The Diagnostic Classification of Critical Limb Ischemia

Nobuyoshi Azuma, MD, PhD

With the global epidemic of diabetes, diagnosis of critical limb ischemia (CLI) has become very complex due to mixture of microangiopathy, infection and sometimes neuropathy with the pure ischemia. We still sometimes encounter the patients with extensive tissue loss due to misdiagnosis of ischemia or infection in previous hospital. For adequate decision making of proper treatment selection for each critical ischemic limb without missing the adequate intervention timing, a new classification system good for not only vascular specialists but also gate keeping clinicians working in the era of diabetes has been desired. Responding to marked demographic shift, Society for Vascular Surgery issued new classification named WIfI system which evaluate the foot lesion comprehensively by three factors; Wound (W), Ischemia (I), and foot Infection (fI). Guidelines for peripheral arterial disease recommend use of WIfI classification system. To decide treatment strategy of CLI as well as managing those limbs after revascularization, it is important to popularize adequate diagnostic system using WIfI classification as common language by not only for vascular specialists but also other clinicians facing CLI patients. (This is a translation of Jpn J Vasc Surg 2018; 27: 187–195.)

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Introduction

Previously, when the Fontaine and Rutherford classifications were proposed, the ratio of diabetes among patients with ischemic limbs was very low. The disease concept for ischemic foot lesions is simple—it is purely caused by ischemia. Since then, however, this concept underwent significant changes due to lifestyle changes and increasing lifestyle-related illness in developed nations. As the population of diabetics has explosively increased, lower limb arterial lesion classifications and diagnoses have also been significantly altered. This paper describes the diagnosis of and the latest classifications for chronic artery occlusive diseases based on an historical context.

Critical Limb Ischemia

History

The term “critical limb ischemia” (CLI) was first coined at the Working Party of the International Vascular Symposium held in 1981. Since then, there have been unceasing debates regarding its definition, target range, and boundary values, with several differences in opinion observed among clinicians and researchers regarding how to use the term. Repeated discussions were held to solve this issue, after which the Society for Vascular Surgery and the North American Chapter of the International Society of Cardiovascular Surgery released reporting standards, including the CLI diagnosis, in 1986. In 1992, the Second European Consensus Document was released, followed by CLI being defined for the first time in a set of guidelines in the TransAtlantic Inter-Society Consensus (TASC) in 2000. This resulted in the concept and definition of CLI becoming widely-known worldwide.

Definition

CLI, as defined in the TASC, must clearly exhibit the following four elements: (1) ischemic rest pain or ischemic ulcer necrosis, (2) it should be limited to chronic ischemia (excluding acute limb ischemia), (3) limb-threatening ischemia usually requiring major amputation within six months if blood flow does not improve, and (4) objective ischemia meeting the hemodynamic standards listed under...
Verifying whether a patient’s symptoms and local limb lesions are truly caused by ischemia is extremely important when determining the treatment modality. The patient should not be simply diagnosed as Fontaine III owing to the presence of pain. It is also a major mistake to diagnose CLI only based on a lower limb exhibiting refractory ulcers and a main trunk of artery being occluded. Presence of occlusions on arteriography only forms a morphological diagnosis. Ischemic resting pain and ischemic ulcers can only be diagnosed based on an objective ischemia evaluation (hemodynamic evaluation) that includes the degree of blood flow from collateral pathways.

Table 1 lists the cutoff values for objective hemodynamic indices that can be used to diagnose CLI. One can discern how difficult it is to draw a line with CLI as different cutoff values have been set based on the symptoms for resting pain and ulcer necrosis. Moreover, cutoff values for ankle pressure, toe pressure, and transcutaneous partial pressure of oxygen (TcPO2) are not standardized. Furthermore, inconsistent with the original definition, several clinical studies have reported cases that improve or completely resolve with conservative treatment despite having been diagnosed with CLI. In particular, one phenomenon commonly observed in clinical trials on regenerative medicine is that most patients diagnosed with CLI based on clear objective ischemic evaluation avoid major amputation even when allocated to the placebo group. This clearly contradicts point (3) of the definition stated above.6)

Thus, although the definitions and boundary values of CLI are not necessarily absolute, one must remember to thoroughly perform an objective evaluation of the ischemia and make a diagnosis and determine the treatment plan by carefully considering the results of such an evaluation.

Table 1 having been demonstrated.4)

**Points of caution**

As of now, the latest severe limb ischemia guidelines are the joint guidelines released by the European Society of Cardiology (ESC) and the European Society for Vascular Surgery (ESVS). These guidelines use the term “chronic limb-threatening ischemia” (CLTI) rather than CLI.7) According to the guidelines, there were three reasons behind proposing the CLTI definition: (1) several patients meeting the definition of CLI or severe limb ischemia avoid amputation in the long-term, as stated above; (2) the incidence of ulcers caused by neuropathy is greatly increasing during this high prevalence period of diabetes; and (3) apart from ischemia, infection also often poses a risk for major amputation of limbs. Thus, a new concept that better expresses chronic ischemia that could lead to lower limb amputation was required.

**Changes in the Classifications of Severe Limb Ischemia**

Table 2 lists the key classifications for severity, including those currently used for limb ischemia and ischemia-related foot diseases.

### Classical limb ischemia classifications

#### Fontaine classification

As previously mentioned, limb ischemia classifications developed at the latter half of the previous century were simple towing to the small number of diabetic patients. Fontaine classification, which is well known and easy to understand, does not include objective diagnostic standards for ischemia.8)

#### Rutherford’s classification

In Rutherford’s classification, numerical targets for ischemic severity have been defined based on an objective evaluation, thereby making up for the lack of such an evaluation in Fontaine classification. Cases of intermittent claudication and tissue loss have also been classified in greater detail.2,9)
Table 2  Comparison of representative classification systems for critical limb ischemia

| Classification | Year | Description regarding ischemia | Description regarding wound | Description regarding infection | Comments |
|----------------|------|--------------------------------|-----------------------------|-------------------------------|----------|
| Fontaine⁵       | 1954 | Grading of ischemic symptoms   | Stage Ia: localized tissue loss | No description | Pure ischemic model |
|                 |      | * No objective criteria of ischemia | Stage Ib: extensive tissue loss | | |
| Rutherford²,⁹   | 1986 | AP <40, TP <30 mmHg for rest pain | Grade 5: minor tissue loss | No description | Pure ischemic model with objective criteria of ischemia |
|                 | revised 1997 | AP <60, TP <40 mmHg for tissue loss | Grade 6: major tissue loss | | |
| Wagner¹⁰        | 1976 | No description | Grade 6: entire foot gangrene | Only description about abscess & osteitis | Classification for diabetic foot proposed by orthopedicians |
| UT¹¹           | 1982 | ABI <0.8 as the criteria of ischemia | Grade 6: partial foot gangrene | | |
|                 |      | * No grading for ischemic severity | | | |
| PEDIS¹²        | 2004 | >0.9, TBI >0.6, TcPO₂ >60 mmHg | Grade 6: systemic infection with SIRS | | |
|                 |      | Grade 2: PAD symptom, ABI <0.9, AP >50 mmHg, TP >30 mmHg, TcPO₂ 30-60 mmHg | Stage 1: no symptom or sign of infection | | |
|                 |      | Grade 3: AP <50 mmHg, TP <30 mmHg, TcPO₂ <30 mmHg | Stage 2: local infection (≤2 cm²) | | |
| SVS WIfI¹³      | 2014 | I (Ischemic) grade | Grade 3: local infection (>2 cm² or deep tissue) | | |
|                 |      | ABI ≥0.80 | Grade 4: systemic infection with SIRS | | |
|                 |      | AP >100 | Stage 5: unsalvageable | | |
|                 |      | ≥60 | | | |
|                 |      | Grade 1: superficial full-thickness ulcer, not penetrating deeper than the dermis | Grade 1: no symptom or sign of infection | | |
|                 |      | Grade 2: deep ulcer, penetrating below dermis to subcutaneous structures involving fascia, muscle or tendon | Stage 1: very low risk | | |
|                 |      | Grade 3: all subsequent layers of the foot involved including bone and/or joint | Stage 2: low risk | | |
|                 |      | clinical description | Stage 3: moderate risk | | |
|                 |      | Grade 0: no wound | Stage 4: high risk | | |
|                 |      | 0 | Stage 5: unsalvageable | | |
|                 |      | 1 | | | |
|                 |      | 1 minor tissue loss | | | |
|                 |      | 2 | | | |
|                 |      | 2 major tissue loss | | | |
|                 |      | 3 | | | |
|                 |      | extensive tissue loss | | | |
|                 |      | 3 | | | |
|                 |      | | | | |

ABI: ankle-brachial index; AP: ankle pressure; TP: toe pressure; TBI: toe-brachial index; TcPO₂: transcutaneous PO₂

However, interpretations of the Rutherford 6 (R6) classification differ based on the researcher and the country. This is because the R6 definition is based on the following three conditions: (i) major tissue loss, (ii) tissue loss extending above the transmetatarsal level, and (iii) the functional foot being unsalvageable. For example, if there was a shallow, small ulcer in the heel, it would be classified as R6 based on only point (ii) above. However, some researchers would classify it as R5 because the term “major tissue loss” does not fit the shallow ulcer. In 2014, the Society for Vascular Surgery Lower Extremity Guidelines Committee published a classification system for threatened lower limbs, categorizing and grading (0–5) the three major risk factors leading to amputation—Wound, Ischemia, and foot Infection (WIfI). The researchers who proposed the WIfI score described it in terms of point (iii) mentioned above. They claimed that performing revascularization despite the limb being unsalvageable when diagnosed as R6 is highly unlikely. Therefore, they reported that the WIfI score be used rather than the Rutherford classification. Certainly, it is inevitable that there will be cases that are difficult to judge when three conditions are established as classification criteria. Additionally, when the question of whether the limb is salvageable is considered, the high likelihood of classifications changing due to the historical background, such as technological innovation, also creates problems.

**Diabetic foot ulcer classifications**

The Wagner ulcer classification system,¹⁰ the University of Texas (UT) diabetic wound classification system,¹¹ and the perfusion, extent, depth, infection, and sensation
(PEDIS) classification system\textsuperscript{12} are the historically important, currently used classifications for diabetic foot ulcers (DFUs).

Wagner ulcer classification system
First proposed in 1975, Wagner ulcer classification system primarily focuses on wound depth. However, it does not evaluate blood flow factors. Moreover, it includes no mention of any infection other than osteomyelitis.

UT diabetic wound classification system
In this system, the depth of the wound and presence of infection have been classified in an easy-to-understand manner, and clinical signs of ischemia have also been considered. Although this classification does address factors not considered in the Wagner classification system, it does not consider the location and extent (spread) of tissue loss. Moreover, the UT system only classifies the presence or absence and not the severity of ischemia.

PEDIS classification system
The International Working Group of the Diabetic Foot developed the PEDIS system, which evaluates the three pathologies “wound, infection, and ischemia” in a well-balanced manner. Particularly, with regards to its infection classification system, it was described as an excellent follow-up strategy in the 2012 IDSA Clinical Practice Guideline for the Diagnosis and Treatment of Diabetic Foot Infections and the 2014 WIfI classification system.\textsuperscript{13} However, this system still only targets DFUs and lacks descriptions covering wound localization and extent of tissue loss required to determine arterial reconstruction and whether the limb is salvageable.

Kobe classification
The Kobe classification was proposed in 2011 by the Department of Plastic Surgery, Kobe University, Japan. It is a four-level system for the pathological classification of DFUs based on etiology and treatment. It focuses on the etiology of DFUs and the pathology of how they increase in severity. Because it is very easy to understand, it has come into particularly wide use among medical staff involved in DFU treatment.\textsuperscript{14}

Ischemic limb classifications in the era of diabetes
Since the previous century, the global population of diabetic patients has explosively increased, and the prevalence of diabetes among patients with peripheral artery disease (PAD) still continues to increase. Patients with PAD and diabetes have several distinctive features, including (1) angiopathy of main trunk arteries (macroangiopathy) involving medial sclerosis that tends to develop in the crural arteries; (2) accompanying microangiopathy; (3) frequent neuropathy and associated foot deformation; (4) increased pain threshold resulting from neuropathy, delaying the detection of ischemia and wound; and (5) susceptibility to infection. Thus, when diabetic patients develop PAD, the focus on vascular lesions moves toward a more peripheral area, and ulceration and necrosis are more likely to occur. Moreover, if tissue loss occurs, healing is delayed and the patient becomes more susceptible to infection.

Another important point is the fact that the natural course from the onset of PAD to exacerbation differs depending on whether the patient has diabetes. The Fontaine and Rutherford classification systems indicate that cases sequentially progress from a milder state to one with increasing exacerbation. However, diabetic patients are more likely to experience a sudden occurrence of ulcers or necrosis without intermittent claudication or pain at rest.\textsuperscript{15,16}

Thus, because of societal changes in disease configurations and increasingly intricate pathophysiology being observed in patients with PAD, more patients are exhibiting an intricate combination of factors such as neuropathy and infection together with ischemia. It is now becoming impossible to accurately define ischemic limbs using only the Fontaine and Rutherford classification systems, which are purely based on the concept of ischemia. In this context, studies have been conducted to develop a classification system that can be used to accurately evaluate such complicated pathologies.

In response to changes in demographics and modern demands, the US Society for Vascular Surgery, in collaboration with podiatrists and other parties, proposed the WIfI classification system.\textsuperscript{13}

Society for Vascular Surgery WIfI classification system
The WIfI system systematically classifies foot lesions by three components—wound, ischemia, and foot infection, in response to complexity of foot disease in diabetic era (Table 2).\textsuperscript{13}

Wound (W) grades
This comprehensive grading system aims to evaluate the presence, spread, and location of the wound. The basic concept is to classify the wound as either an ulcer or necrosis, with necrosis always being graded at one level higher in severity. Based on the location aspect of the W grades, heel ulcers are considered particularly severe, because heel wounds are generally difficult to treat and have a poor prognosis.\textsuperscript{17}

Each grade in the W grades classification not only describes the lesion characteristics but also provides a clini-
critical description. For example, if a very small necrotic area is located at the tip of a toe, close examination may reveal that it is only superficial necrosis, like a scab. Although it indeed is necrosis and shows the characteristics of grade 2 necrosis, such a case should not be straightforwardly classified as grade 2 because it does not satisfy the grade 2 clinical description of “major tissue loss.” When the authors of the WIfI report were questioned, they stated that when such an inconsistency is encountered, the clinical description should be prioritized. In situations such as the one described above, we suggest it should be classified as grade 1, because it would probably become a shallow ulcer once the small scab is removed.

Ischemia (I) grades
A major feature of the WIfI classification is that for ischemia severity, it not only measures the presence of ischemia or whether the case involves CLI but also evaluates severity based on four levels. The classification is objective (grade 0, no obvious ischemia; grade 1, mild ischemia; grade 2, moderate ischemia; grade 3, severe ischemia). The comparison presented under Table 1 shows that when conventional CLI standards are applied, grade 2 and grade 3 satisfy the CLI criteria. Thus, it appears that CLI has been further broken down into two types.

This may sound repetitive; however, the presence of ischemia is absolutely necessary for diagnosis, but it is even more crucial for diagnosing the severity of ischemia. This is because ischemic limbs classified as CLI may include I grade 3 limbs wherein there is hardly any blood flow and I grade 2 limbs that just satisfy the criteria for being described as CLI. If revascularization fails for an I grade 3 limb and repeat stenosis occurs, necrosis will definitely develop. In contrast, if revascularization is performed on an I grade 2 limb and the ulcer heals, it is unlikely to recur, even if the reconstructed artery subsequently re-occluded. This difference is highly significant when selecting the treatment modality or predicting the outcome of revascularization. Describing I grading of treated limbs in literature reveals how severe ischemic limbs authors treated, which is valuable information when we look at revascularization results.

Furthermore, it is interesting to note that I grade 1 cases also exist. If an ulcer develops in such a mildly ischemic limb, the guidelines state that revascularization should not be performed. Meanwhile, if an artery is occluded and a refractory ulcer is present with even a mild ischemia noted, some physicians may consider it best to quickly perform revascularization to rectify the condition. Scant evidence is available regarding the significance of revascularization for such mild cases of ischemia.

Revascularization is not generally recommended for ulcers accompanied by mild ischemia deemed likely to spontaneously resolve; the advantages gained by performing revascularization to enable early healing would be negated by the potentially life-threatening risks of complications associated with restenosis and re-occlusion that could occur after revascularization. In the future, if revascularization becomes a more reliable procedure with better long-term outcomes and a lower level of invasion, its application to mild grade 1 ischemic limbs could be debated upon.

Foot Infection (fI) grades
The WIfI system has inherited the four-level grading of infection used in the PEDIS and IDSA systems. Severe but localized infection is defined as grade 2, whereas systemic infection is defined as grade 3. Infection, particularly infection associated with the ischemic limb, is more dangerous than ischemia because it can directly lead to major amputation. Once infection occurs, tissue pressure increases because of swelling and abscess formation due to inflammation. Increased tissue pressure worsens tissue hemodynamics because arterial blood perfuse to the tissue depending on the pressure gap between capillary/arterial blood pressure and tissue pressure. Furthermore, if the infection is caused by a bacterium with strong tissue-necrotizing abilities, the arteriole network, which had been maintained with great difficulty, will also be destroyed, further exacerbating the ischemia itself. Because diabetic patients are particularly susceptible to infection and have reduced white blood cell functions, such as migration, larger numbers of immune cells should be sent to the site of infection, indicating that more blood flow will be required. Despite the high need for salvaging ischemic limbs, such descriptions of infection have hardly been discussed in previous classifications and guidelines used in the field of vascular surgery. Thus, the fI grading could be described as highly innovative, because it has become an essential part of foot lesion diagnosis, with similar importance as that of ischemia grading.

Although treatment strategies are gradually being established for foot lesions accompanied by infection, there are still reports of delay in treatment for deep infection following revascularization. In such cases, major amputation may be unavoidable despite adequate blood flow having been established. Therefore, treatment modalities for such cases have not yet been definitively established. It is anticipated that clinical research to comprehensively evaluate the WIfI classification system will lead to the development of infection countermeasures for ischemic limbs.

Diagnosis of CLI
The diagnostic procedures and criteria followed when performing medical care during initial outpatient con-
sultation are shown in Fig. 1. Accurately determining the pathophysiology of a highly diverse population of patients with CLI and establishing appropriate treatment plans require a comprehensive process involving the evaluation of the limb, systemic state, and functional aspects.

Diagnosis of impaired lower limb blood flow
The initial outpatient consultation should include palpation of the lower limb arterial pulse (from the inguinal region to the popliteal space and foot region), auscultation for vascular bruit, and ankle brachial index calculation. If blood flow impairment is observed, foot evaluation using WIfI classification is followed.

WIfI I grading
The severity of such an ischemia is also of great importance. Even if ankle pressure is normal, it may not be relevant owing to arterial calcification or arterial disease involvement below the ankle. Even in such a circumstance, if there is a reason to suspect ischemia, toe pressure, skin perfusion pressure, and TcPO₂ should be measured and the severity of any ischemia determined.

If the rest pain or tissue loss is ischemic and the associated objective measurement values satisfy the criteria, CLI can be diagnosed.

WIfI W grading
When examining the foot, the presence of any wound, including between the toes and on the base of the feet, should be investigated. Furthermore, if a wound is present, its depth and location should be recorded and digitally photographed. Because W grade 3 wounds are likely to be accompanied by a deep infection, it is ideal to evaluate the presence or absence of osteomyelitis and deep ulcers via magnetic resonance imaging or other similar tests.²⁹

WIfI fI grading
Because severe ischemia makes it difficult for signs of infection, such as redness and sense of heat, to appear, observations should be carefully made. Moreover, because bacteria are present on chronic wounds and can subsequently lead to severe infections, culture testing should be performed at an early stage. Information regarding infections is also important for implementing countermeasures against hospital-acquired infections.

Dependent rubor, involving reddening over the entire foot region, can also occur in response to ischemia resulting from capillary dilatation (Fig. 2). Care must be taken to not misidentify this as infection.

Evaluation of the general state
PAD is a well-known systemic vascular disease type. Ac-
Accordingly, complications, such as coronary artery lesions, cerebrovascular lesions, and renal artery lesions, are common in patients with PAD. Aortic valvular stenosis frequently complicates cases in older patients and patients undergoing dialysis.

Accordingly, echocardiography and coronary blood flow evaluation must be performed. Because such cases are commonly complicated with cerebrovascular and carotid artery lesions, it is considered ideal to also perform carotid artery ultrasound and head magnetic resonance angiography (MRA). The likelihood of perioperative complications can be reduced if a preoperative imaging diagnosis can be made and if anesthesia and perioperative management are carefully implemented. In addition, if a postoperative cerebrovascular event occurs, it will be clear whether it was present preoperatively or occurred postoperatively, thus making it possible to infer the involved pathophysiology.

Key organ evaluation, including lung function, kidney function, and nutritional state, as well as reserve function assessment is crucial for not only selecting the method of revascularization and anesthesia but also for perioperative management. It is also unquestionably important to understand the state of control of lifestyle-related diseases. To enhance preoperative intervention wherever possible, it must be determined what factors (e.g., hypertension, diabetes, dyslipidemia, smoking, and kidney dysfunction) have contributed to the progression of vascular disease in each patient on a case-by-case basis. Test results for the aforementioned heart, cerebrovascular, and lifestyle-related diseases also provide important information for postoperative secondary prevention strategies. In addition, blood coagulation/fibrinolysis system screening should be routinely performed. If prominent thrombosis or repeated occlusion occurs intraoperatively, the patient may be predisposed to thrombosis such as heparin-induced thrombocytopenia.

**Evaluation of lower limb function**

It should be determined whether the patient can walk. If the patient cannot walk, it should be determined since when he/she could not do so, and factors, such as joint range of motion from a physiotherapy perspective, should be preoperatively evaluated. These data can help predict postoperative functional prognosis, determine the treatment modality (endovascular treatment, surgical treatment, or primary amputation), and establish treatment goals.

**Evaluation of vascular morphology**

Detailed morphological evaluation of the arterial lesion is performed only if the patient is considered eligible for revascularization. The arterial lesion can be assessed using contrast-enhanced computed tomography (CT), ultrasonography, or MRA. In the case of subtle lesions, wherein it is difficult to determine whether intervention should be performed based on CT and MRA findings, diagnostic reliability can be greatly improved by basing the evaluation on morphology and hemodynamics via a duplex scan. It is difficult to perform morphological evaluations of entirely calcified artery using CT and ultrasound; therefore, MRA and digital subtraction angiography (DSA) are used in such cases. Because the contrast medium used does not reach the peripheries of the foot in CLI cases particularly involving severe ischemia, the arteries in the foot often appear invisible on contrast, even if the medium is introduced via the inguinal region using DSA. Revascularization should not be considered impossible based on such findings. Because it is impossible for all of the arteries to be occluded if most of the foot is still living (except in cases of vasculi-

![Fig. 2 Typical photo of dependent rubor (ischemic rubor). This reddish color disappears by elevation of leg or by successful revascularization. This is not due to infection, but is thought due to capillaries dilatation in ischemic foot.](image-url)
to present the initial part of the new treatment guidelines called “the Global Vascular Guidelines (GVG) on the evaluation and management of chronic limb-threatening ischemia.” A full outline of the GVG is yet to be released; it recommends that foot lesions be diagnosed using the WIfI classification, which is becoming the standard of care for vascular specialists worldwide.

Accurate diagnosis is also important for determining the appropriate treatment modality. In Japan, the SPINACH Study (surgical reconstruction versus peripheral intervention in patients with critical limb ischemia), a multicenter prospective clinical study implemented in collaboration with vascular surgeons and interventional cardiologists, released recommendations on what situations require surgical revascularization or endovascular repair. The study reported that surgical revascularization resulted in superior outcomes of endovascular repair for severe foot lesions with WIfI classifications W grade 3 and fl grades 2 and 3.20)

Going forward, the use of the WIfI system in Japan is spreading not only among vascular surgeons but also among physicians performing revascularization and plastic surgeons in general. Thus, efforts must be made to facilitate the use of grades referred to by the WIfI classification system as standard applicable terms, regardless of the treating department or the physician’s specialty.

**Conclusion**

CLI truly presents in a diverse number of ways. Survival of patients with CLI is generally considered very poor; this is certainly the case for the overall CLI population, if one does not consider the diverse pathology presented by individual patients. The limb of some patients is salvageable; the ulcer can be completely cured, and walking ability can be recovered, such that they can return to their daily lifestyle and achieve healthy longevity. However, recently, the number of super-aged, bedridden patients with PAD or dementia has increased; thus, case-by-case treatment goals should also ideally be diverse. Predicting the final extent of tissue loss and the degree of functional prognosis at the time of diagnosis may help select a corresponding treatment modality.

Moreover, physicians are required to quickly make a diagnosis for CLI. Particularly, for WIfI classification I grade 3 or fl grade 2 or 3 cases, revascularization and/or drainage needs to be rapidly implemented.

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