Identifying Critical Limb Ischemia

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Abstract: *Purpose:* To verify the reliability of the recommendation of the TransAtlantic Inter-Society Consensus (TASC) for identifying critical limb ischemia,[1] and to assess the usefulness of an isotope method using thallium-201 chloride (^{201}TlCl).[2] *Patients and Method:* Eighty-four lower limbs with ulcer or gangrene were studied. Ulcer or gangrene was present in 37 limbs of 28 nondiabetic patients and in 47 limbs of 42 diabetic patients. The healing tendency of the ulcer or the stump of a minor amputation was predicted using ankle pressure, toe pressure, and $tcPO_2$ as recommended by the TASC in all 84 limbs, and using an isotope method in 15 limbs. The postocclusive initial and delayed distributions in the foot were each recorded for 15 minutes. *Results:* The three parameters recommended by the TASC were not always predictive of healing due to the presence of false-positive and false-negative results. Ischemic limbs were divided into four types on the basis of the results from applying an isotope method. All limbs that exhibited no increase in isotope uptake at the lesion in both the initial and delayed phases (Type III) did not heal. *Conclusion:* It is difficult to accurately define critical limb ischemia using only the three parameters recommended by the TASC. However, an isotope method employing ^{201}TlCl was useful in identifying critical ischemia. The diagnosis of critical limb ischemia should be made on the basis of an assessment of diverse data that provide information on both circulatory disorders and infection. (J Jpn Coll Angiol, 2005, **45**: 525–531)

Key words: critical limb ischemia, arteriosclerosis obliterans, noninvasive diagnostic methods, TASC

Introduction

Defining critical limb ischemia is a challenge vascular surgeons face. Ankle pressure, toe pressure, and $tcPO_2$ have commonly been utilized for prediction of ulcer healing, and the TransAtlantic Inter-Society Consensus (TASC) has provided recommended quantitative values for defining critical limb ischemia (**Table 1**). However, this recommendation of the TASC uses fuzzy criteria that differ somewhat from previous reports in which definitive criteria have been proposed.[2] Moreover, in our daily practice we often find these values inaccurate in determining the fate of ischemic limbs. The purpose of this study was to verify the reliability of the recommendation of the TASC for identifying critical limb ischemia, and to assess the usefulness of an isotope method using thallium-201 chloride (^{201}TlCl).

Patients and Methods

Eighty-four lower limbs of 70 hospitalized patients with ulcer or gangrene due to arteriosclerosis obliterans (ASO) in our university hospital were included in this study. The mean age of the patients was 70.8 years, with 47 of them men. Ulcer or gangrene was present in 37 limbs of 28 nondiabetic patients and in 47 limbs of 42 diabetic patients.

We assessed the severity of ischemia in the 84 ischemic limbs upon admission using three noninvasive diagnostic methods recommended by the TASC, namely ankle pressure,

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Table 1 Standards definition of critical limb ischemia by TASC[1]

Ankle pressure	< 50-70 mmHg or
Toe pressure	< 30-50 mmHg or
$tcPO_2$	< 30-50 mmHg

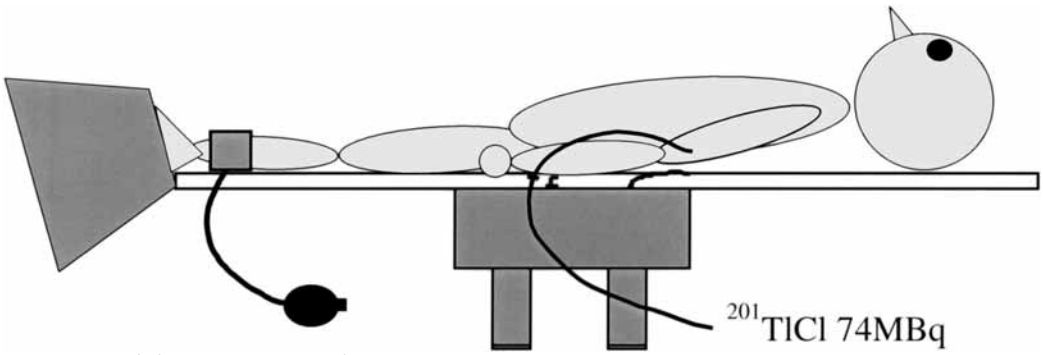

Figure 1 ^{201}TlCl isocount isotope technique.
Three minutes after the cessation of flow at the ankle, the cuff was deflated and simultaneously 74 MBq of ^{201}TlCl was injected rapidly into the basilic vein. The postocclusive initial distribution (immediately after injection) and the delayed distribution (3 hours after injection) in the foot were each recorded for 15 minutes.

toe pressure, and $tcPO_2$. Toe pressure was measured at the big toe using a 2 cm-wide cuff, and $tcPO_2$ was measured at the mid-dorsum. We divided the limbs into nondiabetic and diabetic groups. The clinical outcome was defined as whether or not the lesion exhibited a healing tendency at 2 weeks after medical or minor surgical treatment.

An isotope study was also performed in 15 of the 84 limbs. Three minutes after the cessation of flow at the ankle, the cuff was deflated and simultaneously TlCl was injected rapidly into the basilic vein. The postocclusive initial distribution (immediately after injection) and the delayed distribution (3 hours after injection) in the foot were each recorded for 15 minutes (**Fig. 1**). The perfusion patterns in the ischemic ulcers and gangrenous limbs could be classified into four basic types according to the presence and degree of the relative increase in TlCl uptake proximal to the ischemic lesion. In Type I ischemic ulcers, a hot spot indicative of the inflammatory reactive hyperemia necessary for wound healing was already evident in the initial phase, and increased markedly in the delayed phase (**Fig. 2A**). In Type II ischemic ulcers the hot spot did not appear until the delayed phase (**Fig. 2B**). In Type III ischemic ulcers the hot spot did not appear in either the initial or delayed phase (**Fig. 2C**). There was another special type of ulcer, that appeared in diabetic feet with severe infection. In this type, excessive hyperemia caused the lesion to be severely infected in the initial phase, but decreased in the delayed phase (**Fig. 2D**).

Statistical analyses were performed using StatMate. All results are expressed as mean±SD. The two-sample independent nonparametric student *t*-test or Welch test was used to detect differences between the healing and nonhealing groups. A probability value of $p<0.05$ was considered indicative of statistical significance.

Results

Ankle pressure was measured in 37 nondiabetic and 47 diabetic limbs. The ankle pressures were 83±23 and 42±31 mmHg in the nondiabetic limbs with and without healing tendencies, respectively ($p<0.001$), and 95±49 and 82±66 mmHg in the diabetic limbs with and without healing tendencies, respectively ($p>0.05$). Ankle pressure was not consistently predictive of healing due to a substantial number of false-positive and false-negative results when applying the TASC criteria in both groups (**Fig. 3**).

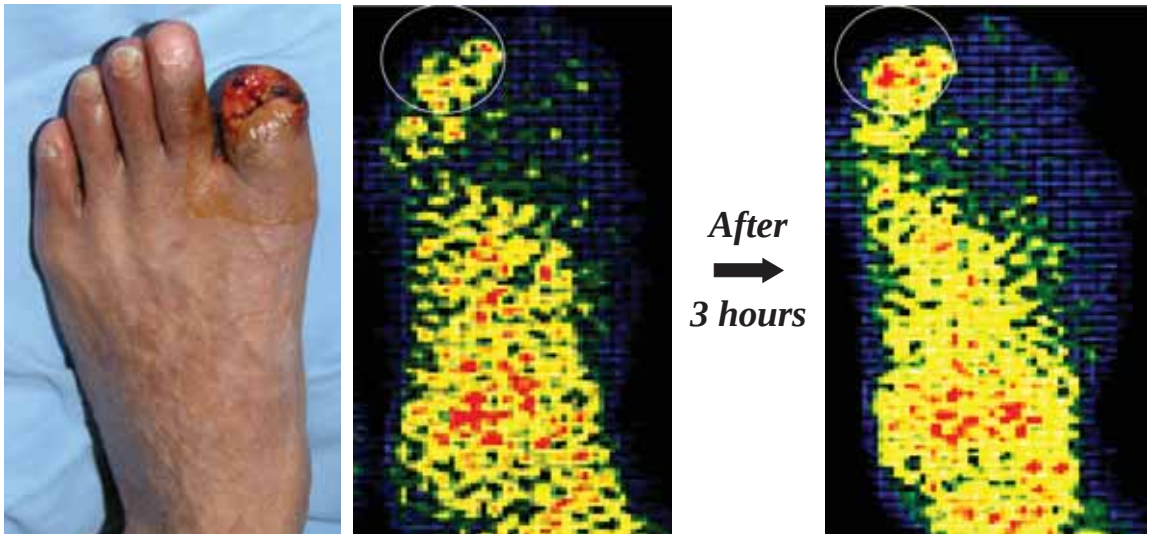

Figure 2A Type I–ischemic ulcer.
Inflammatory hyperemia already appears in the early phase, and it increases in the delayed phase.

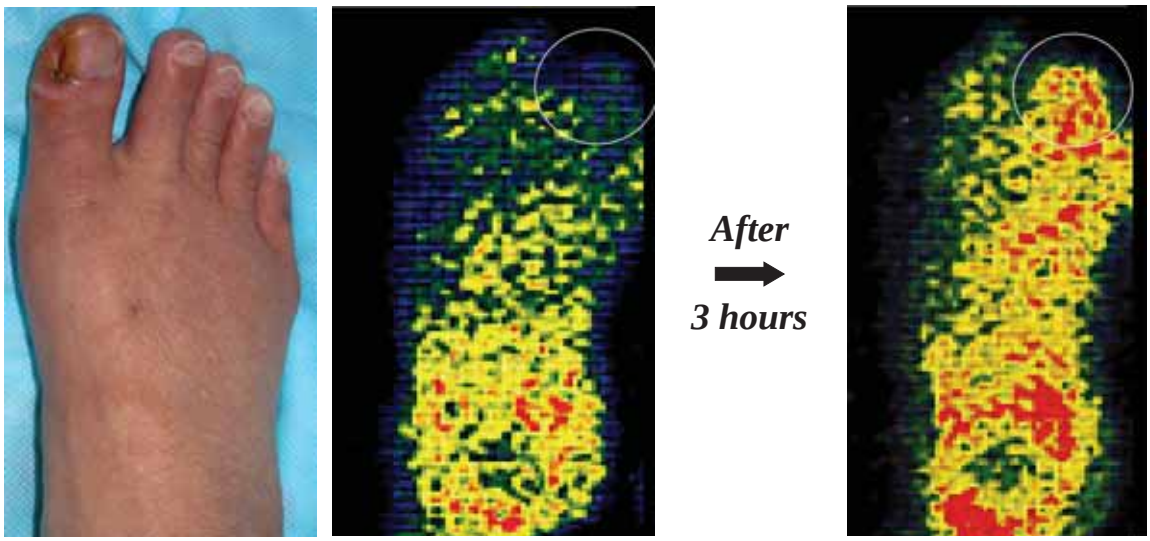

Figure 2B Type II–ischemic ulcer.
Inflammatory hyperemia does not appear in the early phase, but it appears in the delayed phase.

Toe pressure was measured in only 26 nondiabetic and 33 diabetic limbs. The toe pressures were 28±15 and 8±11 mmHg in the nondiabetic limbs with and without healing tendencies, respectively ($p<0.01$), and 30±15 and 11±12 mmHg in the diabetic limbs with and without healing tendencies, respectively ($p<0.001$). It is interesting that there was no false-positive result in either group when using the value (>50 mmHg) recommended by the TASC. However, toe pressure was not predictive of healing due to a substantial number of false-positive results when applying the criteria recommended by the TASC in both groups (**Fig. 4**).

$TcPO_2$ was measured in only 33 nondiabetic and 52

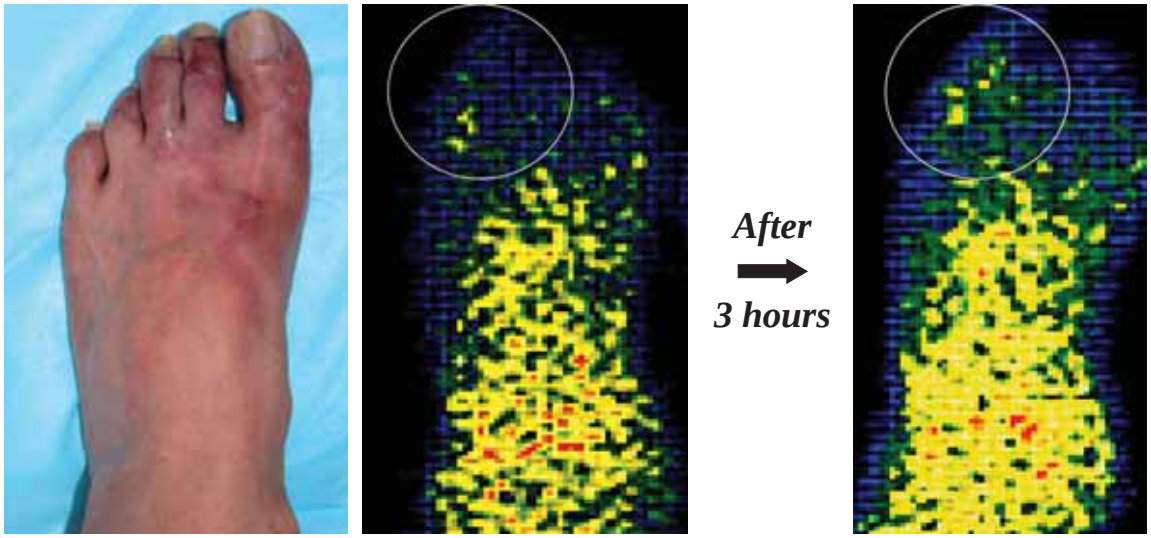

Figure 2C Type III–ischemic ulcer.
Inflammatory hyperemia does not appear in the both phases.

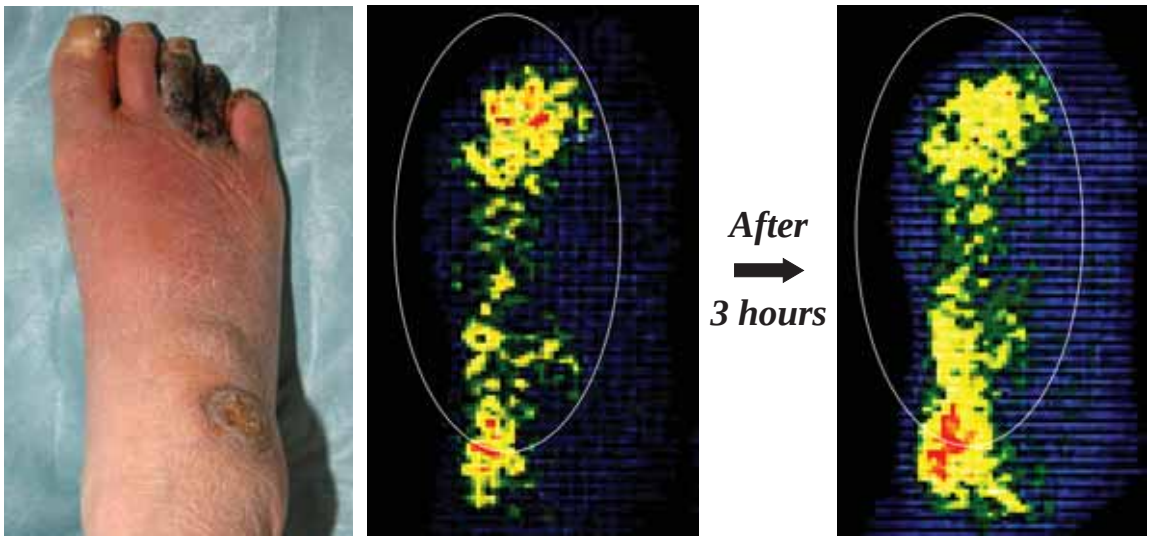

Figure 2D Special type–diabetic gangrene.
Excessive inflammatory hyperemia causes the lesion to be infected in the early phase, and then it decreases in the delayed phase.

diabetic limbs. $TcPO_2$ values were 40±25 and 9±22 mmHg in the nondiabetic limbs with and without healing tendencies ($p<0.001$), and 25±22 and 13±20 mmHg in the diabetic limbs with and without healing tendencies, respectively ($p>0.05$). $TcPO_2$ was also not predictive of healing due to a substantial number of limbs with false-positive and false-negative results when applying the criteria recommended by the TASC in both groups (**Fig. 5**).

The results of the isotope method are given in **Table 2**. Ten limbs with Type I or II lesions exhibited healing tendencies, whereas all four limbs with Type III lesions failed to do so. One limb with the special type of ulcer failed to

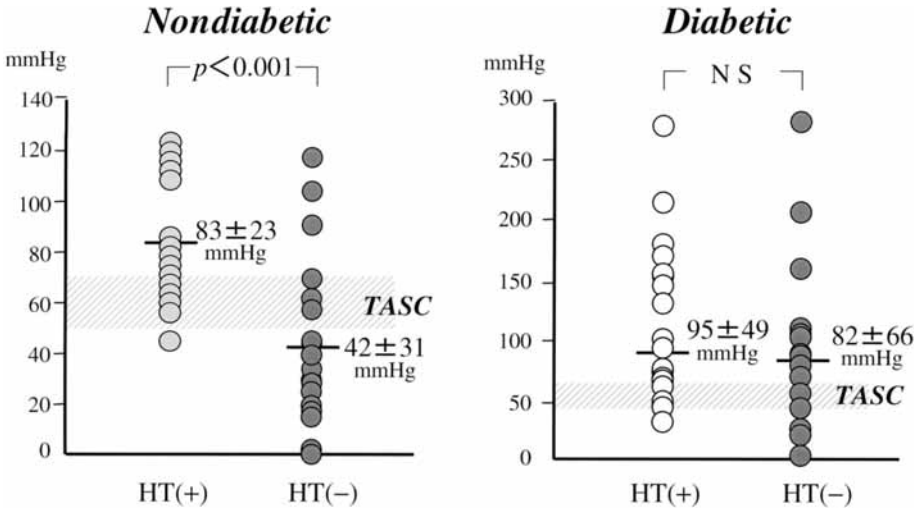

Figure 3 Ankle pressure and healing tendency of the ulcer in nondiabetic and diabetic feet.
HT (+): positive healing tendency, HT (–): negative healing tendency

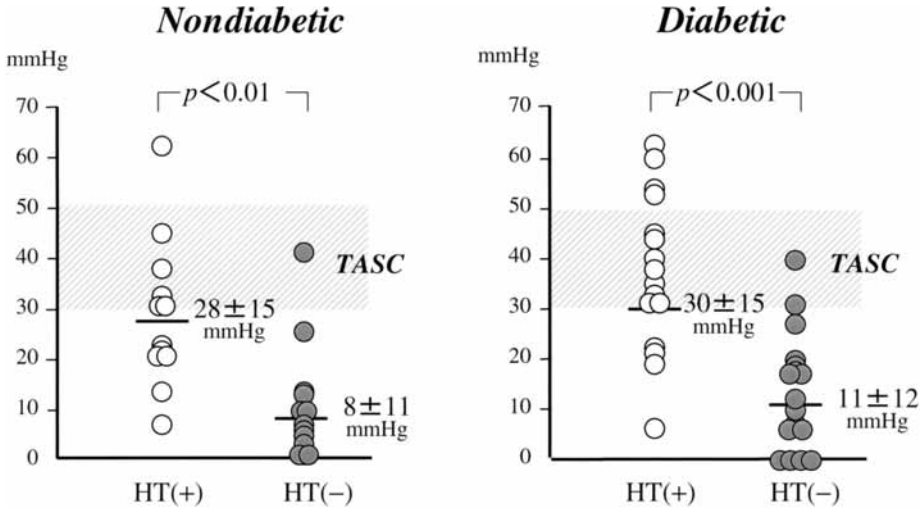

Figure 4 Toe pressure and healing tendency of the ulcer in nondiabetic and diabetic feet.
HT (+): positive healing tendency, HT (–): negative healing tendency

exhibit a healing tendency because of uncontrolled infection. These results indicate that limbs with Type III lesions are critically ischemic.

Discussion

Ankle pressure, toe pressure, and $tcPO_2$ can be used to accurately reveal the hemodynamics of ischemic feet noninvasively,[3-10] whereas our results revealed that none of these parameters were accurately predictive of the healing of ischemic lesions. It is important to assess the presence of inflammatory reactive hyperemia around the lesion since the hyperemic reaction affects the severity of ischemia – the worse hyperemia becomes, the more severe ischemia does. A hyperemic reaction is also observed in infected wounds; this is infectious hyperemia, and must be distinguished from inflammatory hyperemia. Inflammation, a necessary

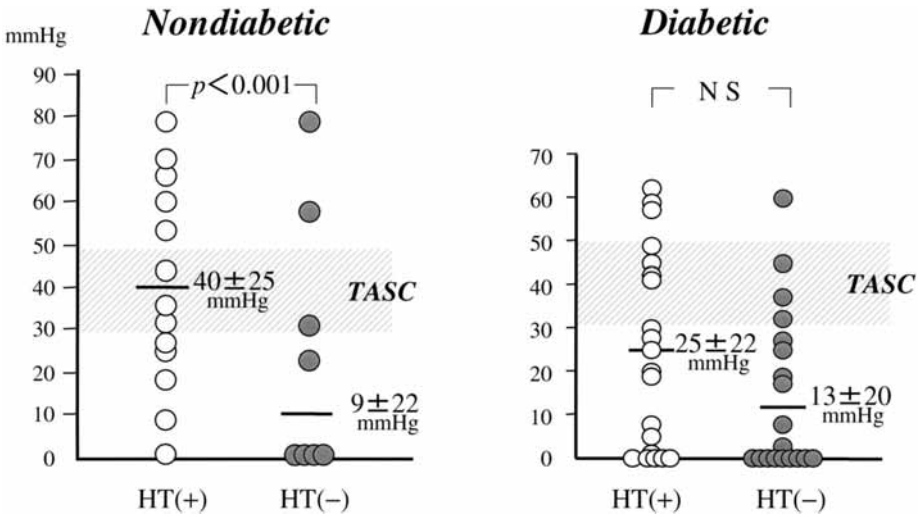

Figure 5 $TcPO_2$ and healing tendency of the ulcer in nondiabetic and diabetic feet.
HT (+): positive healing tendency, HT (–): negative healing tendency

Table 2 Healing tendency assessed by isotope method

Case	Age	Sex	Disease	Type	Outcome
1	70	m	ASO	I	Salvage
2	72	m	ASO + DM	I	Salvage
3	74	m	ASO	I	Salvage
4	60	m	ASO	I	Salvage
5	70	m	ASO	I	Salvage
6	78	f	ASO + DM	I	Salvage
7	76	f	ASO + DM	I	Salvage
8	77	m	ASO + DM	I	Salvage
9	67	m	ASO + DM	I	Salvage
10	79	m	ASO + DM	II	Salvage
11	76	m	ASO + DM	III	BK
12	76	m	ASO	III	AK
13	69	m	ASO	III	BK
14	78	m	ASO	III	BK
15	56	m	ASO + DM	Special	BK

process for wound healing, is disturbed by infection. Assessing the perfusion pattern using the isotope method allowed us to assess the severity and extent of infection.[2] The concept of applying this method to the foot is the same as that in myocardial ^{201}TlCl scintigraphy. The perfusion pattern in the initial phase affects the postischemic stress pattern, while that in the delayed phase relates to the steady-state pattern (**Fig. 6**).

In patients with Type I ulcers, bed rest is not always necessary because inflammatory reactive hyperemia already appears in the initial phase. Medical treatment by vasoactive drugs such as prostanoids may be indicated. In patients with Type II ulcers, bed rest is necessary because inflammatory reactive hyperemia does not appear in the initial phase.

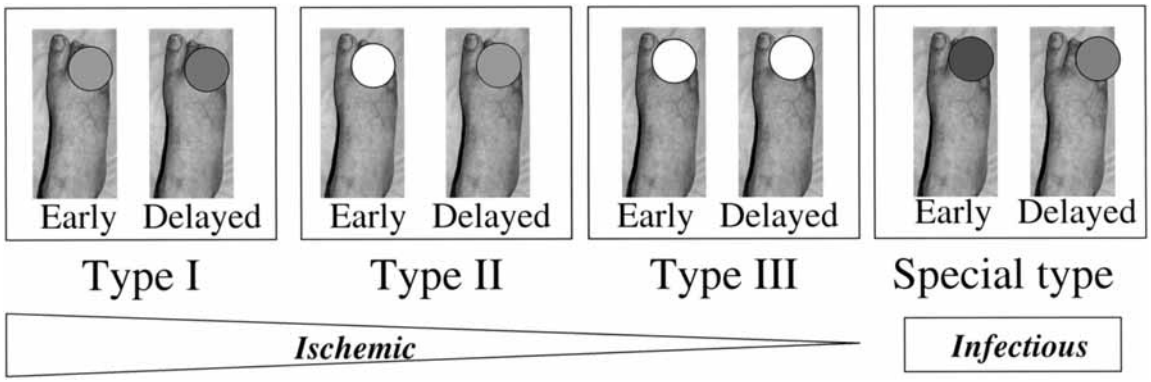

Figure 6 Four types of ischemic ulcerassessed by inflammatory hyperemia at the lesions.

Medical treatment by vasoactive drugs such as prostanoids may be also indicated, but surgical treatment must be considered in patients with delayed wound healing. In patients with Type III ulcers, bed rest is mandatory because inflammatory reactive hyperemia does not appear in either phase. When the feet are critically ischemic, prompt decision to conduct either surgical treatment for improving hemodynamics or limb amputation is extremely important. Special type of ulcers appears to exhibit healing ability due to excessive reactive hyperemia, and the salvage of the limb depends on the aggressive control of infection.

Conclusions

Our results indicate that noninvasive measurements of ankle pressure, toe pressure, and $tcPO_2$ can reveal characteristics of focal hemodynamics such as low perfusion. However, it remains difficult to predict the outcome of an ischemic lesion using only one of these parameters. A poststress isotope imaging method using a single intravenous dose of $^{201}TlCl$ can reveal which feet with Type III ischemic lesions are nonviable and have no healing potential – such feet may be diagnosed as critical ischemia. The diagnosis of critical ischemia should be based on a total assessment of these parameters. Furthermore, while it appears certain that one of the major factors affecting wound healing is ischemia, we must also consider factors such as infection, malnutrition, anemia, and heart failure, especially in diabetic and dialyzed patients.

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