Transcutaneous Oxygen Pressure Measurements on the Buttocks During Exercise to Detect Proximal Arterial Ischemia

Comparison With Arteriography

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Background—We sought to identify whether transcutaneous oxygen tension (tcPO2) measurements could be used to noninvasively detect lesions in the arterial network supplying blood flow to the hypogastric circulation.

Methods and Results—A study was undertaken in vascular patients with suspected (PC, n=43) and not with suspected (NPC, n=34) proximal ischemia. TcPO2 was measured on both buttocks and with a chest reference electrode. Arteriography on the right or left side was positive for stenoses (≥75%) or occlusion of one or more of the following arteries: the aorta, the common iliac arteries, or the internal iliac arteries. The arteriography was compared with the resting tcPO2 values (REST) and with the minimal value (MIN) and maximal change from rest normalized to eventual chest changes (DROP) recorded during or after a treadmill test. REST, MIN, and DROP were, respectively, as follows in positive versus negative arteriograms (mean±SD; in mm Hg): 80.2±10.9 versus 78.6±11.5 (P<0.05), 55.2±20.0 versus 69.9±15.8 (P<0.001), and −31.8±17.6 versus −9.5±6.4 (P<0.0001) in PC and 78.9±14.0 versus 80.5±14.3 (P>0.05), 64.4±21.0 versus 75.1±14.6 (P<0.02), and −24.1±13.5 versus −8.7±4.8 (P<0.0001) in NPC. In PC and NPC respectively, with a cutoff point of −16 and −15 mm Hg, DROP showed, respectively, 83%/82% and 79%/86% sensitivity specificity in the diagnosis of positive arteriograms.

Conclusions—Proximal ischemia is a frequent finding in vascular patients. TcPO2 measurement on the buttocks during exercise is a sensitive and specific indicator for lesions in the arterial tree toward the hypogastric circulation. Potentially it could objectively assess the response to endovascular or surgical approaches to iliac lesions. (Circulation. 2003;107:1896-1900.)

Key Words: peripheral vascular disease ■ diagnosis ■ claudication ■ regional blood flow ■ exercise

In claudication resulting from proximal ischemia, exercise-related symptoms can mimic nonvascular diseases, such as neurologic claudication, sciatica,1,2 or neuromuscular or osteoarticular symptoms.3,4 Most of the cases of buttock claudication presented in the literature are isolated observations,1–6,7–11 suggesting that proximal ischemia might be rare. In most reported cases, angiography is the only examination that allowed for the diagnosis of isolated internal iliac lesions.1,2,6,12 It is likely that the real number of patients suffering from proximal ischemia with or without claudication is underestimated13 because of the lack of effective, noninvasive investigation tools to aid in the diagnosis of this condition. It is controversial whether a more extensive approach toward revascularization of the internal iliac arteries is needed to limit the risk of postsurgical proximal ischemia in aortobifemoral bypass.12,14,15 This may be attributable to the difficulty in proving the vascular origin of the symptoms by using noninvasive methods. Recently, there has been a renewed interest in hip/buttock claudication caused by lesions in one or both of the internal iliac arteries because of the development of endovascular procedures that allow easier access to these vessels compared with surgical techniques.16 Wolpert et al16 recently underlined the need for objective measurements of hip/buttock ischemia using noninvasive studies for the objective evaluation of the effects of surgical interventions. The superior and inferior gluteal arteries supplying blood to the buttocks are the main branches of the internal iliac artery.17 The purpose of this study was to analyze whether transcutaneous oxygen pressure (tcPO2) measurements during exercise on the buttocks could serve as a noninvasive, sensitive, specific technique for detecting proximal ischemia resulting from lesions at the level of or above the internal iliac arteries (arteriography being considered the gold-standard). We studied the ability of tcPO2 to detect arteriographically proven lesions and not the relationship between tcPO2 and proximal limb pain.
Methods

Population
In a prospective analysis, a study on 77 vascular patients referred for surgery and complaining of stage II claudication was undertaken according to protocol approved by the Institutional Review Board of Angers. All patients underwent a treadmill test with tcPO2 readings and an arteriography within 3 months of the exercise test. All patients had previously undergone noninvasive vascular investigations with ankle to brachial systolic pressure indices measurements at rest (ABI). Results for the Doppler and ABI values were not made known at the time of exercise tests. When clinical complaints included symptoms that would suggest possible proximal ischemia (Table 1), patients were included in the suspected proximal ischemia (PC) group. Patients reporting isolated calf claudication consistent with Rose criteria were included in the no suspected proximal ischemia (NPC) group. Characteristics of the patients in each group are reported in Table 2. Fifteen of the 43 PC patients had undergone vascular surgery at least 3 months before the exercise test, including 5 aortobifemoral terminolateral bypasses, 6 percutaneous angioplasties (1 femoral, 2 common iliac, 3 external iliac), 2 femoropopliteal bypasses, and 2 aortoiliac bypasses. Ten of the 34 NPC subjects had undergone vascular surgery at least 3 months before the exercise test, including 5 aortobifemoral terminolateral bypasses, 4 percutaneous external iliac angioplasties, and 2 femoropopliteal bypass. Digitized arteriograms were performed using the Seldinger technique with 4 French pigtail catheters. The preangiography walking test results were not made known at this time. For each side, arteriography was considered positive in the presence of an occlusion or a significant stenosis (>75%) of at least one of the following arteries: the aorta, the ipsilateral common iliac artery, or the ipsilateral internal iliac artery, irrespective of the presence of lesions on the external iliac or the gluteal arteries. Inversely, arteriography was considered negative in the absence of a significant stenosis in any of these arteries. In all terminolateral aortobifemoral bypasses, the perfusion was done a retro through the external iliac arteries toward the hypogastric system when it was patent. Then in these patients the external iliac artery was used for the analysis instead of the common iliac artery.

Exercise Test
After a 20-minute resting period, patients were installed in a room with a temperature of 21°C. Measurements were performed using tcPO2 devices (TINA TCM3 Radiometer) (Figure). A one-point calibration to air was performed before each experiment. The calibration value was set according to actual barometric pressure. The temperature of the probe was 44.5°C to allow for maximal vasodilation, thereby decreasing the arterial to skin surface oxygen pressure gradient. Afterward, the tcPO2 measurements were automatically temperature-corrected to 37°C by the transcutaneous device. A reference electrode was placed on the chest to measure eventual systemic changes. One electrode was positioned on each buttock, 4 to 5 cm behind the bony prominence of the trochanter. Before fixing the electrode, the skin was cleaned and dead cells from the epidermal surface were removed by gently rubbing the skin with gauze. Once the electrodes were in position, a pretest heating period of 15 to 20 minutes in the standing position was required to allow stable resting values to be reached. Stable values were defined as tcPO2 changes <2 mm Hg within 5 minutes. A 12-lead ECG was used to control the heart rate and to detect any arrhythmias or abnormal depolarization events during the whole exercise test procedure.

The treadmill test was performed using a 10% slope and a progressive increase of speed according to the following procedure. The speed was started at 1 km/h1 and increased by 0.5 km/h1 every minute up to 2.5 km/h1. After 1 minute at this rate, the treadmill speed was stabilized at 3.2 km/h1 for an additional 16 minutes. Patients were encouraged to perform at the highest possible speed for the longest time possible. Exercise was discontinued on the patient’s request or in the absence of claudication after a total walking duration of 20 minutes.

Exercise tests were performed and analyzed blinded to the results of arteriography in the cases where arteriography was performed first. TcPO2 values were recorded for 2 minutes in the standing position before the treadmill was started, during the walking period, and for 10 minutes in the standing position after the end of the exercise test. The data were recorded on a computer via an analogue to digital converter (Biopac System, Inc) with a sample rate of 3 Hz on 16 bits. Moving average of over 15 samples was performed on raw data to decrease the electronic artifacts on the signal. Then the values were averaged over 5-second intervals for additional analysis. The tcPO2 values at rest (REST) were the mean of tcPO2 values over the 2 minutes of the resting period (24 intervals of 5 seconds). The minimal value (MIN) was the lowest value recorded on a 5-second interval during or in the 10 minutes after exercise. On each 5-second interval, the tcPO2 change from rest in each buttock was corrected with the corresponding absolute value of the chest electrode tcPO2 change, chest tcPO2 changes being subtracted (if chest tcPO2 increased) or added (if chest tcPO2 decreased) from the results of tcPO2 changes at the buttocks.

For the analysis, the lowest negative value resulting from this calculation on a 5-second interval during or in the 10 minutes after exercise was used. This maximal decrease of the value of delta from rest of oxygen pressure at the buttocks level is referred to as DROP throughout this study and expressed in mm Hg.
Analysis of the Results

Comparisons of the ABI and tcPO₂ values between positive and negative arteriograms were performed with unpaired t tests. Paired t test were used to compare MIN values to REST values within each group of positive or negative arteriograms. We used the receiver operating curve (ROC) analysis to study the relationship between ABI and tcPO₂ parameters and the results of the arteriogram. This technique is based on calculating the sensitivity and specificity of a test for each value of the studied variable in the diagnosis of a disease. This approach has the double advantage of allowing for the objective determination of the performance of a test through the calculation of the area under the sensitivity/specificity relationship curve and the objective determination of the cutoff point to be proposed for clinical use. In the first case, the sensitivity and specificity range was from 0% to 100%. A perfect test would provide a surface of 10,000, whereas a surface of 5000 would be the result of a random choice. In the second case, the distance from the point of sensitivity versus specificity to the 100%/100% sensitivity/specificity angle is calculated. The value of the variable resulting in the lowest distance to this angle is considered to be the best compromise of sensitivity and specificity for an arbitrarily defined equal cost of false-positive or false-negative tests. Using this cutoff point, we calculated the optimal sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the parameter studied. Statistical analysis for the comparison of the area under the ROC (area=SE of area) was performed with the method described by Hanley and McNeil. For all statistical tests, a 2-tailed probability level of P<0.05 was used to indicate statistical significance.

Results

None of the patients in the PC or NPC groups presented symptoms of dyspnea, angina, arrhythmia, or depolarization abnormalities justifying early termination of the walking test. Results for ABI, REST, MIN, and DROP in PC and NPC patients according to the result of arteriography are reported in Table 3. Eight ABI values are missing in each group because of cardiac arrhythmia, incompressible arteries (ankle pressure >250 mm Hg), or distal cutaneous lesions.

PC Group

Eight of the patients were able to perform the walking test up to 20 minutes. In 2 of these 8 cases, exercise did not bring on any symptoms, whereas in the other 6, the usual symptoms of the patients were present but did not force them to discontinue the walking test. Among the 86 studied axes, 58 were classified positive after the arteriography, among which 20 were bilateral positive arteriograms.

In the diagnosis of stenosis or occlusion of the arterial branches supplying the hypogastric circulation, area under the ROC was 6083±723 for the 78 measurable ABI values. For the whole PC group, area under the ROC was 4541±664 for REST and 7266±577 for MIN (P<0.0001 from REST). According to the ROC analysis, using the DROP value provided the highest diagnostic performance with an area of 9107±295 (P<0.0001 from REST and from MIN). The optimal cutoff point for resting value was 81 mm Hg and showed a 58.6% sensitivity, 32.8% specificity, 66.0% PPV, and 30.6% NPV. Sensitivity, specificity, PPV, and NPV increased to 62.1%, 85.7%, 85.7%, and 50.0% with the use of MIN using a cutoff point of 63 mm Hg. Last, the optimal DROP cutoff point was −16 mm Hg. With that cutoff point, sensitivity, specificity, PPV, and NPV were, respectively, 82.8%, 82.1%, 90.6%, and 69.7%.

NPC Group

In 7 patients the test was discontinued after 20 minutes. In 4 of these 7 patients, exercise did not result in symptoms, whereas the 3 who were symptomatic were not forced to terminate the walking test. Among the 68 studied axes, 33 were classified positive by arteriography, with 1 patient having a subocclusion of the subrenal aorta.

In the diagnosis of stenosis or occlusion of the arterial branches supplying the hypogastric circulation, area under the ROC was 6083±723 for the 60 measurable ABI values. For the whole NPC group, area under the ROC was 5229±707 for REST and 6528±663 for MIN (P<0.0001 from REST). DROP provided the highest diagnostic performance with an area of ROC of 8628±474 (P<0.0001 from MIN and from REST).

The optimal cutoff point for resting value was 89 mm Hg and provided a 78.8% sensitivity but only a 37.1% specificity, 54.2% PPV, and 65% NPV. Sensitivity, specificity, NPV, and PPV were increased to 54.5%, 68.6%, 62.1%, and 61.5% with the use of MIN value observed during the test, with a cutoff point of 68 mm Hg. Using the DROP cutoff point of −15 mm Hg, sensitivity, specificity, PPV, and NPV were, respectively, 78.8%, 85.7%, 83.9%, and 81.1%.

Discussion

In proximal ischemia, lesions at the level of the distal aorta, common or internal iliac artery, or branches of the internal

<table>
<thead>
<tr>
<th>Arteriogram</th>
<th>PC</th>
<th>NPC</th>
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</thead>
<tbody>
<tr>
<td>ABI</td>
<td>0.86±0.24</td>
<td>0.92±0.32</td>
</tr>
<tr>
<td>Measurable</td>
<td>53</td>
<td>25</td>
</tr>
<tr>
<td>REST, mm Hg</td>
<td>80.2±10.9</td>
<td>78.6±11.5</td>
</tr>
<tr>
<td>MIN, mm Hg</td>
<td>55.2±20.0</td>
<td>69.9±15.8</td>
</tr>
<tr>
<td>DROP, mm Hg</td>
<td>−31.8±17.6</td>
<td>−9.5±6.4</td>
</tr>
</tbody>
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For each limb, arteriogram was considered positive (+) in the presence of significant lesions on the aorta, ipsilateral common, or internal iliac artery and negative (−) in the absence of a significant lesion in any of these arteries. NS indicates a nonsignificant difference.
iliac arteries, or a combination of these is described. They may result from atherosclerosis or as a complication of aortoiliac or aortofemoral surgery, or other rare causes. Impaired vascularization to the hypogastric area may result in buttoc or hip claudication but also in vascular impotence, colonic ischemia, or combination of these symptoms. Even in these symptomatic patients, the diagnosis of the vascular origin of lower limb pain may be particularly elusive and lead to prolonged undiagnosed cases if distal pulses are palpable or physical examination unremarkable, as may sometimes occur in cases of isolated internal iliac artery lesions.

Arteriography MRI or angioscanners do show lesions on the aortoiliac tree; however, they are invasive, costly, and cannot be used as primary investigation. Transpaperial or transanal ultrasound imaging or Doppler may allow for the direct visualization of the trunk of the internal iliac artery, but the transpaperial scanning is limited to nonobese patients with no intestinal gas. Finally, neither of these 2 imaging techniques proves the causal relationship between symptoms or ischemia and the presence of the arterial lesions.

For this purpose, functional investigations in the hypogastric territory should be performed. Among them, in male patients, ankle-brachial index could be better replaced by penile-brachial index. Much has been published on impotence but not on proximal claudication. Furthermore, even using the Doppler rather than plethysmography, differentiation between right and left arterial lesions is difficult. Thermography or near infrared spectroscopy could also be proposed. The latter technique seems promising because it provides a rapid estimation of tissue oxygen saturation up to a depth of 2 cm, compared with surface measurements of tcPO₂ or thermography. In obese patients, because of the thickness of subcutaneous fat in the buttocks, one might be measuring a superficial value rather than the muscle saturation itself. This, as well as the high price of available devices, might explain the fact that no research has yet been reported at the buttock level. Whole-body thallium scintigraphy during and following exercise can also be used, allowing for direct measurement of muscle ischemia. Scintigraphy has shown a 82% sensitivity specificity compared with arteriography in the detection of proximal ischemia in patients with claudication, but the use of radioactivity, technical requirements, and costs limit it to highly specialized centers.

tcPO₂ is a sensitive and a reliable index in the diagnosis of peripheral arterial disease, particularly after exercise, but to the best of our knowledge its use on the buttocks in the diagnosis of proximal ischemia has never been reported. Ideally, a reference electrode should be used in a control area, usually on the chest. Chest tcPO₂ changes have been shown to correlate with arterial oxygen pressure changes. This reference electrode takes into account potential exercise-related systemic arterial PO₂ changes in healthy or diseased subjects. These systemic changes, as well as the unpredictable gradient between the surface and underlying arterial oxygen pressure, are the rationales behind the use of DROP rather than absolute MIN values in gathering diagnostic information from tcPO₂. Indeed, although low absolute MIN values may result from arterial occlusion, they could also result from a high transcutaneous pressure gradient or from exercise-related systemic hypoxia. The DROP calculation being independent on these two factors provides the highest diagnostic value in our study. The relatively lower sensitivity in NPC compared with PC patients likely resulted from the fact that distal claudication limited the exercise early in some NPC patients, thus preventing proximal ischemia from developing. Finally, the possibility that either isolated gluteal lesions (arteriography considered negative) or revascularization through collateral circulation in case of isolated internal iliac occlusion (resulting in the absence of ischemia) decreased sensitivity specificity cannot be totally ruled out. Nevertheless, the diagnostic performance of tcPO₂ remains close to the one reported for scintigraphy.

Proximal ischemia with or without claudication is found in 40% of diabetic patient with abnormal whole-body thallium scintigraphy. The present study illustrates, as suggested from recent reports, that proximal ischemia even without symptoms is a frequent (and likely underestimated) event.

We suggest that transcutaneous oxygen pressure measurement on the buttocks during exercise, although a surface measurement, is useful in the management of patients suspected of exercise-related proximal ischemia. As a noninvasive, objective test, its use could serve the following purposes. First, it could determine future studies for analyzing isolated, suspected proximal claudication with the aim of decreasing the prolonged diagnostic phase often observed. Here, tcPO₂ could help in the selection of patients needing arteriographic investigation. Second, it could provide objective measurements of the hypogastric perfusion during exercise before and after aortofemoral or aortoiliac bypasses and thus facilitate the analysis of whether an aggressive approach toward the hypogastric arteries is needed. Third, it could estimate the effect of either internal iliac intentional occlusion or contrary hypogastric stenosis dilatation before and after endovascular procedures.

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