



UvA-DARE (Digital Academic Repository)

The value of non-invasive techniques for the assessment of critical limb ischaemia

Ubbink, D.Th.; Tulevski, I.I.; den Hartog, D.; Koelemay, M.J.W.; Legemate, D.A.; Jacobs, M.J.H.M.

DOI

[10.1016/S1078-5884\(97\)80101-3](https://doi.org/10.1016/S1078-5884(97)80101-3)

Publication date

1997

Published in

European Journal of Vascular and Endovascular Surgery

[Link to publication](#)

Citation for published version (APA):

Ubbink, D. T., Tulevski, I. I., den Hartog, D., Koelemay, M. J. W., Legemate, D. A., & Jacobs, M. J. H. M. (1997). The value of non-invasive techniques for the assessment of critical limb ischaemia. *European Journal of Vascular and Endovascular Surgery*, 13, 296-300. [https://doi.org/10.1016/S1078-5884\(97\)80101-3](https://doi.org/10.1016/S1078-5884(97)80101-3)

General rights

It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations

If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: <https://uba.uva.nl/en/contact>, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.

UvA-DARE is a service provided by the library of the University of Amsterdam (<https://dare.uva.nl>)

The Value of Non-invasive Techniques for the Assessment of Critical Limb Ischaemia

D. Th. Ubbink*, I. I. Tulevski, D. den Hartog, M. J. W. Koelemay, D. A. Legemate and M. J. H. M. Jacobs

Department of Surgery, Academic Medical Centre, Amsterdam, The Netherlands

Objective: The European Consensus Document (ECD) defines critical ischaemia (CI) according to clinical (Fontaine) and blood pressure parameters. However, clinical symptoms may be non-specific and CI may exist without severely reduced blood pressures. This study prospectively investigated the additive value of transcutaneous oxygen tension (pO_2) and toe blood pressure measurements to assess the presence of CI.

Methods: Forty-nine patients with 65 legs clinically classified as Fontaine stages III ($n=23$) and IV ($n=26$) were studied. Ankle and toe systolic blood pressures and pO_2 were measured to assess the presence of CI (cut-off values were 50, 30 and 30 mmHg, respectively). The surgeon was blinded for the toe pressure and pO_2 results. The treatment received within 1 month after presentation was recorded as being either conservative or invasive (vascular surgery or PTA).

Results: An ankle pressure of ≤ 50 mmHg classified only 17% of the legs as having CI. By adding toe pressure and pO_2 , significantly more legs (63%; $p<0.0001$) were classified as CI, of which 68% received invasive therapy. Forty-nine percent of the legs with an ankle pressure >50 mmHg were treated invasively, whereas only 32% of the legs classified as not having CI by means of toe pressure and pO_2 underwent invasive therapy. If the need for invasive treatment is used as the "gold standard" for the presence of CI, 54% of the legs would accurately be classified on the basis of the ankle blood pressure. The combination of toe pressure and pO_2 would have yielded 71% and the ECD criteria 72% accurately classified legs. The odds ratio for invasive therapy given a pO_2 or toe pressure above the cut-off value was 14.

Conclusion: Ankle blood pressure measurements have limited diagnostic value. Adding toe and/or oxygen pressures enhances the detection of CI requiring invasive therapy.

Key Words: Critical limb ischaemia; Diagnosis; Ankle blood pressure; Toe blood pressure; Transcutaneous oximetry.

Introduction

According to the European Consensus Document (ECD) critical limb ischaemia is defined on the combination of clinical findings and non-invasive blood pressure measurements: persistent ischaemic rest pain requiring analgesics for more than 2 weeks or ulceration or gangrene, with an ankle systolic pressure of ≤ 50 mmHg and/or a toe pressure of ≤ 30 mmHg.¹ The present therapeutic policy of vascular surgeons is based not only upon the definition of the ECD, but also upon surgical risk profile, natural course of the disease, the estimation of imminent limb death and technical surgical possibilities.²

A major pillar of the clinical diagnosis of critical limb ischaemia is the Fontaine classification.³ This

classification may be criticised as it does not discern the various causes for pain at rest apart from arterial insufficiency, such as arthritis or neurological disorders. Ankle blood pressure measurements are useful to assess the presence, but not the severity of, leg ischaemia and are unreliable in patients with medial sclerosis,^{4,5} especially in diabetics.⁶ Toe blood pressure measurement is not generally applied probably due to its limitations, e.g. the variety of cut-off values proposed for critical ischaemia,⁷ the frustration of measurements at low temperatures⁸ or the impossibility to measure when local ulcers are present or after a distal amputation. Moreover, critical limb ischaemia exists despite an ankle pressure >50 mmHg and a toe pressure of >30 mmHg.^{9,10} Thus, the solidity of the definition of critical limb ischaemia, as proposed by the ECD, is questionable.^{9,11} This situation gives rise to an individual, non-standardised therapeutic approach, which may lead to inaccurate appreciation of the severity of the ischaemia and/or inappropriate conservative or late surgical treatment. A consensus

* Please address all correspondence to: D. Th. Ubbink, Department of Surgery, Suite G4-105, Academic Medical Centre, P.O. Box 22700, 1100 DE Amsterdam, The Netherlands. e-mail: D.Ubbink@amc.uva.nl

is, however, useful to define patient groups in comparative studies.

Other diagnostic tools have been proposed to enhance discrimination of the severity of the disease, including skin microcirculatory investigation¹² (especially transcutaneous oxygen tension measurements^{10,13}), the assessment of peripheral resistance in crural vessels peroperatively¹⁴ or by using pulse-generated run-off.^{15,16} Yet, most of the latter methods have their shortcomings, being either too complicated, too expensive or time consuming. In this prospective study we investigated what the additional effect of two simple, non-invasive measurements, i.e. toe blood pressure and transcutaneous oxygen pressure measurements, could be on the therapeutic policy in 49 patients having 65 legs with chronic critical limb ischaemia.

Patients and Methods

From October 1994 to September 1995 all patients with Fontaine Stages III or IV were included. Patients with an acute arterial occlusion, a congenital arteriovenous malformation or clinical evidence of venous insufficiency were excluded. Thus, 49 patients, 27 males and 22 females, with 65 ischaemic legs consented to participate in the study.

Investigations were performed after acclimatisation in a room with a temperature of 22–23°C. Ankle systolic blood pressures in the dorsal pedal, the posterior tibial, and peroneal artery were measured using a 8 MHz Doppler probe (Stöpler, PV lab) and a cuff around the ankle. The ankle pressure was defined as the highest value among the three ankle arteries measured. The peroneal artery pressure, although rarely used in the assessment of the ankle blood pressure, may contribute substantially to the perfusion of the foot in critical ischaemia through collaterals, and was therefore also taken into account. Critical ischaemia according to the ankle pressure was diagnosed when all three ankle arteries showed a pressure ≤ 50 mmHg. Toe systolic pressures were measured in the big and second toe by means of photoplethysmography and a digital cuff with a width of 1.9 or 2.5 cm, depending on the size of the toe. The toe pressure was defined as the highest of both toe pressures measured. In doing so the reliability was appreciated as an alternative measurement in patients whose big toe was ulcerated or amputated. A cut-off value of 30 mmHg was used. Transcutaneous pO_2 (Radiometer, TCM3) was measured on the dorsum of the foot at an electrode temperature of 44°C. The pO_2 cut-off value used for the

detection of critical ischaemia was 30 mmHg.¹³ Duplex investigation of the aortoiliac or femoropopliteal arteries was performed when the vascular surgeon decided therapeutic intervention was necessary on the basis of the clinical situation and the ankle pressure measurement.

The vascular surgeon involved was blinded for the results of all non-invasive measurements, except for the ankle blood pressure. The therapeutic decision was registered and was classified as conservative (i.e. local wound care, analgesics, antibiotics, or toe amputation) if the patient had not undergone a therapeutic intervention (i.e. vascular reconstruction or percutaneous transluminal angioplasty [PTA]) within 1 month after the first measurement, since the presence of critical ischaemia was regarded as requiring a decision for intervention within that period. The need for invasive therapy was regarded as the "gold standard" for the presence of critical ischaemia. Patients were classified as critically ischaemic when at least one out of the combination of parameters (ankle+toe pressures [ECD]; toe + oxygen pressure; ECD + oxygen pressure) showed a reading below its cut-off value.

Statistics

Statistical analysis of the differences in measurement results between the two Fontaine stages was investigated using the non-parametric Mann-Whitney U-test, differences in the numbers of critically ischaemic legs detected by means of the different parameters was tested using the Wilcoxon matched pairs test. Logistic regression analysis was done to identify independent predictors of invasive therapy. The probability of invasive therapy was expressed as an odds ratio. In this study the odds ratio was the odds of invasive therapy given a test result below the cut-off value divided by the odds for invasive therapy given a test result above the cut-off value. A probability of 0.05 was used for entry into and of 0.10 for removal from the model.

Results

The patients' mean age was 72 years (range 47–94 years). The median duration of their symptoms was 2 months (range 2 weeks to 24 months). Twenty-three of the patients were Fontaine stage III and 26 stage IV. The mean ulcer size in Fontaine IV patients was 1.6 cm, ranging from 1 to 3 cm. Diabetes occurred

Table 1. Numbers and percentages of the Fontaine III and IV legs complying to criteria for critical ischaemia using different parameters.

	Critical ischaemia	No critical ischaemia	Inconclusive
Ankle pressure	11 (17%)	51 (78%)	3 (5%)
ABI	13 (20%)	47 (72%)	5 (8%)
Toe pressure	23 (35%)	34 (52%)	8 (13%)
ECD	26 (40%)	39 (60%)	0 (0%)
pO ₂	29 (45%)	32 (49%)	4 (6%)
Toe pressure + pO ₂	37 (53%)	28 (47%)	0 (0%)
ECD + pO ₂	41 (63%)	24 (37%)	0 (0%)

ABI = Ankle-to-brachial blood pressure index; ECD = European Consensus Document criteria (ankle + toe pressure).

in 22 (45%) of the patients, smoking in 22 (45%), hypertension in 19 (40%), cardiac diseases in 14 (29%), cerebrovascular disorders in 12 (24%) and hypercholesterolaemia in 7 (18%) of the patients. Marked differences between legs in Fontaine stages III and IV were found only when measuring pO₂ (33 vs. 25 mmHg; $p=0.05$) and toe pressure in the second toe (42 vs. 24 mmHg; $p=0.05$). Fontaine III patients underwent fewer interventions than did Fontaine IV patients, but this difference was not statistically significant. Three major amputations were observed in the first month after starting either conservative or invasive therapy. Thirty-six legs (55%) underwent invasive treatment within the 1 month period. Of the remaining 29 legs treated conservatively, 11 underwent Duplex scanning or angiography.

The results of the different parameters and the percentage of legs that showed values below the cut-off value for critical ischaemia are shown in Table 1. The ankle pressure criterion of ≤ 50 mmHg classified only 11 (17%) legs and an ankle-to-brachial pressure index $\leq 35\%$ classified only 13 (20%) as critically ischaemic, which was significantly lower than the number of critically ischaemic legs classified with a combination of toe pressure and pO₂ (up to 63%). Adding the pO₂ parameter to the ECD criteria led to a significantly better detection of critical ischaemia than with the ECD criteria alone ($p<0.001$). Pressure measurement in the peroneal artery, in addition to the other two ankle arteries, influenced classification in only 3% of the legs. The toe pressure criterion (≤ 30 mmHg) classified 13 more legs (20%) as having critical ischaemia, but failure of the measurement occurred more than when using other parameters (12% of the legs). Additional measurement of the pressure in the second toe changed the classification in only 3% of legs.

The relation between the detection of critical ischaemia by means of the different parameters and the

Table 2.

	Surgery/PTA	Conservative	Total
Ankle pressure			
Critical ischaemia	9	2	11
No critical ischaemia	25	26	51
Unattainable	2	1	
Ankle-to-brachial pressure index			
Critical ischaemia	11	2	13
No critical ischaemia	22	25	47
Unattainable	3	2	
Toe pressure			
Critical ischaemia	19	4	23
No critical ischaemia	13	21	34
Unattainable	4	4	
ECD			
Critical ischaemia	22	4	26
No critical ischaemia	14	25	39
Unattainable	0	0	
pO ₂			
Critical ischaemia	22	7	29
No critical ischaemia	12	20	32
Unattainable	2	2	
Toe pressure + pO ₂ combined			
Critical ischaemia	27	10	37
No critical ischaemia	9	19	28
ECD + pO ₂ combined			
Critical ischaemia	28	13	41
No critical ischaemia	8	16	24

subsequent therapy is shown in Table 2. The diagnostic characteristics of each of the (combined) parameters are presented in Table 3. When ankle pressures were below 50 mmHg, nine out of 11 legs received invasive treatment (positive predictive value [PPV] = 82%). However, 25 out of 51 legs with an ankle pressure above 50 mmHg also underwent invasive therapy (negative predictive value [NPV] = 49%). The ECD criteria scored the highest PPV (85%), but its sensitivity was relatively low (61%). When the combination of toe and oxygen pressure parameters showed no critical ischaemia, only nine patients were treated invasively (NPV = 68%). If those two parameters had been added to the ankle pressure given to the surgeon, 30 more legs would have been classified as having critical ischaemia, and only eight legs without critical ischaemia would have been treated invasively (PPV = 68%). Sixteen legs had a pO₂ between 31 and 40 mmHg. If the highest cut-off value of 40 mmHg were used, as is sometimes proposed in the literature, a total of 69% of the legs could have been classified as having critical ischaemia. The sensitivity to detect critical ischaemia would increase to 89% if the higher pO₂ cut-off value had been combined with the ECD criteria. This combination, however, would not enhance its predictive values (PPV = 62%; NPV = 69%).

The legs that underwent a major amputation all had critical ischaemia according to the combination of ECD and pO₂ parameters. A minor (toe) amputation was

Table 3. Diagnostic characteristics of the various (combinations of) parameters used to detect critical ischaemia requiring invasive treatment.

	Ankle pressure	ABI	Toe pressure	ECD	pO ₂	Toe pressure + pO ₂	ECD + pO ₂
Sensitivity	25%	31%	53%	61%	61%	75%	78%
Specificity	90%	86%	72%	86%	69%	66%	45%
Accuracy	54%	55%	62%	72%	65%	71%	68%
PPV	82%	85%	83%	85%	76%	73%	68%
NPV	51%	53%	62%	64%	63%	68%	67%

ECD = European Consensus Document; ABI = ankle-to-brachial blood pressure index; PPV = positive predictive value; NPV = negative predictive value.

performed in three conservatively treated patients, whose pO₂ and toe pressure, but not the ankle pressure, showed critically ischaemic values. Logistic regression analysis showed that toe pressure and pO₂ contributed significantly ($p < 0.03$ and $p < 0.05$, respectively) to the treatment choice, as opposed to the patient's ankle blood pressure, age, sex or Fontaine stage. Both parameters had an odds ratio of 14, i.e. the chance of receiving invasive therapy because of critical ischaemia in case of a test result below the cut-off value was 14 times higher than in case of a test result above the cut-off value. In contrast, the ankle pressure parameter had an odds ratio of 0.3 and the ankle-to-brachial index 1.0.

Discussion

This study shows that in the detection of critical ischaemia the ankle blood pressure is of limited diagnostic significance as critical ischaemia requiring surgery can exist with an ankle pressure above the cut-off value of 50 mmHg. The addition of toe blood pressure and/or transcutaneous oxygen tension measurements leads to a higher sensitivity. Moreover, adding these parameters results in a higher negative predictive value, i.e. more patients without critical ischaemia according to these parameters are treated conservatively.

In this study a relatively low percentage (up to 63%) of patients belonging to Fontaine stages III and IV were classified as having critical ischaemia using any of the non-invasive parameters, and would therefore, according to the European Consensus, need therapeutic action. However, every patient with Fontaine III or IV due to arterial insufficiency requires therapy. Non-invasive techniques are useful to assess the presence of arterial insufficiency, which may not always be clear from the clinical symptoms. In particular adding the skin oxygen pressure to the ankle and toe pressures appears useful to detect critical ischaemia,

which is in accordance with previous studies in atherosclerotic¹³ and diabetic patients.¹⁷ The sensitivity to detect critical ischaemia by means of transcutaneous oximetry could be further enhanced by raising the cut-off value to 40 mmHg. The assessment of critical ischaemia by means of non-invasive measurements could also be ameliorated by the combination of several techniques. This amelioration is likely to be due to the fact that toe blood pressure and oxygen tension are local measurements nearer to the ischaemic site, as opposed to the ankle blood pressure. Measurement of peroneal artery pressure or toe pressure in the second digit was not technically difficult, but appeared useful only when other parameters are unattainable.

Taking the need for invasive therapy as a "gold standard" for the presence of critical ischaemia is of course debatable, since the choice for invasive therapy is influenced by other factors, such as non-reconstructability or contra-indications, e.g. concomitant diseases or a poor general condition. This results in patients being treated conservatively, but who do have critical ischaemia. This can be illustrated by the finding that a considerable number of legs (38%) treated conservatively underwent duplex scanning or angiography. This suggests the surgeon did intend to treat invasively. Furthermore, some patients received invasive treatment after the predefined period of 1 month. This may explain the relatively high percentage (18–32%, depending on the diagnostic parameter(s) used; see Table 2) of the legs classified as critically ischaemic, which were treated conservatively.

The treatment of choice is sometimes difficult to assess because of the uncertainty of the Fontaine classification, since rest pain or ulceration may not be due to arterial insufficiency. Hence, duplex scanning and/or angiography are usually performed to assess the need for and type of invasive therapy. The findings of this study are promising as the extra non-invasive data may aid the surgeon in the decision of whether to treat the patient with invasive or conservative treatment. Those patients who do not have critical isch-

aemia according to these criteria may be spared angiography and be treated conservatively. However, some patients without critical ischaemia according to pressure parameters are still treated invasively, solely on the basis of their clinical situation. For the final answer we need a prospective study, because the diagnostic merit of a larger number of non-invasive parameters is valuable only when also the outcome of the treatment is improved.

In conclusion this study has shown that the detection of critical ischaemia on the basis of the clinical situation and the ankle blood pressure can be improved by adding the toe blood pressure measurement, as proposed by the ECD, and/or the skin oxygen pressure measurement, a simple, non-invasive technique, using a cut-off value of 30 mmHg. Ankle blood pressure measurements alone are insufficient for this purpose.

References

- 1 EUROPEAN WORKING GROUP ON CRITICAL LEG ISCHAEMIA. Second European Consensus Document on chronic critical limb ischaemia. *Eur J Vasc Surg* 1992; 6: (Suppl. A).
- 2 JACOBS MJHM, UBBINK DTh, HOEDT TEN R, BLASI GM. Current reflections of the vascular surgeon on the assessment and treatment of critical limb ischaemia. *Eur J Vasc Endovasc Surg* 1995; 9: 473-478.
- 3 FONTAINE R, RIVEAUX R, KIM M, KIENY R. Résultats des opérations hyperémiantes (sympathectomies lombaires et artériectomies) dans les oblitérations artérielles chroniques spontanées des membres. *Rev Chir* 1953; 72: 204-230.
- 4 BOLLINGER A, BARRAS JP, MAHLER F. Measurement of foot artery blood pressure by micromanometry in normal subjects and in patients with arterial occlusive disease. *Circulation* 1976; 53: 506-512.
- 5 VINCENT DG, SALLES-CUNHA SX, BERNHARD VM, TOWNE JB. Noninvasive assessment of toe systolic pressures with special reference to diabetes mellitus. *J Cardiovasc Surg* 1983; 24: 22-28.
- 6 GOSS DE, DE TRAVORD J, ROBERTS VC, FLYNN MD, EDMONDS ME, WATKINS PJ. Raised Ankle/brachial pressure index in insulin-treated diabetic patients. *Diab Med* 1989; 6: 576-578.
- 7 CARTER SA. The relationship of distal systolic pressures to healing of skin lesions in limbs with arterial occlusive disease, with special reference to diabetes mellitus. *Scand J Clin Lab Invest* 1973;31 (Suppl.): 239-243.
- 8 SAWKA AM, CARTER SA. Effect of temperature on digital systolic pressures in lower limb in arterial disease. *Circulation* 1992; 85: 1097-1101.
- 9 THOMPSON MM, SAYERS RD, VARTY K, REID A, LONDON NJM, BELL PRF. Chronic critical leg ischaemia must be redefined. *Eur J Vasc Surg* 1993; 7: 420-426.
- 10 JACOBS MJHM, UBBINK DTh, KITSLAAR PJEHM, TORDOIR JHM, SLAAF DW, RENEMAN RS. Assessment of the microcirculation provides additional information in critical limb ischaemia. *Eur J Vasc Surg* 1992; 6: 135-141.
- 11 TYRREL MR, WOLFE JHN. Critical leg ischaemia: an appraisal of clinical definitions. Joint Vascular Research Group. *Br J Surg* 1993; 80: 177-180.
- 12 BOLLINGER A, FAGRELL B. *Clinical capillaroscopy: a guide to its use in clinical research and practice*. Toronto: Hogrefe & Huber, 1990.
- 13 UBBINK DT, JACOBS MJHM, TANGELDER GJ, SLAAF DW, RENEMAN RS. The usefulness of capillary microscopy, transcutaneous oximetry and laser Doppler fluxmetry in the assessment of lower limb ischaemia. *Int J Microcirc* 1994; 14: 34-44.
- 14 PARVIN SD, EVANS DH, BELL PRF. Peripheral resistance measurement in assessment of severe peripheral vascular disease. *Br J Surg* 1985; 72: 751-753.
- 15 SCOTT DJA, VOWDEN P, BEARD JD, HORROCKS M. Non-invasive estimation of peripheral resistance using Pulse Generated Runoff before femorodistal bypass. *Br J Surg* 1990; 77: 391-395.
- 16 THOMPSON MM, SAYERS RD, BEARD JD, HARTSTONE T, BRENNAN, PRF BELL. The role of Pulse-generated Run-off in the assessment of patients prior to femorocrural bypass grafting. *Eur J Vasc Surg* 1993; 7: 37-40.
- 17 BALLARD JL, EKE CC, BUNT TJ, KILLEEN JD. A prospective evaluation of transcutaneous oxygen measurements in the management of diabetic foot problems. *J Vasc Surg* 1995; 22: 485-492.

Accepted 23 August 1996