phase of 1 minute from flat grade and 0 km/h, to 3.2 km/h and 10% slope. In the absence of limiting symptoms, after 15 minutes the speed and grade were increased by steps of 1 minute until exhaustion or limiting symptoms, as previously described⁹. For patients that were unable to walk the 10 m in 15 sec the speed was limited to 2 km/h only. We recorded maximum walking time (MWT). Walking was performed under 12 lead electrocardiographic supervision, and was stopped on patient's request or in case of medical indication (e.g.: severe arrhythmia).

TcpO₂ measurements

We used eight 44.5 ° C heated probes on PF5010 device (Perimed; Stockholm, Sweden) connected to a computer preinstalled with the AcqTcpO₂ program that automatically calculated the decrease from rest of oxygen pressure (DROP) from absolute Ex-tcpO₂ values, for buttocks, thighs and calves using the left chest probe as a reference^{10, 11}. The right chest probe was used for DROP calculations, except in cases of disconnection of the right chest probe, of a history of right thoracotomy, or of the presence of a stenosis or occlusion of the right sub-clavicular artery. In these cases the left chest results were used. The DROP index (Decrease from Rest of Oxygen Pressure) corresponds to the limb changes from rest minus chest changes from rest. By construction, DROP is zero before exercise and it returns to zero at the end of the recovery period. The nadir value of DROP changes (DROPm) recorded during or following exercise was used as an estimation of the severity of regional blood flow impairment (RBFi).

After a pre-heating period of at least 15 minutes, DROP values from both buttocks, both thighs and both calves were recorded for 2 minutes at rest, throughout exercise and for a minimum of 10 minutes during recovery. If the DROP value was not returned to zero within the 10 minutes of the recovery period, recovery was extended to 15 minutes or 20 minutes if necessary.

A minimal DROP value (DROPm) < -15 mmHg during or following walking was used to define the presence of ischemia.¹¹. We calculated the time required to reach 50% of its minimal value (50%RT) or 10% of its minimal value (90%RT). These 50%RT and 90%RT were calculated from the end of the walking period, even if DROPm occurred during the recovery period.

Inclusion criteria and ethical approval:

As a routine, patients were systematically recalled that their recording and medical database can be used for research purposes and of their right to deny such a use. If patients deny, this was recorded in the hospital database but according to French law, this analysis of routine practice does not require written individual consent. The database was ethically approved and was fully declared to national authorities. The present analysis of the recording and database received local ethics committee approval with reference 2020/42 and conforms to the Declaration of Helsinki. It was registered to the American National Institutes of Health database clinicaltrials.gov under reference NCT04376099. For the present work, we analysed all the patients referred for exercise-tcpO₂ during the first semester of 2018. Exclusion criteria were: No recording in the database (denied use of the medical file, or missing recording despite a TcpO₂ test), absence of TcpO₂ (test not performed for technical reasons or contra-indication to the test), corrupted recording (recovery period not recorded, recording failure), non-standard probe positioning or missing limb probe, duplicate recording, or absence of ischemia on any of the 6 limb probes.

Statistical analysis:

Population description was dichotomized into patients with calf pain by history (With or without associated non-calf symptoms) and patients with non-calf claudication only.

Recovery time and distribution (Gaussian/ non-Gaussian) was performed with rounding the recovery duration by intervals of 30 seconds

The coefficient of correlation of recovery time to DROPm with the hypothesis that recovery time would be proportional to the severity of exercise-induced ischemia and/or duration of walking.

We determined the graphical relationship between the lowest calf vs. non-calf DROPm and highest calf vs. non-calf 50%RT and 90%RT for the whole group and for patients with calf claudication assuming the longest recovery would be associated to the lowest DROPm values, and compared the ischemia and recovery times on calf and non-calf localizations with Wilcoxon paired tests.

We performed a multi-variate determination of the factors that influence the recovery times with step by step linear regression analyzing, using Lowest DROPm age, resting arterial systolic pressure, sex, body mass index, use of beta-blockers, maximal walking time as potential explanatory variables.

Statistical analyses were performed using SPSS (IBM SPSS statistics V15.0, Chicago USA). Results are reported as mean±standard deviation (SD). Comparison between groups were performed with unpaired t-test from numerical data and Chi test for categories. For all statistical tests, a 2-tailed probability level of p<0.05 was used to indicate statistical significance. Non-significant results are reported as NS.

RESULTS

Among the 216 patients referred for treadmill tests during the study period, exclusion criteria resulted in 132 files that were available for the analysis in the present study as shown in figure 1. Population characteristics are reported in table 1. As shown, we had a relatively large proportion (18.2%) of patients that reported isolated non-calf pain by history. Few differences were found between patients that reported calf (+/- non-calf) pain and those that reported non-calf pain only, specifically on ABI. Nevertheless of interest is to note that the proportion of patients with calf (+/- Non-calf) pain that had non-calf ischemia was high and almost similar to the proportion of patients reporting non-calf pain only but that showed calf ischemia. Examples of recording and recovery time calculations are shown in figure 2, illustrating the fact that DROPm may occur after the end of the walking period, and that the location showing the lowest DROPm value is not necessarily the one having the longest recovery times.

As shown in figure 3, the duration of hemodynamic recovery with TcpO₂ was shorter than 10 min consistently with the clinical definition of claudication in most patients. Of the 792 recovery time values, only 3 (0.4%) and 23 (2.9%) were in excess of 10 minutes (600 sec) for 50%RT and for 90%RT, respectively. The times required for 95% of recorded values to reach 50%RT and 90%RT were 5.83 min and 9.80 min, respectively.

On a univariate basis, a very weak although significant correlation was found between each of the 792 DROPm and 50%RT ($r=-0.270$, $p<0.001$) as well as for 90%RT ($r=-0.311$ $p<0.001$). As a result of this weak correlation, and as shown in figure 4, the calf was the location of maximal severity of ischemia and simultaneously of the longest recovery time in only 41 (30.1%) for 50%RT and 46 (34.8%) and 90%RT, and in only 40 (37.0%) for 50%RT and 44(40.7%) for 90%RT, of the whole 132 patients, and of the 108 patients that complained calf claudication by history, respectively. Last, on the average the duration of 50%RT and 90%RT at the calf level, were not superior to non-calf 50%RT and 90%RT: $p=0.191$ and $p=0.676$, respectively.

Last, multivariate analysis showed that for 50%RT, only lowest DROPm and BMI were associated to the duration of 50% recovery. The r correlation coefficient was 0.241 ($p<0.01$), and standardized b coefficient were -0.240 ($p=0.005$) for lowest DROPm and 0.169 ($p=0.047$) for BMI. The analysis for 90%RT found that the r correlation coefficient was 0.411 ($p<0.001$), with standardized b coefficient being -0.348 ($p=0.002$) for lowest DROPm, 0.202 ($p=0.014$) for BMI, and -0.204 ($p=0.015$) for systolic blood pressure. Neither age, sex, the use of betablockers, nor the duration of the walking period played a significant role in the models.

DISCUSSION:

The prevalence of non-calf claudication is highly variable in previous studies¹²⁻¹⁵, and calf pain remains the dominant symptom in intermittent claudication. Almost all studies analyzing hemodynamic recovery in patients with claudication have focused on calf only. To the best of our knowledge, no study has ever compared hemodynamic results in the recovery period after exercise at the proximal (non-calf) and distal (calf) levels simultaneously. This aspect is of particular importance in accompanying and advising patients with claudication to wait for a sufficient period of time to allow forthcoming walking period following recovery from previous exercise-induced ischemic pain.

Dissipation of pain could appear as the most intuitive and easy way of estimating hemodynamic normalization after exercise. The problem arises from the fact that duration of pain dissipation is constantly shorter than hemodynamic normalization¹⁶. Further studies of pain dissipation provide some puzzling results. While studying claudication recovery time after a progressive, graded treadmill protocol (2 mph, 0% grade with 2% increase every 2 minutes), Addison et al. reported that LEAD patients with sarcopenia had higher claudication recovery time (592 ± 98 s vs 395 ± 29 s; $P<.05$) than did individuals without sarcopenia¹⁷. The issue here is that the results imply that almost half of the patients with sarcopenia did not fulfill vascular type claudication because their recovery time was superior to 10 minutes. Further, Garner et al. while studying the dissipation of claudication pain after walking with various treadmill grades found significant differences in time to onset of claudication and time to maximal claudication pain, but strictly no effect on time needed for claudication pain to dissipate¹⁸. Last, the estimation of pain dissipation remains subjective and objective measurable markers should probably be preferred. One of the simplest way of estimating recovery in claudication is to use heart rate as a surrogate measurable marker of peripheral hemodynamic recovery in LEAD patients. Fecchio *et al.* suggested that most heart rate recovery indices were reproducible and reliable in patients with claudication following maximal graded treadmill exercise¹⁹. We showed that heart rate recovery is dependent on both the severity and diffusion of lower limb ischemia as assessed with Tcpo2²⁰. Nevertheless, heart rate recovery is sensitive to fitness²¹, and highly dependent of cardiac dysfunction or of presence of diabetes²². Last, heart rate provides no information on a leg-by-leg basis and on the localization of ischemia.

Lower limb hemodynamic measurements seem preferable for the direct estimation of post exercise recovery from ischemia. The measurement of ankle to brachial systolic pressure index (ABI) is largely used as an easy tool for estimating hemodynamic responses to exercise in LEAD patients²³. Although many studies report the fall in ABI value immediately at the end of exercise^{24, 25}, only few have studied the duration of this ABI fall and the recovery time to pre-exercise values. Sakurai et al showed that after treadmill exercise (2.4 km/h and 10% grade), the recovery time for ABI to reach 90% of its pre-exercise value was superior to 10 min in most of patients²⁶. Average values as high as 15.6 to 28.3 minutes were observed in LEAD patients (without or with micro-albuminemia) after treadmill walking (2.4km/h 12% slope)²⁷. Of interest is to note that recovery time for ABI seems to be influence by the duration of constant load walking while the decrease in ABI from its pre-exercise value was not influenced by walking time duration²⁶. Contrary to previous results, Ohta reported that training reduced not only recovery time for ABI but also the ABI fall observed after the walking period²⁸. This seems consistent to what was observed in athletes performing

maximal incremental exercise²⁹. The major limit of ABI, is that it provides no indication as to the level of hemodynamic impairment and is only a poor marker of the blood delivery (collateral vessels can normalize flow under low pressure). In theory, thigh pressure could differentiate proximal from distal hemodynamic recovery parameters³⁰. Nevertheless, although thigh pressure seems to be able to diagnose iliac stenosis after maximal heavy load exercise in athletes³¹, it failed to diagnose aortoiliac stenosis in LEAD patients after exercise³². Last, ABI will not be the optimal approach to the evaluation of buttock or thigh ischemia that might result from stenosis or occlusion of arterial branches that are not participating to the distal perfusion (i.e. profunda femoris or internal iliac artery). Many authors have proposed the use of near infrared spectrometry (NIRS) to estimate oxygen debt throughout exercise and recovery³³⁻³⁷, although there is a debate on the influence of skin flow over the NIRS signal³⁸. Some authors reported that NIRS derived parameters correlate with pain rating or walking distance^{39, 40}. A correlation was also observed between the oxygenated hemoglobin recovery time and the ABI recovery time after walking exercise. Although the recovery times measured by NIRS were shorter than the recovery time for the ABI^{41, 42}. The period of recovery of NIRS derived parameters postexercise should be considered in perspective of the fact that a shorter lived but significant decrease is also observed in normal subjects⁴³, making the interpretation of which proportion of the time is related to ischemia an interesting but unsolved issue. A recent study proposed an NIRS-guided training intensity maintaining a 15% reduction in skeletal muscle saturation to improve claudication without pain with attractive results.⁴⁴ This is a clever approach since simultaneous measurement of NIRS at the thigh and calf is possible. Nevertheless, on the one hand the physiological responses seem to differ at those two level⁴⁵, on the other hand to the best of our knowledge post exercise multisite (proximo-distal) recording have never been reported in LEAD patients. Last, NIRS can be used in claudicating buttocks⁴⁶, but seems to be disappointing at the buttock level possibly due to fat thickness⁴⁷. Positron emission tomography⁴⁸, 31phosphorus magnetic resonance spectroscopy⁴⁹⁻⁵¹, magnetic resonance angiography :⁵² are potential candidate for research purposes but, to date, can hardly be used in routine.

Transcutaneous oxygen pressure is clearly of advantage to estimate calf and non-calf oxygen mismatch during exercise and recovery with the possibility to estimate regional perfusion impairment on buttocks, thighs, and calves simultaneously. Although a surface technique, it was shown accurate and reliable in the evaluation of RBF⁵³. As expected, the recovery time was inferior to 10 minutes in most patients and did correlate with MWT and the severity of ischemia (as estimated by DROPm value). The relatively slow response of TcpO₂ in case of an abrupt change in the values to be recorded should be kept in mind. The 90% response to abrupt change was estimated to range 20 to 30 seconds and the observed recovery times probably overestimate true recovery time by the same delay. Whether TcpO₂ could be used to guide rehabilitation in patients with claudication as was done with NIRS is an exciting perspective for future investigations.

There are limitations to the present study. First, it is possible that our results in a 3.2km/h and 10% grade treadmill test are not applicable to other testing procedures. We recently shown the changing walking speed in patients unable to walk one minute at this speed resulted in increased MWD but had no influence on DROPm, but the recovery time for DROP was not studied. Second, we did not record the time for pain dissipation and cannot correlate the estimation of hemodynamic recovery to symptoms in our patients. Third, a population bias is

possible with patients referred to us for exercise TcpO₂ being frequently cases of atypical claudication or claudication of debatable vascular origin. Forth, the DROP provides only an estimation of the mismatch between oxygen delivery and oxygen consumption in the area of interest. Then, the normalization of DROP does not implies that perfusion has normalize, but only that oxygen mismatch has normalized. As a matter of fact, chest TcpO₂ was generally superior to chest values at rest at the end of the recovery period, confirming that physiological effect of exercise on arterial oxygen content are still measurable far after DROP has normalized. Fifth, patients were allowed to hold the treadmill bar during the recovery period, which may influence the time for recovery. This is true but we advocate that recovery in the standing position is closer to usual recovery position than the lying position required for ABI or radiological investigations. Sixth and last, the changes in TcpO₂ are highly reliable⁵³, the position of the probe on the limb is important and ischemia of the distal part of the thigh close to the knee without ischemia close to the groin is observed in case of superficial artery occlusion⁵⁴. The same issue applies also to eventual foot ischemia although isolated foot ischemia without calf ischemia is a relatively rare observation⁷. Whatever, due to the retrospective analysis of recording and the use of standard position of probes, it can be that we missed the most ischemic areas (feet, lower back).

CONCLUSION :

This is the first study analyzing calf and non-calf (buttock and thigh) hemodynamic recovery after exercise in patients with claudication. The median half time recovery (50%RT) is 2 minutes, and almost all patients reach 90%RT in less than 10 minutes. Although recovery duration correlates significantly with the severity of RBF_I of the same location, a wide discrepancy exists and when calf and non-calf localizations are considered. Non-calf recovery time exceeds calf recovery time in almost half of the patients. We suggest that non-calf ischemia should be measured when one aims at objectifying the biological effects of exercise or the effects of treatments on recovery from exercise. We also think that these observations might be of particular interest to guide the duration of stops in rehabilitation programs.

CONFLICT OF INTEREST

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AUTHOR CONTRIBUTIONS

PA SH conceived and designed the study. PR JP, JH PA SH Participated to the recruitment of patients, MF, JH PR participated to the data analysis and interpretation. PA and SH prepared the manuscript draft, the other authors critically revised the manuscript. All authors approved the final version of the manuscript

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TABLES AND FIGURES

Table 1: Characteristics of the patients and results for the exercise test. TcpO2 is transcutaneous oxygen pressure and DROP is for decrease from rest of oxygen pressure.

		Total	Calf pain +/- non-calf pain by history	Isolated non-calf pain by history	p
		N=132	N=108	N=24	
Patients characteristics					
Age	<i>years</i>	64.6 ± 9.6	64.5±9.4	64.8±11.0	0.581
Male gender	<i>Nb (%)</i>	110 (83)	90 (83)	20 (83)	1.000
Body weight	<i>kg</i>	76.5 ± 15.3	75.1±15.4	82.7±13.2	0.027
Height	<i>cm</i>	167 ± 8	170±8	171±9	0.610
BMI	<i>kg/m²</i>	26.5 ± 5.0	26.0±4.8	28.5±5.3	0.025
Systolic blood pressure	<i>mmHg</i>	136 ± 17	136 ± 18	138 ± 16	0.932
Diastolic blood pressure	<i>mmHg</i>	77 ± 10	77 ± 11	80 ± 9	0.964
ABI	-	0.70 ± 0.25	0.68±0.27	0.78±0.16	0.102
Ongoing treatments					
Antiplatelet agents	<i>Nb (%)</i>	118 (89)	97 (90)	21 (88)	0.739
Antihypertensive drugs	<i>Nb (%)</i>	83 (63)	65 (60)	18 (75)	0.174
Cholesterol lowering drugs	<i>Nb (%)</i>	95 (72)	75 (69)	20 (83)	0.171
Anticoagulants	<i>Nb (%)</i>	9 (7)	6 (6)	3 (13)	0.222
Beta blockers	<i>Nb (%)</i>	45 (34)	35 (32)	10 (42)	0.387
Symptoms by history					
Self-reported symptoms: calves	<i>Nb (%)</i>	108 (82)	108 (100)	0 (0)	0.000
Self-reported symptoms: non calves	<i>Nb (%)</i>	74 (56)	50 (46)	24 (100)	0.001
Tcpo2 values at rest					
Chest	<i>mmHg</i>	62 ± 14	62 ± 12	62 ± 15	0.869
Left buttock	<i>mmHg</i>	64 ± 14	64 ± 14	64 ± 12	0.815
Left thigh	<i>mmHg</i>	69 ± 12	69 ± 12	69 ± 10	0.892
Left calf	<i>mmHg</i>	67 ± 11	67 ± 11	67 ± 9	0.753
Right buttock	<i>mmHg</i>	64 ± 12	64 ± 12	64 ± 12	0.884
Right thigh	<i>mmHg</i>	71 ± 10	70 ± 10	72 ± 9	0.467
Right calf	<i>mmHg</i>	69 ± 13	70 ± 12	68 ± 17	0.443
Treadmill test					
Duration of walking	<i>years</i>	572 ± 430	558 ± 427	635 ± 448	0.426
Left buttock DROP min	<i>mmHg</i>	-17 ± 13	-16 ± 11	-22 ± 15	0.051
Left thigh DROP min	<i>mmHg</i>	-15 ± 13	-15 ± 13	-15 ± 10	0.829
Left calf DROP min	<i>mmHg</i>	-23 ± 14	-24 ± 14	-17 ± 8	0.013
Right buttock DROP min	<i>mmHg</i>	-17 ± 13	-16 ± 11	-23 ± 19	0.023
Right thigh DROP min	<i>mmHg</i>	-16 ± 12	-16 ± 11	-17 ± 14	0.874
Right calf DROP min	<i>mmHg</i>	-21 ± 11	-22 ± 12	-16 ± 7	0.012
Non-calf ischemia	<i>Nb (%)</i>	97 (73)	74 (69)	23 (96)	0.006
Calf ischemia	<i>Nb (%)</i>	117 (89)	100 (93)	17 (71)	0.002
Maximal non calf 50%RT	<i>sec</i>	206 ± 123	207 ± 128	203 ± 101	0.907
Maximal calf 50%RT	<i>sec</i>	219 ± 121	220 ± 118	217 ± 136	0.932
Maximal non-calf 90%RT	<i>sec</i>	387 ± 187	377 ± 183	398 ± 166	0.172
Maximal calf 90%RT	<i>sec</i>	393 ± 167	434 ± 200	366 ± 174	0.395

Figure 1: Flowchart of the study.

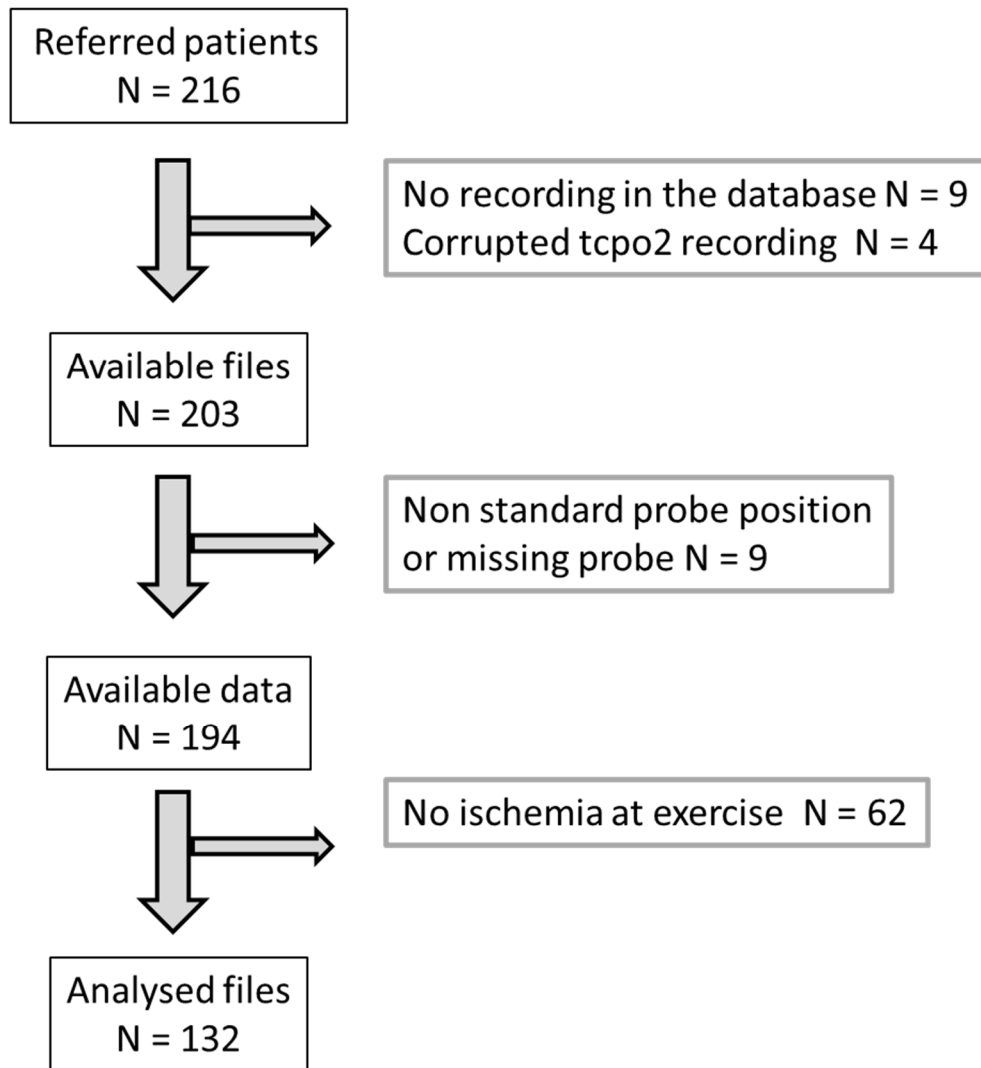


Figure 2: (Color figure) Typical examples of transcutaneous oximetry recordings and the corresponding radiological imaging. Upper panel is a patient with occlusion of the left common iliac artery (White arrow) with ischemia dominantly at the left thigh level (pink graph). Note that minimal DROP occurs almost 3 minutes after the end of the exercise period (grey area). Middle panel is a patient with severe right external iliac stenoses (white arrows), with ischemia dominantly on the left calf (red line) and left thigh (violet line). Note that the recovery time for the left thigh is longer than for left calf. Lower panel is a patient with a complete occlusion of the left, and sub-occlusion of the right, internal iliac arteries (White arrow). Note that a significant ischemia was observed in the left thigh (pink line) and left calf (yellow line) as a result of associated external iliac and femoral lesions but that the recovery time at the left (Blue line) and right (green line) buttocks, largely exceed the recovery time of distal ischemia. Colors for DROPs are the same on all figures: the black lines are the second chest electrodes. As shown its DROP value is almost flat confirming that chest changes were similar on the two chest probes.

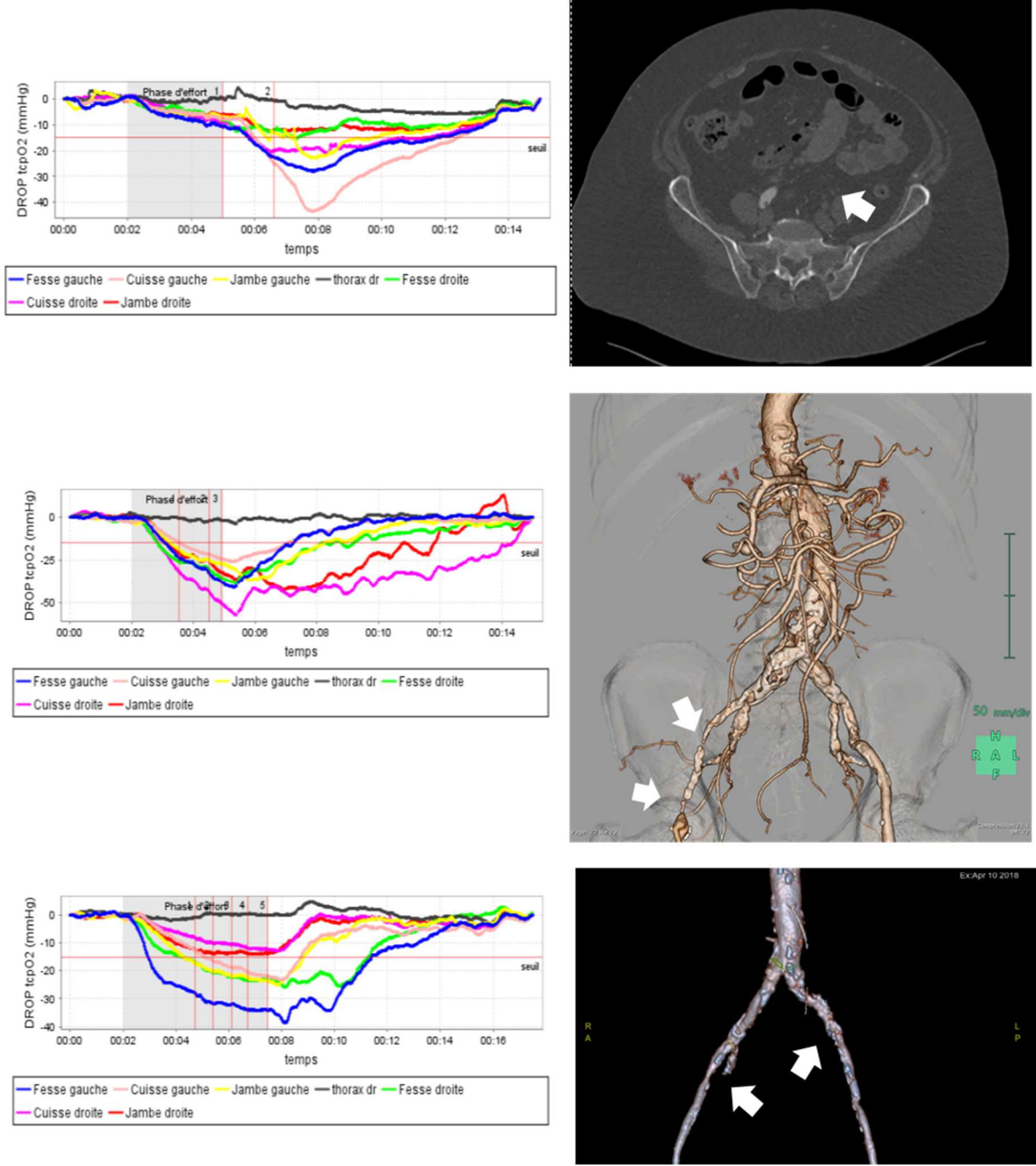


Figure 3: Distribution of the 50% and 90% recovery times (by intervals of 30 sec) for all calf and non-calf (buttocks and thighs) localizations. Median values are 124 and 272 sec respectively.

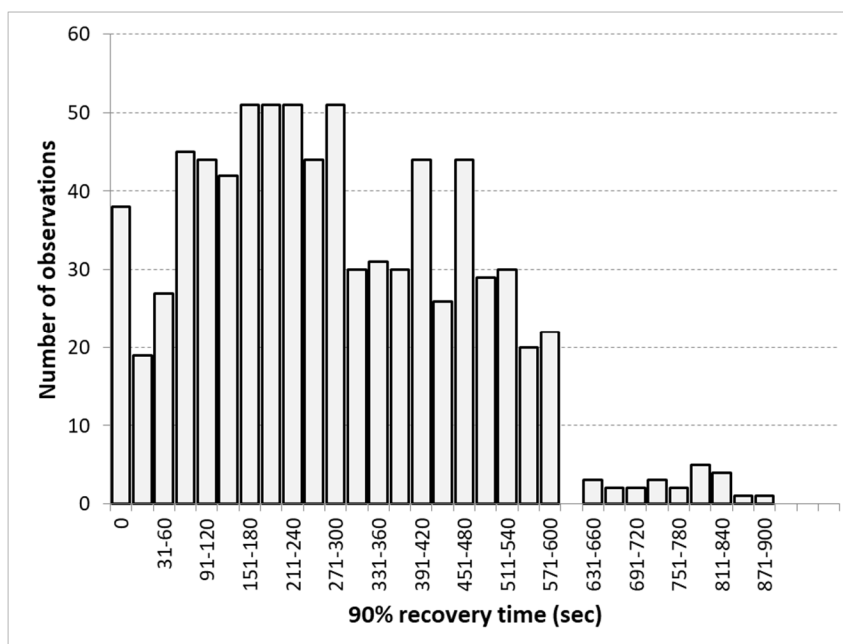
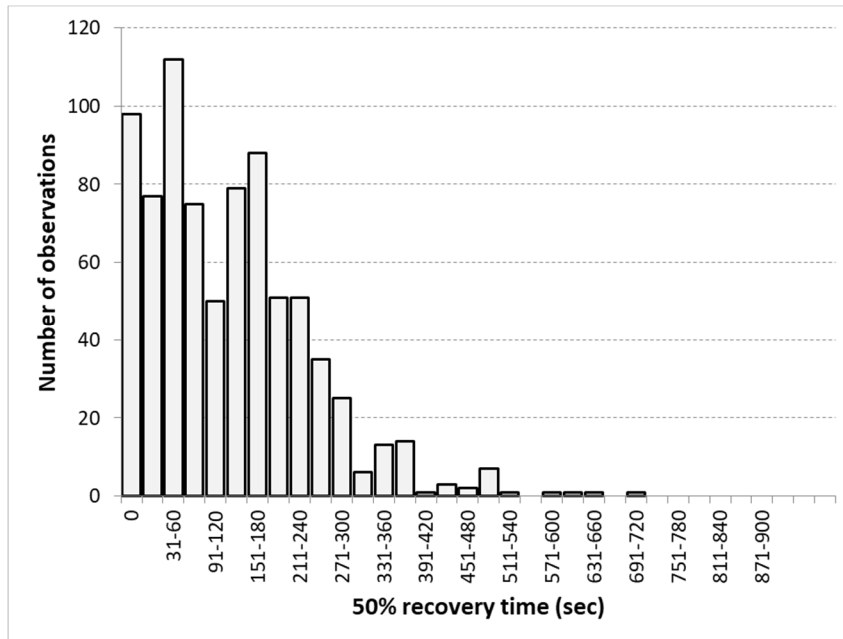


Figure 4: Comparison of ischemia (DROp<-15 mmHg) at the calf (CI) and non-calf (NCI) area and of longest recovery time at the calves (CRT) and non-calves (NCRT) area, for the whole population (upper panels; N = 132) and for patients with calf pain by history (lower panels; N = 108). Results are presented for 50% and 90% recovery time. NCI>CI and NCI< CI means that non-calf ischemia is more severe (lower DROp) and less severe (higher DROp) than calf ischemia, respectively. NCRT>CRT and NCRT< CRT means that non-calf recovery time is longer and shorter than calf recovery time, respectively. Note that for all graphs this situation represents approximately half of the cases.

