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Korean Guidelines for Interventional Recanalization of Lower Extremity Arteries

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Peripheral arterial occlusive disease caused by atherosclerosis can present with intermittent claudication or critical limb ischemia. Proper diagnosis and management is warranted to improve symptoms and salvage limbs. With the introduction of new techniques and dedicated materials, endovascular recanalization is widely performed for the treatment of peripheral arterial occlusive disease because it is less invasive than surgery. However, there are various opinions regarding the appropriate indications and procedure methods for interventional recanalization according to operator and institution in Korea. Therefore, we intend to provide evidence based guidelines for interventional recanalization by multidisciplinary consensus. These guidelines are the result of a close collaboration between physicians from many different areas of expertise including interventional radiology, interventional cardiology, and vascular surgery. The goal of these guidelines is to ensure better treatment, to serve as a guide to the clinician, and consequently, to contribute to public health care.
Index terms: *Guideline; Peripheral arterial disease; Diagnosis and management; Intervention*

INTRODUCTION

Background and Purpose

Peripheral arterial occlusive disease (PAOD) is primarily caused by atherosclerosis. The purpose of treatment is to reduce the symptoms of limb ischemia such as claudication and to salvage the limbs. Interventional procedures (angioplasty or stent placement) for the recanalization of lower extremity arteries in patients with chronic stenosis or occlusion of lower extremity arteries have been widely performed in recent years as medical equipment and technology have developed.

The indications for these interventional procedures are gradually increasing with the rapid development of

equipment and procedures, and there are a variety of views about the indications for patients and procedure methods among medical institutions and operators. In the United States, the American Heart Association (AHA) presented guideline recommendations for interventional procedures in lower extremity arteries in 2005 and announced an amendment in 2011 as procedures developed. In Europe and North America, Transatlantic Intersociety Consensus (TASC), a working group formed in 2001 and centered on interventional radiology, vascular surgery, and cardiology, issued guidelines for interventional procedures and a revision in 2007. Furthermore, in 2011, new guidelines were issued with the European Heart Association as the focus. Through these efforts, by establishing the standard for procedures and raising the awareness of physicians on the front lines of medicine to the importance of the procedures, a cautious approach is encouraging. Moreover, these guidelines can be used as basic standards for social insurance wages and judgment standard for reducing medical costs.

However, even though a number of studies like this have been conducted, correct clinical guidelines for our situation in Korea have not yet been established. Thus, experts from academies (the Korean Society of Interventional Radiology [KSIR], the Korean Society for Vascular Surgery, the Korean Society of Interventional Cardiology, and the Korean Society of Radiology and Nursing) related to interventional procedures in Korea came together and agreed to develop clinical guidelines. We would like to agree on the proposal of recommendation by presenting evidence-based treatment recommendations through a multidisciplinary approach, to serve as a guide for interventional procedures by providing up-to-date and accurate information to health care providers working at primary, secondary and tertiary hospitals. Furthermore, we would like to help patients themselves choose appropriate medical services by recognizing accurate information and further contribute to public health promotion.

Guideline Development Method

Considering that the development of *de novo* domestic clinical guidelines is a difficult undertaking, these guidelines were developed by adapting the pre-existing guidelines of other countries. But if there were no existing guidelines, we evaluated existing documents with good quality using the systemic document review methodology. We proposed initial recommendations based on the two

sources described above then developed a new proposal by implementing the rule to suitably transform the guidelines of other countries for domestic circumstances in Korea.

Subject of Application and Scope

Adult men and women with limb ischemia symptoms caused by chronic stenosis or occlusion of the lower extremity arteries that occurred due to atherosclerosis or diabetes were targeted. Acute limb occlusion and chronic limb occlusion caused by other underlying diseases other than diabetes or atherosclerosis were excluded. The guidelines were limited to proposing recommendations for interventional recanalization, therefore the proposal of recommendations for medical treatment, exercise therapy, and surgical operations were excluded. Cases with lack of evidence and controversial cases were excluded from the guidelines.

Level of Evidence and Classification of Recommendation

The level of evidence (LOE) and the classification of recommendations (COR) followed the criteria used in the American College of Cardiology/American Heart Association (ACC/AHA) 2005 guideline. COR was separated into three categories: Recommendation I (strong recommendation), Recommendation II (weak recommendation), and Recommendation III (contraindication). Recommendation I was defined as conditions for which there was solid evidence for and/or general agreement that a given procedure or treatment is effective, useful, and beneficial and will not be changed by further research. Recommendation II was defined as conditions with conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment. IIa was defined as cases for which the weight of evidence/opinion was in favor of usefulness/efficacy. IIb was defined as cases for which the usefulness/efficacy was less well established by evidence/opinion. Recommendation III was defined as conditions for which there was evidence and/or general agreement that a procedure/treatment is not useful/effective and may be harmful in some cases (Table 1). LOE was classified into three steps: A, B, and C. Evidence A was defined as data derived from multiple randomized clinical trials or meta-analysis. Evidence B was defined as data derived from a single randomized clinical trial or non-randomized studies. Evidence C was defined as only consensus opinion of experts, case studies, or standard of care (Table 2).

Table 1. Classification of Recommendations

Class	Description
I	Conditions for which there is evidence for and/or general agreement that given procedure or treatment is beneficial, useful, and effective
II	Conditions for which there is conflicting evidence and/or divergence of opinion about usefulness/efficacy of procedure or treatment
IIa	Weight of evidence/opinion is in favor of usefulness/efficacy
IIb	Usefulness/efficacy is less well established by evidence/opinion
III	Conditions for which there is evidence and/or general agreement that procedure/treatment is not useful/effective and is some cases may be harmful

Table 2. Levels of Evidence

Level	Description
A	Data derived from multiple randomized clinical trials or meta-analysis
B	Data derived from single randomized clinical trial or nonrandomized studies
C	Only consensus opinion of experts, case studies, or standard of care

Independence of Support and Editing

This study was developed as a project for creating the clinical guidelines of the Korean Society of Radiology and the KSIR. During the entire process of guideline development, there was no influence from the Korean Society of Radiology and the KSIR and there was no external support from any other academies, institutions and interest groups. All members who participated in this clinical guideline development process have signed agreements confirming that there was no conflict of interest in connection with the studies.

Guideline Revision

We will conduct revision at intervals of 3–5 years by using an adaptation development method when new examination and treatment methods for interventional recanalization of lower extremity arteries are introduced and research results are accumulated.

Guideline Adaptation Process

Configuration and Role of the Committee

The steering committee was composed of the president and executives of the KSIR. The steering committee fixed the subject and the goal, assigned the guideline development chairman and committee members and approved the guideline development budget. The guideline development committee was made up of 20 committee members including a chairman and a secretary.

Guideline development committee members were educated about guideline development methodology and the evaluation of guidelines based on the Appraisal of Guideline for Research and Evaluation II (AGREE II). This was accomplished by inviting methodology experts and hosting workshops. After the workshops, we discussed the purpose of the guidelines, the range of development including writing topics, the subjects of application and user groups, development method, the determination of the LOE, COR, the selection of the consensus development method, internal and external review processes, revision processes and formation of the committee of detail associated with guideline development during the first conference of the guideline development committee. The committee of detail was composed of the guideline evaluation committee, the writing committee, and the editing committee. Five members were involved in the guideline evaluation committee and evaluated the pre-existing guidelines based on AGREE II. Eight members were involved in the writing committee and were in charge of drawing up the guideline draft and the proposal of recommendations. The editing committee was composed of 5 members and was in charge of reviewing the recommendation levels, the LOE, and the guideline draft by performing peer review.

Evaluation and Selection of Guidelines in Other Countries

In order to select a high-quality guideline for reference in the adaptation process, we searched for existing guidelines. We recovered 70 documents by mixing search index words such as PAOD, endovascular treatment, limb ischemia and guidelines with the use of the PUBMED, OVID, SCOPUS, WEB OF SCIENCE, and COCHRANE search engine.

The guideline evaluation committee determined the inclusion and exclusion criteria for quote-worthy documents among the obtained documents. The inclusion criteria were set as evidence-based guidelines, international guidelines written in English, and recent guidelines written since

2005. Guidelines that did not represent the organization, those written by one person and translations of single guidelines were excluded.

A total of 6 guidelines were chosen based on this inclusion criterion. 4 guideline evaluation committee members evaluated these guidelines based on AGREE II, which is the most commonly used tool internationally for the quality assessment of guidelines. AGREE II is made up of 23 sub-items within 6 assessment categories and each item is given a score on a 7-point Likert scale. All guidelines evaluation committee members received systemic education about AGREE II with methodology experts through case-by-case analysis by participating in the workshop. In comparing the results of 4 evaluation committee members, cases for which the difference between the highest record and the lowest record was more than 4 points were defined as a disagreement. If more than 5 items were disagreed upon, reevaluation was conducted after coordinating opinions about inconsistent evaluation items. Based on the re-evaluated results after opinion coordination, 5 guidelines that had standardized scores of more than 50% in all categories and in particular, over 70% in the rigour of development category, were finally selected (1-5).

Deduction and Selection of Key Question

The guideline development committee shared roles by assigning committee members according to sub-themes of writing items for the deduction of the clinical question at the second conference. The third conference of the guideline development committee selected the final key question after reviewing whether population, intervention, comparison, and outcome (PICO), the essential structural component of the key question, was well equipped and appropriate as a clinical question. The key question was agreed upon using the nominal group technique. Consensus was defined as more than 75% of the panel selecting 1 and 2 on the 5-Likert scale (1, agree entirely; 2, agree generally; 3, agree partially; 4, do not agree generally; 5, do not agree entirely). If the consensus was less than 75%, a second round of voting was carried out after discussion and a modification of phrases. If agreement was not reached in the second round of voting, the key question was dismissed. Ten development committee members participated in the panel. Seventeen of a total of 40 key questions that were drawn up were agreed upon by committee members and were selected as the final clinical question. The selected key questions were arranged and the <Key Question PICO

Data Extraction Form> was developed (Table 3).

Document Search

Because of the adaptation development process, the deduction of the proposal of recommendations for the clinical question mostly referred to existing selected guidelines. However, for clinical questions without existing guidelines, a library search expert was involved in order to find good quality documents by sub-themes. PubMed and Cochrane library databases were used for evidence based documents searches. The searching parameters were restricted to publications before June 30, 2013, studies done on humans only, and studies published in English. After developing the searching formulas for each sub-theme, the search results were reviewed and evidential studies were selected for each related key question. When a more recent systemic review or meta-analysis study was found, papers previously published with a lower LOE were excluded along with the corresponding case reports. The search terms for PAOD were Peripheral Arterial Disease (MeSH), and Arterial Occlusive Disease (MeSH), and related search terms were input by connecting AND/OR.

The search formulas by sub-themes using Mesh terms in PubMed and Cochrane library were as follows:

Diagnosis of Peripheral Arterial Occlusive Disease
   (Peripheral Arterial Disease/diagnosis [MeSH]) AND (Arterial Occlusive Diseases/diagnosis [MeSH]) AND (Ankle Brachial Index [MeSH Major Topic] OR Ultrasonography, Doppler, Duplex [MeSH] OR Computed Tomography Angiography OR Magnetic Resonance Angiography [MeSH] OR Angiography [MeSH])

Patient Care for Contrast Medium-Related Nephrotoxicity
   (Kidney Diseases/prevention and control [MeSH] OR Kidney Diseases/therapy [MeSH]) AND (Contrast induced [Title]) AND (Angiography [MeSH])

Indication of Recanalization and the Establishment of Procedure Plan
   (Peripheral Arterial Disease/therapy [MeSH]) AND (Arterial Occlusive Diseases/therapy [MeSH]) AND (Endovascular Procedures/instrumentation, methods, therapy [MeSH])

Interventional Procedure Method
   (Peripheral Arterial Disease [MeSH]) AND (Arterial Occlusive Diseases [MeSH]) AND (Endovascular Procedures/

Table 3. Key Question PICO Data Extraction Form

Sub-Themes	Clinical Questions	P (Population)	I (Intervention)	C (Comparison)	O (Outcome)
Diagnosis	Screening test for diagnosis of peripheral arterial occlusive disease	Intermittent claudication, critical limb ischemia patients or adult with risk factor of peripheral arterial occlusive disease	Hemodynamic examination	Imaging examination	Sensitivity, specificity
	Vascular imaging examination for localization of peripheral arterial occlusive disease	Patients with peripheral arterial occlusive disease	Noninvasive imaging examination	Invasive imaging examination	Sensitivity, specificity
Indications for interventional recanalization	Implementation subject of recanalization (including intervention and surgery) of lower extremity artery (divided into intermittent claudication and critical limb ischemia)	Patients with intermittent claudication or critical limb ischemia	Intervention or surgery	Medication or exercise therapy	Improvement of symptom, quality of life, morbidity, mortality
	Which lesion can be applied for interventional recanalization of lower extremity artery compared with surgery?	Patients with intermittent claudication or critical limb ischemia	Intervention	Surgery	Patency rate, quality of life, amputation free survival rate, morbidity, mortality
Patients care before interventional procedure	Laboratory test evaluating contrast medium related renal injury and preprocedural care for preventing renal injury	Patients with intermittent claudication or critical limb ischemia who have plan for interventional recanalization	Laboratory test or care for preventing contrast medium related renal injury	Observation	Incidence of contrast induced nephropathy, morbidity, mortality
	Is drug therapy needed before and after procedure?	Patients with intermittent claudication or critical limb ischemia	Drug therapy	Observation	Morbidity, mortality
Establishment of procedure plan	Selection criteria of target artery for treatment	Patients with intermittent claudication or critical limb ischemia	Intervention	Conservative treatment	Improvement of symptom, quality of life, morbidity, mortality
	Treatment plan of multiple lesions	Patients with multiple stenotic or occlusive lesions in lower extremity artery	Intervention	Conservative treatment	Improvement of symptom, quality of life, morbidity, mortality
Aorto-iliac artery interventional procedure	In which case is primary stent placement needed for interventional racanalization of aortoiliac artery?	Patients with stenotic or occlusive lesions in aortoiliac artery	Primary stent placement	Balloon angioplasty	Patency rate, complication
	When is bailout stent placement needed during interventional recanalization of aortoiliac artery	Patients with stenotic or occlusive lesions in aortoiliac artery	Bailout stent placement	Balloon angioplasty	Patency rate, complication
	Is kissing stent needed for treatment of lesions involving aortoiliac bifurcation?	Patients with stenotic or occlusive lesions in aortoiliac bifurcation	Kissing stent placement	Stent placement, balloon angioplasty	Patency rate, complication

Table 3. Key Question PICO Data Extraction Form (Continued)

Sub-Themes	Clinical Questions	P (Population)	I (Intervention)	C (Comparison)	O (Outcome)
Femoro-popliteal artery interventional procedure	Is primary stent placement needed for short segment stenotic or occlusive lesion of femoropopliteal artery?	Patients with short segment stenotic or occlusive lesions in femoropopliteal artery	Primary stent placement	Balloon angioplasty	Patency rate, limb salvage rate, complication
	When is bailout stent placement needed during interventional recanalization of femoropopliteal artery?	Patients with stenotic or occlusive lesions in femoropopliteal artery	Bailout stent placement	Balloon angioplasty	Patency rate, limb salvage rate, complication
	Is subintimal angioplasty needed for long segment occlusive lesion of femoropopliteal artery?	Patients with long segment occlusive lesions in femoropopliteal artery	Subintimal balloon angioplasty	Stent placement	Patency rate, limb salvage rate, complication
	Are new procedures more effective than plain old balloon angioplasty or stent placement for interventional recanalization of femoropopliteal artery?	Patients with stenotic or occlusive lesions in femoropopliteal artery	Plain old balloon angioplasty or stent placement	Drug eluting balloon angioplasty, drug eluting stent, cutting balloon angioplasty, atherectomy, laser therapy, stent graft	Patency rate, limb salvage rate, complication
Infrapopliteal artery interventional procedure	How would guide wire passage during interventional recanalization of infrapopliteal artery?	Patients with stenotic or occlusive lesions in infrapopliteal artery	Intraluminal guide wire passage	Subintimal guide wire passage	Success rate, patency rate, complication
	In which case is stent placement needed for interventional racanalization of infrapopliteal artery?	Patients with stenotic or occlusive lesions in infrapopliteal artery	Stent placement	Balloon angioplasty	Patency rate, limb salvage rate, complication

instrumentation, methods [MeSH]) AND (Iliac Artery [MeSH] OR Popliteal Artery [MeSH] OR Femoral Artery [MeSH] OR Infrapoplliteal Artery) AND (Angioplasty [MeSH] OR Stents [MeSH] OR Drug-Eluting Balloon [All Fields] OR Drug-Eluting Stents [MeSH] OR Stent Graft [All Fields] OR Atherectomy [MeSH] OR Cryoplasty [All Fields])

Deduction of Recommendations

Writing committee members who were assigned to specific sub-themes drew up the proposal of recommendations for clinical questions. A single draft of the proposal of recommendations was deduced by collecting common information and removing unnecessary information after analyzing the recommendations extracted from the selected guidelines. If there was no data for reference in existing guidelines of clinical questions, a new proposal of recommendations was developed based on the results of evaluating the quality of documents through the documents search and review process. Thus a total of 63 proposals of recommendations were drawn up. We created a recommendation data extraction form, which the panel used as a reference during the Delphi consensus process.

At the 4th guideline development committee member conference, a preliminary examination of the draft was conducted under the agreement of 11 development committee members who participated in the conference. In this process, vague phrases and sentences were checked and the draft of the proposal of recommendations was modified prior to the Delphi consensus process. Fourteen of the recommendations were deleted because no final agreement was reached due to opinions that information remained ambiguous and difficult to understand despite modification of phrases or sentences or the recommendations were unpractical in Korea, etc. The remaining 49 recommendations were selected by Delphi consensus survey and a <Recommendation Data Extraction Form> was created (Table 4). The nominal group consensus was used for the agreement method and the criteria of adoption and rejection was the same as the selection of key questions.

Agreement Method and Panel Selection for Recommendation Adoption

For formal mutual agreement of the final adoption of recommendations, a modified Delphi technique was applied. By sending an official document for cooperation explaining the objectives and necessity of a guideline for interventional recanalization of the lower extremity

Table 4. Recommendation Data Extraction Form

Recommendation	G	RCT	NRCS	SR/MA	NR	CS
1. Ankle brachial index is useful as screening test for peripheral arterial occlusive disease (Class I, Level A).	5					
2. In patients who are already diagnosed with peripheral arterial occlusive disease, it is necessary to measure ankle brachial index to evaluate their basic condition (Class I, Level B).	1					
3. Ankle pressure is high and credibility of ankle brachial index is low when artery is not compressed because of severe calcified sclerosis. In this situation, toe brachial index is useful for diagnosis of peripheral arterial occlusive disease (Class I, Level B).	2					
4. Segmental limb pressure measurement is useful diagnostic test because it helps to determine approximate location of lesions and helps to establish appropriate treatment plan (Class I, Level B).	2					
5. PVR is useful test for not only early diagnosis of PAOD but also to assess state after revascularization because it is able to identify the approximate location and degree of lesion (Class IIa, Level B).	2					2
6. Exercise test may be performed to diagnose peripheral arterial occlusive disease when resting ankle brachial index is normal in patients in whom peripheral arterial occlusive disease is suspected (Class I, Level B).	5					
7. Exercise test may be performed in order to objectively assess how much a patient's leg function is limited and how much function is recovered after treatment (Class I, Level B).	1					
8. Measurement of transcutaneous oxygen pressure can be used to evaluate degree of oxygen supply to feet or around wound and whether oxygen supply is improved after recanalization in patients with critical limb ischemia (Class IIa, Level B).	0	2	4		1	3
9. Duplex ultrasonography is one of primary imaging modalities that can be performed in patients in whom peripheral arterial occlusive disease is suspected for purpose of confirmative diagnosis (Class I, Level B).	1			2	1	3
10. Duplex ultrasonography is useful for purpose of identifying location and extent of lesions in patients with peripheral arterial occlusive disease (Class I, Level A).	5		4		1	3
11. Duplex ultrasonography is useful as follow-up imaging modality for evaluation of patency of lower extremity arteries recanalized by intervention (Class IIa, Level B).	1			2	2	
12. Computed tomography angiography is very useful for identifying location and extent of lesions in patients with peripheral arterial occlusive disease (Class I, Level B).	5					
13. Computed tomography angiography may be considered as substitute for magnetic resonance angiography for those patients with contraindications to magnetic resonance angiography (Class I, Level B).	1					
14. Magnetic resonance angiography can be conducted for purpose of evaluating location and degree of lesions in patients diagnosed with peripheral arterial occlusive disease (Class I, Level B).	5	1	2	3		
15. Magnetic resonance angiography is also useful as standard test for determining target patients for interventional recanalization (Class I, Level B).	1	1	2	1		
16. During magnetic resonance angiography, it is desirable to obtain images using contrast medium (Class I, Level B).	1					
17. Magnetic resonance angiography is useful as follow-up imaging modality for evaluation of patency of lower extremity arteries recanalized by intervention (Class IIa, Level B).	1				1	4
18. It is desirable to perform angiography on assumption of vascular recanalization rather than for diagnostic purpose (Class I, Level B).	3					

Table 4. Recommendation Data Extraction Form (Continued)

Recommendation	G	RCT	NRCS	SR/MA	NR	CS
19. By checking patient's medical history and laboratory tests before performing angiography, most appropriate puncture sites can be determined. Amount of contrast medium usage should be minimized as much as possible by performing selective angiography (Class I, Level C).	1					
20. If angiography of lower extremity artery needs to be performed, digital subtraction angiography is useful (Class I, Level A).	2					
21. If there is no significant improvement after conservative treatment in patients with intermittent claudication, recanalization should be considered (Class IIa, Level C).	5					
22. If there is lesion in aorto-iliac artery in patients with intermittent claudication, recanalization should be considered as primary treatment method (Class IIa, Level C).	2					
23. Recanalization should be performed for purpose of limb salvage for all technically possible lesions in patients with critical limb ischemia (Class I, Level A).	4					
24. In aorta-iliac arteries and femoral-popliteal arteries, interventional treatment should be considered first for TASC II A–C lesions (Class I, Level C).	1		1			
25. In aorta-iliac arteries and femoral-popliteal arteries, interventional treatment may be considered first for TASC II D with severe co-morbidities (Class IIb, Level C).	1					
26 When remaining life is less than 2 years or autogenous vein is not available for bypass surgery, angioplasty is proper method to increase distal blood flow in patients with critical limb ischemia (Class IIa, Level B).	1	2	1			2
27. In patients with infrapopliteal artery occlusive disease, interventional treatment should first be considered for critical limb ischemia (Class IIb, Level B).	2	1				
28. Assessment of risk of contrast medium-related acute renal injury should be performed prior to procedure in all patients (Class I, Level C).					1	
29. Patients should be supplied with adequate fluids before procedure (Class I, Level B).		2	1			
30. Usage of contrast medium should be minimized in chronic renal disease (eGFR < 60 mL/min or sCr ≥ 1.4 mg/dL) (Class I, Level B).				1	3	
31. Aspirin (75–325 mg/d) and clopidogrel (75 mg/d) combination therapy is recommended as most safe and effective antiplatelet therapy before procedure (Class I, Level B).	2					
32. When stenosis is more than 75% of diameter in patients with intermittent claudication, interventional treatment can be performed, and when the stenosis is 50–75% of diameter, physician should judge by measuring intra-arterial pressure during resting phase or after using vasodilator (Class I, Level C).	2					
33. During infrapopliteal artery recanalization in patients with critical limb ischemia, figuring out location of wound and state of blood vessels supplying blood flow to wound with concept of angiosome should be considered first when establishing procedure plan (Class IIa, Level B).			1	1	1	
34. During infrapopliteal artery recanalization in patients with critical limb ischemia, recanalization of more than one other artery that serves as at least collateral circulation is necessary because recanalized artery is frequently re-occluded (Class IIb, Level C).					1	
35. If inflow lesions and outflow lesions of lower extremity artery coexist, recanalization of inflow lesions should be performed first (Class I, Level C).	1					
36. When symptoms continue even after recanalization of inflow lesions in patients with both inflow and outflow lesions, recanalization of outflow lesions should be performed (Class I, Level B).	1					
37. If it is not clear whether hemodynamically significant inflow disease exists, intra-arterial pressure of each suprainguinal lesion should be measured before and after vasodilator infusion (Class I, Level C).	1					

Table 4. Recommendation Data Extraction Form (Continued)

Recommendation	G	RCT	NRCS	SR/MA	NR	CS
38. If short-term and long-term outcome is similar and there is no difference in co-morbidities in patients with critical limb ischemia accompanied by ipsilateral femoro-popliteal artery lesion and infrapopliteal artery lesion, angioplasty is recommended first (Class IIa, Level C).	2					
39. Primary stent placement is first considered in long segment stenosis or complete occlusion of common and external iliac artery (Class I, Level A).	2	1		1		
40. Bailout stent placement is performed in cases with more than 5 mm Hg pressure difference crossing lesion, more than 30% residual stenosis, or flow-limiting intimal dissection after balloon angioplasty (Class IIa, Level C).	2					
41. Kissing stent can be considered first in cases where degree of risk for aorto-bifemoral bypass surgery is significant in stenotic or occlusive lesions involving aortic bifurcation and bilateral common iliac artery (Class IIb, Level C).						8
42. Primary stent placement is not recommended for short segments of femoral-popliteal artery (Class III, Level A).	1	7		1		1
43. Bailout stent placement is recommended when there is residual stenosis of more than 30% or flow-limiting dissection after balloon angioplasty (Class IIa, Level C).	1					
44. Subintimal balloon angioplasty can be performed to improve limb salvage rate in patients who have limitations in surgical treatment and who also have occlusive lesions longer than 10 cm in femoro-popliteal artery (Class IIb, Level C).				2		1
45. Efficacy of drug-eluting stent, atherectomy, cutting balloon angioplasty, and laser therapy in interventional treatment of femoro-popliteal artery has not been established yet (Class IIb, Level A).	1	9			1	
46. Angioplasty with drug eluting balloons had good patency rate compared to plain old balloon angioplasty, but clear clinical effect has not been proved yet with respect to cost and risk of bailout stent placement (Class IIb, Level A).		3	1			
47. During infrapopliteal angioplasty, guide wire passage into true lumen of lesion is primarily attempted for stenotic lesions (Class IIb, Level A).					1	3
48. During infrapopliteal angioplasty, intraluminal guide wire passage at proximal part of lesion is primarily attempted for calcified complete occlusion lesions, and if fails, tandem subintimal guide wire passage is attempted (Class IIb, Level B).					1	6
49. Primary stent placement in infrapopliteal arteries is not desirable, but it can be considered as bailout method after balloon angioplasty (Class IIa, Level A).		6	3	4	1	5

CS = case series study, G = guideline, NR = non-systemic narrative review, NRCS = non-randomized controlled study, RCT = randomized controlled study, SR/MA = systemic review/meta-analysis

arteries to associated academies, namely the Korean Society of Interventional Cardiology and the Korean Society for Vascular Surgery, panels with representatives and expertise from the associated academies were assigned evenly. The panel was composed of 36 members (the KSIR, 15; the Korean Society of Interventional Cardiology, 9; and the Korean Society for Vascular Surgery, 12). Members of the guideline development committee, who were involved in the deduction of clinical questions and recommendations during the process of developing the guidelines, were excluded. To assist the panel, the recommendation data extraction form and related references were provided by e-mail. The vote was performed anonymously. After sending the disclosure sheet on conflict of interest to all panel members, the members signed the document confirming that they did not receive any support from interest groups related to the recommendation. The degree of consensus was quantitatively analyzed using a 9-Likert scale (1, strongly disagree; 9, entirely agree). In the response scale, 7–9 points were considered to agree with the recommendations. When more than 70% of the panel agreed, the proposal of recommendations was considered to have reached consensus. For recommendations without consensus, a second round of voting was conducted after

providing all information to panelists through an online discussion session on matters that required clarification. If an agreement was not reached, the recommendations were rejected. Twenty five out of 36 panel members participated in the vote (the KSIR, 12; the Korean Society of Interventional Cardiology, 4; the Korean Society for Vascular Surgery, 9). During the first round of voting, one recommendation did not meet the agreement condition. The agreement condition for a different recommendation was barely met, but with many disputes. After providing all information, re-voting was conducted, but the two recommendations did not reach agreement.

Guideline Drafting

Based on the adopted recommendations, the writing committee members assigned to specific sub-themes wrote a guideline draft.

Review and Guideline Determination Process

The editing committee evaluated the written guideline draft based on the selected recommendations. The guidelines were internally evaluated through an expert advisory conference to discuss the expertise of relevant academies associated with the guideline including problems in the recommendations, background and description of the evidence, etc. After the guidelines were determined by internal evaluation, the final guidelines were established through a public hearing with the relevant field experts and stakeholders.

CONTENTS

Diagnosis of Peripheral Arterial Occlusive Disease

Peripheral arterial occlusive disease should be diagnosed from a combination of the patient's symptoms, physical, hemodynamic, and vascular imaging examination. Symptoms are intermittent claudication and critical limb ischemia (CLI). Diseases that need to be distinguished from intermittent claudication are chronic compartment syndrome, venous claudication, nerve root compression, Baker's cyst, spinal stenosis, arthritis of foot and ankle etc. CLI should be differentiated from diabetic neuropathy, complex regional pain syndrome, nerve root compression, night cramp, and Buerger's disease. Physical examination includes blood pressure in both arms, cardiac sound, color and temperature of foot, the presence of leg muscle atrophy, loss of leg hair, palpation of femoral artery, radial

artery, ulnar artery, brachial artery, carotid artery, popliteal artery, dorsalis pedis artery and posterior tibial artery.

Hemodynamic Examination

Ankle Brachial Index

The ankle brachial index (ABI) is the ratio of the ankle artery blood pressure to the patient's arm blood pressure. ABI is the simplest and most non-invasive examination among the tests available for the diagnosis of PAOD because blood pressure is easily measured at the same time in both arms and ankles using a cuff. Therefore, ABI can be used as a screening test for PAOD.

Resting ABI should be measured in all patients with intermittent claudication or incurable foot wounds, all patients aged 50–69 years with diabetes or smoking history, and all persons over the age of 70 (1-6).

The possibility of wound healing and limb salvage as well as patient survival can be predicted to some extent through ABI. ABI is useful as an evaluation index of the therapeutic effect of interventional recanalization of lower extremity arteries. ABI is also measured to assess basic status in patients who are already diagnosed with PAOD.

The method of ABI measurement is as follows. Systolic blood pressure is measured using a cuff enclosing each brachial artery, dorsalis pedis artery, and posterior tibial artery in both the right and left side with the patient lying down. The same cuff should be wrapped around all four arteries and a cuff with a 10–12 cm width is usually used (1). A hand held Doppler is recommended to detect blood flow, but plethysmography or a stethoscope, and automatic blood pressure measurement devices can also be used. Higher brachial pressure in either arm and higher ankle pressure in the dorsalis pedis artery and the posterior tibial artery are considered variables for ABI (1, 3). Under normal conditions, ankle blood pressure is 10–15 mm Hg higher than that of the brachial artery, so ABI should be more than 1.00. If the resting ABI is less than 0.9, PAOD can be diagnosed with 95% sensitivity and 100% specificity (7).

Ankle blood pressure is higher than normal when the blood vessel is not compressed because of severe calcified sclerosis of the arteries caused by diabetes, old age or dialysis. As a result, additional tests should be required for patients with diabetes, old age, and those receiving dialysis, because it is difficult to diagnose PAOD or determine its severity in these patients using only ABI. ABI greater than 1.4 can be attributed to the severe calcified

ankle artery and additional tests are required. Typical tests that can be added are toe brachial index (TBI), pulse volume recording (PVR), transcutaneous oxygen pressure, and vascular imaging examination (1, 3). Toe pressure is usually measured by placing the cuff around the big toe or the second toe and attaching a blood volume measurement instrument to the tip of the toe. TBI is obtained by comparing with brachial pressure, similar to the ABI. The normal range of TBI is more than 0.7 and under 0.7 may indicate PAOD (1, 3).

Recommendation

1. Ankle brachial index is useful as a screening test for peripheral arterial occlusive disease (Class I, Level A).
2. In patients who are already diagnosed with peripheral arterial occlusive disease, it is necessary to measure the ankle brachial index to evaluate their basic condition (Class I, Level B).
3. The ankle pressure is high and the credibility of the ankle brachial index is low when the artery is not compressed because of severe calcified sclerosis. In this situation, toe brachial index is useful for diagnosis of peripheral arterial occlusive disease (Class I, Level B).

Segmental Limb Pressure

Segmental limb pressure (SLP) can be used to measure arterial blood pressure divided into several segments from thigh to ankle. Systolic blood pressure is measured by wrapping a cuff around four areas (upper thigh, lower thigh, upper leg, and ankle) then inflating and deflating each cuff in a manner similar to when measuring ankle blood pressure. In some cases, measurements may be performed with only three areas (thigh, upper leg, ankle).

Measuring SLP is very helpful for establishing a treatment plan because the approximate location of lesions can be estimated. A significant difference in blood pressure between the brachial and upper thigh indicates lesions in the aorta and iliac artery, a difference between the upper thigh and lower thigh indicates lesions in the superficial femoral artery, a difference between the lower thigh and upper leg indicates lesions in the distal superficial femoral artery or popliteal artery, and a difference between the upper leg and ankle indicates stenosis of the infrapopliteal artery (1, 3).

Recommendation

1. Segmental limb pressure measurement is a useful diagnostic test because it helps to determine the approximate location of lesions and helps to establish an appropriate treatment plan (Class I, Level B).

Pulse Volume Recording

Pulsatile arterial inflow to the limbs causes periodic changes in blood volume in the leg. PVR is used to measure this change. Plethysmography is a device that records volume changes in organs or limbs. According to the measurement method, it is classified into: pneumoplethysmography, a recording wave formed by converting the volume change of air injected into the pneumatic cuff into pressure, photoplethysmography, which detects color changes in skin that occur with the cardiac beat using infrared sensors on the skin, and strain gauge plethysmography, displayed as a wave form by converting the volume change of the limb concurrent with the cardiac beat into electrical resistance using a thin rubber tube filled with mercury or indium-gallium. Among these, pneumoplethysmography is most commonly used.

Using plethysmography, not only can SLP be measured but PVR can also be obtained. In general, it senses volume changes and produces a wave form when the pressure is increased to 65 mm Hg by the injection of a suitable amount of air measured by the pneumatic cuff. Change in pressure according to volume changes in the measured part is calculated by a formula. It is similar to the change in arterial blood pressure, and can estimate the degree of arterial occlusion through the change in the wave form and amplitude.

Normal PVR is similar to the artery waveform and consists of rapid systolic up-stroke, rapid down-stroke, and prominent dicrotic notch. If the degree of arterial occlusion is severe, the waveform is weakened, the slope becomes flat, the width becomes wide and the dicrotic notch disappears. PVR can determine the approximate location of the lesion because it is measured on each segment of the limbs and can also determine the degree of stenosis through waveform analysis. Thus, it is a useful test not only for early diagnosis of PAOD but also to assess the state after revascularization (7). It is also a useful test in the case of severe calcification because change in volume according to blood flow is not associated with the presence of calcification on the vascular wall (3).

Recommendation

1. Pulse volume recording is a useful test for not only early diagnosis of PAOD but also to assess the state after revascularization because it is able to identify the approximate location and degree of the lesion (Class IIa, Level B).

Exercise Test

The exercise test is useful for identifying decreases in arterial pressure caused by stenotic lesions that are not apparent in the resting phase due to collateral flow by increasing blood flow demand in the leg muscles with exercise. The exercise test is helpful for diagnosis when resting ABI is normal in patients in whom PAOD is suspected. It is also helpful for evaluating how much the leg function of a patient with PAOD is limited and how much function is recovered after treatment. Furthermore, it enables differentiation of claudication caused by PAOD from other causes, and can also provide personalized data for exercise treatment that may be needed in the future (3). An exercise test should be carried out by a protocol defined under the strict surveillance of the patient's condition, and patients should have knowledge about potential symptoms that may occur during the test.

The treadmill is employed universally as an exercise load method. The patient is tested by walking until pain occurs (up to 5 minutes) at the speed of 3.2 km/hr (2 mile/hr) and with a 10–12% slope. If treadmill exercise is not possible, climbing stairs or walking down the aisle can be used. If the patient cannot move, other methods that involve repeating active pedal plantar flexion or inducing reactive hyperemia by blocking blood flow in the thigh using a cuff for 3–5 minutes until the pressure exceeds systolic arterial pressure and then letting it flow (1).

In the resting phase, initial ABI is measured and ABI is measured again after the patient exercises. A decrease in ABI of 15–20% after exercise would be indicative of PAOD (1).

Recommendation

1. The exercise test may be performed to diagnose peripheral arterial occlusive disease when resting ankle brachial index is normal in patients in whom peripheral arterial occlusive disease is suspected (Class I, Level B).
2. The exercise test may be performed in order to objectively assess how much a patient's leg function

is limited and how much function is recovered after treatment (Class I, Level B).

Transcutaneous Oxygen Pressure

Transcutaneous oxygen pressure is a test for directly measuring the diffusion of oxygen in the blood stream passing through the skin by attaching a probe to the skin. Ultimately, it is a test that reflects microcirculation in the skin rather than a measurement of blood pressure in the foot. Therefore, it can evaluate whether blood flow and oxygen are properly supplied to the wound site in CLI or not. It can also assess whether blood flow to the wound site is sufficiently restored for wound healing after recanalization (8). In cases where amputation is inevitable, it is also measured in order to predict wound healing on the amputated limb (9).

Recommendation

1. The measurement of transcutaneous oxygen pressure can be used to evaluate the degree of oxygen supply to the feet or around a wound and whether the oxygen supply is improved after recanalization in patients with critical limb ischemia (Class IIa, Level B).

Vascular Imaging Examination

Duplex Ultrasonography

Duplex ultrasonography (DUS) is a fast and non-invasive diagnostic modality that can be directly applied in outpatient clinics or at the bedside. It has several advantages including direct visualization of the arterial wall using gray scale imaging, observation of blood flow using color Doppler and power Doppler, measurement of blood flow, and assessment of the degree of stenosis through Doppler waveform analysis. The sensitivity and specificity of DUS are 90% and 95%, respectively for diagnosis of stenosis with a diameter of more than 50%. Thus, DUS can be used as a primary imaging test for definite diagnosis for patients in whom PAOD is suspected (10, 11). Furthermore, DUS is also useful for evaluating the anatomical location and degree of stenosis (12). On the basis of DUS information, interventional recanalization of lower extremity arteries or bypass surgery can be performed. However, the results can be different depending on the examiner's skill and experience, and it is difficult to evaluate the iliac artery, which is located in a deep place and hidden by the intestine. There is also a limitation for evaluating vessels

with severe calcification and multiple stenotic lesions. The sensitivity of DUS is too low at 60–65% for finding stenotic lesions in the lower extremities of patients with multiple stenotic lesions. Therefore, other imaging modalities are needed to detect these lesions according to the situation in many cases. DUS is considered useful as a follow-up imaging modality of lower extremity arteries recanalized by intervention (10), but whether it improves long-term patency has not yet been fully validated.

Recommendation

1. Duplex ultrasonography is one of the primary imaging modalities that can be performed in patients in whom peripheral arterial occlusive disease is suspected for the purpose of confirmative diagnosis (Class I, Level B).
2. Duplex ultrasonography is useful for the purpose of identifying the location and extent of lesions in patients with peripheral arterial occlusive disease (Class I, Level A).
3. Duplex ultrasonography is useful as a follow-up imaging modality for the evaluation of patency of lower extremity arteries recanalized by intervention (Class IIa, Level B).

Computed Tomography Angiography

With the introduction of multidetector computed tomography (CT), scan time is shorter and the occurrence of artifacts is minimized. Therefore, vascular imaging using CT has been dramatically improved by the introduction of three-dimensional images. CT angiography (CTA) has advantages in that it can observe surrounding tissue, images comparable to angiography can be obtained with three-dimensional reconstruction, and it is possible to evaluate the entire blood vessel at a glance as well as to perform a detailed analysis of the blood vessel wall and lumen through tomography (13, 14).

In the initial study using a single detector, in cases of stenosis with more than 50% diameter in the lower extremity artery, sensitivity was 89–100% and specificity was 92–100% (13, 14). According to a meta-analysis published in 2009, the sensitivity for iliac artery stenosis with more than 50% diameter was 93–100%, the sensitivity and specificity for femoral-popliteal artery stenosis with a diameter of more than 50% were 96% and 98%, respectively (15). Thus, CTA is very useful for determining the location and severity of lesions in patients with PAOD.

However, it has a disadvantage in that it is difficult to analyze lesions with severe calcification of the blood vessel wall, and analysis of small arteries of the foot is limited. As there are nephrotoxicity in accordance with contrast medium injection and radiation exposure, it is barely suitable as a screening test for PAOD. However, it can be performed as a secondary test in patients in whom PAOD is suspected and it can also be performed for the purpose of evaluating the location and degree of lesion prior to treatment.

Recommendation

1. Computed tomography angiography is very useful for identifying the location and extent of lesions in patients with peripheral arterial occlusive disease (Class I, Level B).

Magnetic Resonance Angiography

With the development of magnetic resonance imaging technology, it is possible to obtain a good image of the lower extremity artery comparable to angiography and CTA. For the image acquisition of proper magnetic resonance angiography (MRA) around the lower extremity artery, a high magnetic field, use of the appropriate coil, and fast image acquisition sequence is necessary. Also, contrast medium should be used when the image is obtained.

Compared to digital subtraction angiography, the sensitivity (93–100%) and specificity (93–100%) were very high. Therefore, it can be performed for the purpose of evaluating the location and severity of lesions in patients with PAOD. It can also be used as a standard test to determine target patients for interventional recanalization (16, 17). Furthermore, it is useful to evaluate lesions that underwent recanalization. Compared to angiography, the sensitivity and specificity for detecting anastomosis site stenosis after bypass surgery were both excellent at 90–100%. The accordance rate of angiography to identify re-stenosis after interventional recanalization was also excellent at 80–95% (18, 19).

There are some disadvantages: the lesion is likely to be overestimated, calcification is not detected, and imaging analysis is difficult because of artifacts in the presence of a metal, etc. The usefulness of the technique can therefore be limited in patients with metal objects (such as cardiac pacemaker, implantable cardioverter defibrillator, neurostimulator, and cochlear implant) transplanted. There is also a disadvantage in that contrast medium usage is limited in severe renal failure patients.

Angiography

Angiography is a standardized test for vascular imaging that most accurately represents the state of the arterial lumen. However, since it is an invasive procedure and complications associated with arterial puncture and contrast medium may occur, it is desirable to perform on the assumption of treatment rather than for a diagnostic purpose (1-3). There are several indications of diagnostic purpose: in cases where a non-invasive vascular imaging test is limited because of artifacts caused by vascular calcification, in cases where the patient's position and state is not suitable for non-invasive vascular imaging tests, and cases where each branch of the arteries should be observed in detail for skin flap transplantation, etc. These criteria should be determined by the attending physician in charge.

Angiography has several disadvantages as follows; it is difficult to evaluate the entire leg arterial system, it cannot directly observe the wall of the artery, and three-dimensional analysis of the blood vessel is difficult. Thus, it is desirable to use in concert with non-invasive vascular imaging techniques. Therefore, tests such as CTA are recommended before performing angiography to determine the overall position and severity of lesions and to evaluate the surrounding tissue, perform three-dimensional analysis of the lesions, and determine collateral flow. This can be very helpful prior to angiography and recanalization using a less invasive and planned method (3).

It is good to obtain images with digital subtraction angiography whenever possible for lower extremity arteries (1, 3). When performing angiography, the medical history of patient's contrast medium-related side effects and renal function should be checked and the use of contrast medium should be minimized (3).

Indications for Recanalization of Peripheral Arterial Occlusive Disease

Asymptomatic PAODs usually do not require prophylactic recanalization and only symptomatic PAOD patients are the subjects of recanalization (2).

Intermittent Claudication

The treatment of patients with intermittent claudication is focused on improving prognosis and symptoms through appropriate risk factor regulation. Treatment methods for relieving symptoms can be separated into non-invasive treatments such as medication or exercise treatment and invasive treatments such as surgery or interventional recanalization. The primary treatments are exercise under supervision and medication treatment including risk factor improvement and antiplatelet therapy. As the number of interventional treatments for the purpose of increasing walking distance without a break increases, a comparative study of exercise under supervision is needed.

In a recent randomized controlled trial involving 151 patients with intermittent claudication, there was no significant difference in the quality of life at 12 months after recanalization (20). When additional interventional treatment was performed in patients with mild to moderate claudication with the best medical treatment and exercise under supervision, there was no difference in the quality of life after 2 years, but walking distance increased compared to the group that did not receive additional interventional treatment (femoro-popliteal artery lesions increased by 38%, aorto-iliac lesions increased by 78%) (21).

In the CLEVER study, exercise under supervision had better results in improving treadmill performance ability compared to a primary stent, but the actual quality of life was much better in the stent group, so further research is needed (22). Thus, when there is no improvement of symptoms

after performing conservative treatment over 3–6 months in intermittent claudication patients, the exact location and nature of the lesion should be identified through imaging examination and recanalization should be considered as needed (1-5). However, interventional recanalization can be considered for aorta-iliac artery lesions without a wide range of medical treatments (1, 2). Lesions of infrapopliteal arteries in intermittent claudication patients are not an indication for recanalization.

Recommendation

1. If there is no significant improvement after conservative treatment in patients with intermittent claudication, recanalization should be considered (Class IIa, Level C).
2. If there is lesion in the aorto-iliac artery in patients with intermittent claudication, recanalization should be considered as a primary treatment method (Class IIa, Level C).

Critical Limb Ischemia

Critical limb ischemia refers to the presence of ischemic resting pain, ischemic ulcerated lesion or gangrene. The primary goal of treatment is to improve the patient's function and quality of life and to increase the chance of survival by relieving ischemic pain, healing ischemic ulcers, and preventing amputation of lower limbs (1).

Critical limb ischemia is a chronic condition, so it should be distinguished from acute limb ischemia. Ankle blood pressure less than 50 mm Hg is recommended as a diagnostic criterion, which means that symptoms cannot be improved without recanalization (2). Therefore, recanalization should be considered immediately in patients with CLI and should be performed by multidisciplinary consensus after clinical and imaging examination.

Recommendation

1. Recanalization should be performed for the purpose of limb salvage for all technically possible lesions in patients with critical limb ischemia (Class I, Level A).

Indications for Interventional Recanalization of Peripheral Arterial Occlusive Disease

Intermittent Claudication

There is still controversy on whether to choose either interventional or surgical recanalization of PAOD because of the lack of a randomized controlled trial. The reason for the lack of a randomized controlled trial is that it is difficult to perform direct comparative research between two groups because the devices and technology used for interventional treatment are rapidly developing.

The selection of a proper treatment method for the recanalization of the lower extremity artery is determined depending on anatomic lesions, co-morbidities, doctor's expertise and patient's choice.

According to anatomical position, interventional treatment is primarily recommended for TASC II A– C of lesions in aorta-iliac arteries (1). In this case, interventional treatment shows a success rate of more than 90% with low morbidity and mortality. However, the main limitation of recommendations for interventional treatment is that there are no randomized controlled trials reported by comparing two groups. According to a limited report, there was a study showing that the iliac artery stent procedure resulted in better patency rates than surgical treatment (23). In cases of TASC II D lesion, interventional treatment can be attempted first if the operator has lots of experience and severe co-morbid diseases are also present (1).

In femoro-popliteal artery cases, interventional treatment is often selected first for even long and complex lesions due to technological developments, the increase in operator experience and low risk of the procedure. Therefore, interventional recanalization is recommended for TASC II A–C of lesions in femoro-popliteal arteries. It can also be attempted first if there are interventionists with lots of experience as well as in the presence of severe co-morbidities (1).

Recommendation

1. In aorta-iliac arteries and femoral-popliteal arteries, interventional treatment should be considered first for TASC II A–C lesions (Class I, Level C).
2. In aorta-iliac arteries and femoral-popliteal arteries, interventional treatment may be considered first for TASC II D with severe co-morbidities (Class IIb, Level C).

Critical Limb Ischemia

The choice of interventional recanalization or surgical recanalization in patients with CLI is still debated. There is only one randomized controlled study related to this problem called Bypass versus Angioplasty in Severe Ischemia of the Leg (BASIL). In this study, there was no difference in limb salvage rate for the first 3 years between the

interventional treatment group and the surgical treatment group (1 year, 68% vs. 71%; 3 years, 57% vs. 52%). In follow-up observation for more than 3 years, patients who underwent bypass surgery showed higher amputation-free survival and overall survival than patients who received interventional treatment (24, 25). However, less invasive angiography can be a solution in cases where the patient's remaining life is less than 2 years, the autogenous vein is not available for bypass surgery, and there is a wound accompanied by complications.

Most patients with CLI and infrapopliteal artery occlusive diseases have multi-level concomitant lesions. Therefore, the treatment purpose for these lesions is mostly limb salvage and there is no goal to treat claudication. There is growing evidence supporting the salvage of limbs by first performing interventional treatment in patients with CLI and by allowing direct blood flow to the foot through at least one infrapopliteal artery (26).

Recommendation

1. When remaining life is less than 2 years or autogenous vein is not available for bypass surgery, angioplasty is a proper method to increase distal blood flow in patients with critical limb ischemia (Class IIa, Level B).
2. In patients with infrapopliteal artery occlusive disease, interventional treatment should first be considered for critical limb ischemia (Class IIb, Level B).

Patients Care before Interventional Procedure

Contrast Medium-Related Nephrotoxicity

Contrast medium-related renal injury is the most common cause of iatrogenic acute renal injury and is defined when an increase of serum creatinine of more than 25% or 44 µmol/L occurs within 3 days after contrast medium is administered (27). In cases of chronic renal disease (estimated glomerular filtration rate [eGFR] < 60 mL/min or serum creatinine [sCr] ≥ 1.4 mg/dL), the risk of contrast medium-related nephrotoxicity is higher. Other important risk factors are as follows: age over 70 years, dehydration, diabetic nephropathy, congestive heart failure, gout, anemia, cirrhosis, taking nephrotoxic drugs, excessive use of contrast medium, and repeated use of contrast medium (28). Thus, for the prevention of contrast medium-related nephrotoxicity, renal function tests such as eGFR or serum creatinine should be performed within 7 days before interventional procedure in patients with risk factors. At

this time, if patient's renal function is abnormal (eGFR < 60 mL/min or sCr ≥ 1.4 mg/dL), proper action should be taken before the procedure. To prevent renal function deterioration caused by contrast medium in patients with poor renal function, the use of contrast medium should be minimized, alternatives (CO_2) to iodine contrast medium should be considered and proper management before the procedure should be ensured in order to preserve renal function (27, 28).

The standard management before the procedure is to supply sufficient fluid. Reasonable fluid therapy according to various studies is intravenous isotonic saline (1.0 to 1.5 mL/kg per hour) administration starting 3–12 hours before the procedure and administered continuously for 6–24 hours after the procedure (29). There are various opinions about the preventative effects of N-acetyl-L-cystein for contrast medium-related nephrotoxicity, but there were no preventative effects on renal toxicity in most large-scale randomized studies of Acetylcysteine for Contrast-Induced Nephropathy Trial (30). Therefore, pharmacological prophylaxis is not usually recommended because the evidence supporting the prevention of renal toxicity caused by contrast medium is insufficient (30).

Recommendation

1. Assessment of the risk of contrast medium-related acute renal injury should be performed prior to the procedure in all patients (Class I, Level C).
2. Patients should be supplied with adequate fluids before the procedure (Class I, Level B).
3. The usage of contrast medium should be minimized in chronic renal disease (eGFR < 60 mL/min or sCr ≥ 1.4 mg/dL) (Class I, Level B).

Pre-Procedure Medication

Aspirin (75–325 mg/day) and clopidogrel (75 mg/day) combination therapy is recommended as a safe and effective antiplatelet therapy before the procedure (3). To administer the two drugs before the procedure, the regimen to load aspirin up to 300 mg at least 3 days prior to the procedure or to administer clopidogrel 75 mg once a day up to three times a day etc. is carried out in various ways according to operators and institutions. However, it is recommended to take more than 100 mg of aspirin and more than 75 mg of clopidogrel beginning at least 2 days before the procedure.

Heparin is used to prevent thrombosis within blood vessels or around the catheter during the procedure.

Heparin (50–100 units/kg) is administered after puncture and it is administered additionally at 1000 units per hour. The sheath can be removed when activated clotting time (ACT) is less than 200 seconds. Even if ACT is more than 200 seconds, the sheath can be removed using the closing device if continuous administration of heparin after the procedure is necessary. To remove the effects of heparin due to bleeding complication, protamine should be administered. 1 mg of protamine can typically neutralize 100 units of heparin and up to 50 mg can be administered at a time (3).

Recommendation

1. Aspirin (75–325 mg/day) and clopidogrel (75 mg/day) combination therapy is recommended as the most safe and effective antiplatelet therapy before the procedure (Class I, Level B).

Establishment of Procedure Plan

Selection of Therapeutic Target Vessel

Securing proper inflow and outflow is essential to maintain the re-opening of the blood flow in any recanalization. For this, it is important to determine anatomical position, shape and degree of lesions with a variety of imaging techniques before treatment. When the lesion has more than 75% diameter stenosis in patients with intermittent claudication, interventional treatment can be performed. In cases with 50–75% diameter stenosis, it is useful to measure the pressure in both upper and lower arteries of the suspected area to confirm the significance. In particular, arterial pressure can evaluate clinical significance through quantification of hemodynamic changes in lesions. Systolic pressure gradient of more than 5–10 mm Hg in the resting phase or systolic pressure difference of more than 10–15 mm Hg after using the vasodilator is considered clinically significant (31). Using these methods, the need for the procedure with lesions where disturbance of blood flow is suspected can be determined as well as success or failure after the procedure.

The most important thing for establishing procedure plans for patients with CLI is the state and location of the wound in the foot of the patient at the time of referral and the state of lower extremity arteries corresponding to the wound. Among the arteries below the knee, the status of the anterior tibial artery and the posterior tibial artery is particularly important and if there are severe lesions in the two arteries, the status of the peroneal artery which serves as collateral circulation is also important. Introducing the concept of angiosome to determine the state of arteries below the knee which supply blood to the wound should be considered first when establishing a procedure plan (32).

By prioritizing blood vessels that need the procedure, recanalization of the most important blood vessels can be conducted. Furthermore, recanalization of more than one other artery that acts as at least collateral circulation is necessary because re-occlusion frequently develops (33).

Recommendation

1. When the stenosis is more than 75% of the diameter in patients with intermittent claudication, interventional treatment can be performed, and when the stenosis is 50–75% of the diameter, the physician should judge by measuring intra-arterial pressure during a resting phase or after using a vasodilator (Class I, Level C).
2. During infrapopliteal artery recanalization in patients with critical limb ischemia, figuring out the location of the wound and the state of blood vessels supplying blood flow to the wound with the concept of angiosome should be considered first when establishing a procedure plan (Class IIa, Level B).
3. During infrapopliteal artery recanalization in patients with critical limb ischemia, recanalization of more than one other artery that serves as at least collateral circulation is necessary because the recanalized artery is frequently re-occluded (Class IIb, Level C).

Treatment Plan of Multiple Lesions

There is a lack of evidence regarding the recanalization implementation principle for multiple lesions. However, according to the AHA/ACC Guidelines, recanalizing the inflow lesions first is recommended. If the symptoms persist despite the recanalization of inflow lesions, the recanalization of outflow lesions should be conducted (3). If it is not clear whether hemodynamically significant inflow disease exists, the intra-arterial pressure of the suprainguinal lesion should be measured before and after vasodilator infusion (3).

In patients with CLI and infrapopliteal artery lesions, the presence of associated proximal or distal part lesions is important for establishing a treatment plan. Even if the target infrapopliteal artery is properly re-opened, the patency rate may deteriorate in cases where there is flow disturbance of proximal parts such as in the iliac artery or

the femoral artery or where the blood flow below the ankle is not good. Thus, recanalization of associated proximal or distal lesions is needed.

In cases where lesions are localized in the infrapopliteal artery and are accompanied by lesions in the femoro-popliteal artery, each treatment plan is established differently. If there are also lesions in the femoral-popliteal artery, either all lesions are treated by angioplasty or a bypass surgery is performed for the femoral-popliteal artery lesions and angioplasty is used for the infrapopliteal lesions. This hybrid technique combining surgical bypass surgery and angioplasty has been spot-lighted and its usage is expected to increase. Even though the long-term patency rate of surgical bypass surgery is significantly superior to that of angioplasty for the treatment of femoral-popliteal artery lesions, angioplasty for femoro-popliteal artery lesions has many advantages in terms of lower morbidity, mortality and shorter hospital stay if the artery remains open for at least 6 months in CLI which is enough period for wound healing (34).

Recommendation

1. If inflow lesions and outflow lesions of lower extremity artery coexist, recanalization of inflow lesions should be performed first (Class I, Level C).
2. When the symptoms continue even after the recanalization of inflow lesions in patients with both inflow and outflow lesions, recanalization of outflow lesions should be performed (Class I, Level B).
3. If it is not clear whether hemodynamically significant inflow disease exists, the intra-arterial pressure of each suprainguinal lesion should be measured before and after vasodilator infusion (Class I, Level C).
4. If the short-term and long-term outcome is similar and there is no difference in co-morbidities in patients with critical limb ischemia accompanied by ipsilateral femoro-popliteal artery lesion and infrapopliteal artery lesion, angioplasty is recommended first (Class IIa, Level C).

Aorto-Iliac Artery Interventional Procedure

Balloon angioplasty and stent placement performed with reference to the TASC II classification are the most commonly used procedures for patients with clinical symptoms who also have hemodynamically significant lesions in the aorto-iliac artery. Stent placement is effective in iliac artery lesions because the long-term patency rate of

iliac artery stents is excellent. Iliac artery stents have low complication rates and the procedure is non-invasive.

Balloon Angioplasty

Becker et al. (35) reported the results of balloon angioplasty for iliac artery lesions after analyzing 2679 cases. The technical success rate was 92% and the 2-year and 5-year patency rates were 81% and 72% respectively. In the meta-analysis of balloon angioplasty compared to stent by Bosch and Hunink (36), the 4-year patency rates of stenotic lesion and occlusive lesion balloon angioplasty in the claudication patient group were 65% and 54%, respectively, while that of the stent was 77% and 61%, respectively. The 4-year patency rates of stenotic lesion and occlusive lesion balloon angioplasty in the CLI patient group were 53% and 44%, respectively, while that of stent was 67% and 53%, respectively. Thus, the stent group had a higher success rate and lower long term failure.

Lesions for which hemodynamically excellent results can be expected with only balloon angioplasty without complications are usually short lesion of less than 3 cm or concentric stenosis lesions. It is difficult to achieve favorable outcomes with balloon angioplasty alone for lesions accompanied by long segment stenosis or multiple stenosis, complete occlusion, severe calcifications because of frequently developed flow-limiting dissection or other complications. Stent placement is recommended for these lesions.

Stent Placement

Stent placement can be performed as a primary or selective procedure after angioplasty. The indication for selective stent placement is flow-limiting dissection or residual stenosis of more than 30%. Occasionally, blood pressure measurement in the proximal and distal part of the lesion is necessary in order to evaluate the exact hemodynamic significance of the residual lesion. The highest systolic pressure difference of 5–10 mm Hg (10–15 mm Hg after using a vasodilator) is considered a criteria for significant stenosis (31).

In the practical field and in most clinical cohort studies, angioplasty alone is often insufficient for complete occlusive lesions of the iliac artery and often increases the risk of distal embolization, arterial rupture and intimal dissection. Therefore, primary stent placement is preferred in order to reduce these risks. The most recent randomized clinical study reported that performing primary

stent placement rather than simple balloon angioplasty for occlusive lesions of the iliac artery can improve the technical success rate and reduce major complications (37).

Although predilatation before primary stent placement can be helpful for the procedure, a study reported that it is common to place stents without predilatation if there is no technical problem with stent advancement, and that doing so can reduce re-stenosis after the procedure (38). Primary stent placement is preferred in complex lesions such as eccentric, calcified, ulcerated plaque, and plaque with spontaneous dissection (39). Even though there is theoretical evidence supporting the reduction of distal embolization in these lesions by preventing the protrusion of the atherosclerotic plaque or intimal dissection, there is no direct evidence for the clinical effectiveness of primary stent placement according to the particular type of lesion.

According to the meta-analysis result, the long-term patency rate of primary stent placement was better than selective stent placement for common and external iliac artery cases (40). There are no differences reported yet between early and long-term patency rates according to specific stent products or materials and the mesh types used for stents. In a randomized study for a self-expandable stent made of nitinol and stainless steel, there was no difference in the 1-year patency rate, complications, and clinical symptoms. The advantages of a balloon-expandable stent are that radial stiffness is higher and precise placement is possible at the desirable location. Thus, it is generally preferred in cases of calcified lesions where elastic recoil is expected as well as cases in which eccentric plaque is located at the ostium of the common iliac artery and the external iliac artery (41). A self-expandable stent is preferred for lesions with long length, without severe calcification, and tortuous arterial course. Stents should be placed to include the entire lesion. Even if the stent is placed across the origin of the internal iliac artery, blood flow into the internal iliac artery is maintained.

During aorta and iliac artery stent placement, according to the TASC II guidelines for aorto-iliac occlusive lesions published in 2007, interventional treatment is preferred for A and B classifications, surgical bypass is preferred for D, and in the case of C, if the degree of surgical risk is low considering co-morbidities, surgery can be considered and interventional treatment can be carried out depending on the circumstances (1). However, according to recently published European Society of Cardiology (ESC) guidelines and AHA guidelines, in all cases of TASC II A–

C, interventional treatment is recommended as the primary treatment and surgical treatment is preferred for TASC II D (2, 3). Furthermore, it has been gradually established that the result of interventional treatment for TASC II D lesions can be close to surgery thanks to technological developments and accumulation of data (23).

In the meta-analysis of endovascular treatment for TASC II C/D lesions analyzing 958 patients in 16 articles, the technical success rate was 92.8% and the 1-year patency rate was 88.7%. When TASC II D was also analyzed separately among these patients, the technical success rate was 90.1% and 1-year patency rate was 87.3% (40). 19 non-randomized cohort analyses revealed that 5-year long-term follow-up results for extensive aortic-iliac artery occlusive disease showed more than 86% patency rate by considering secondary intervention, which is close to the surgical outcome (42). Interventional treatment has an advantage in that secondary intervention can be easily conducted even if the actual patency rate is slightly lower than for surgical bypass. As a result, the patency rate can be increased further so that the therapeutic effect of the lesion is close to the outcome of a surgical bypass.

A retrospective study regarding the 10-year patency rate based on the TASC II classification showed that there was no difference with stent placement between the TASC II A/B and TASC II C/D groups even though the long-term patency rate of the TASC II C/D group was lower than for the TASC II A/B group when only balloon angioplasty was conducted (43). The result of a large-scale randomized controlled trial for TASC II D has not yet appeared, and sufficient long-term results of studies with only the TASC II C/D group have not yet accumulated. However, considering the results so far, even in the case of TASC II C or D, interventional treatment can provide good long-term results in cases where there is concern about performing surgery due to the patient's general condition or co-morbidity.

Aorto-bifemoral bypass surgery has the best long-term patency rate for lesions involving the aorta and bilateral common iliac artery so far, but complications and mortality for surgery are higher than for interventional treatment. For interventional treatment of steno-occlusive lesions involving aortic bifurcation, the kissing stent technique is usually performed on both sides. The procedure is safe compared to surgery and the risk of complication is low. It has been reported that a 4-year patency rate was 81% for aorto-iliac artery bilateral kissing stenting (44).

Surgical bypass is recommended for Leriche disease,

which is a complete occlusion of the aorto-biiliac artery according to TASC II. Stent placement in Leriche disease was reported to have a 1-year patency rate of 85% and a 3-year patency rate of 66% (45), which is lower than the 86% 5-year patency rate for aorto-bifemoral bypass surgery. A large-scale randomized controlled trial has not yet been reported, but considering the results so far, the long-term patency rate for stent placement in Leriche disease appears to be lower than for surgical treatment. However, due to the safety and lower risk of complication, stent placement can be considered as a treatment method in patients with high risk of surgery. However, large-scale studies are needed before broader agreement can be reached.

Recommendation

1. Primary stent placement is first considered in long segment stenosis or complete occlusion of the common and external iliac artery (Class I, Level A).
2. Bail-out stent placement is performed in cases with more than 5 mm Hg pressure difference crossing the lesion, more than 30% residual stenosis, or flow-limiting intimal dissection after balloon angioplasty (Class IIa, Level C).
3. Kissing stent can be considered first in cases where the degree of risk for aorto-bifemoral bypass surgery is significant in stenotic or occlusive lesions involving aortic bifurcation and the bilateral common iliac artery (Class IIb, Level C).

Femoro-Popliteal Artery Interventional Procedure

Surgical bypass is known as the gold standard of treatment in stenotic or occlusive lesions in the femoro-popliteal artery. The best results can be expected when using the greater saphenous vein as the conduit rather than an artificial graft. According to a multicenter randomized controlled trial of the BASIL study, the comparison results of primary angioplasty and bypass surgery showed that there was no difference in amputation-free survival until 6 months. However, in the group that survived more than 2 years after the first treatment, overall survival and amputation-free survival were better in the bypass surgery group (25). Therefore, there was no evidence that interventional treatment showed results close to bypass surgery.

According to the AHA and ESC guidelines, treatment for the femoro-popliteal artery is recommended based on TASC II classifications. Interventional treatment is recommended

for stenotic lesions of less than 10 cm in length and occlusive lesions of less than 5 cm in length (2, 3). Initial outcome and long-term results of interventional treatment for the femoro-popliteal artery are not good compared to the iliac artery because there are many factors that have an adverse effect on the results of interventional treatment such as a lot of mechanical and physical stress in the femoro-popliteal artery. Furthermore, there are many problems resulting from co-morbidities at other sites including cardiovascular, cerebrovascular and renal arteries. Therefore, many types of therapeutic techniques have been studied to overcome these problems.

Balloon Angioplasty

Balloon angioplasty in the femoro-popliteal artery is the most widely used interventional treatment. The meta-analysis results of balloon angioplasty analyzing 923 cases in 19 articles showed that the procedure success rates of stenosis and occlusion were 98–100% and 81–94%, respectively, in the intermittent claudication patient group and 69–88% and 62–75%, respectively, in the CLI patient group. The 3-year patency rates of stenosis and occlusion were $61 \pm 2.2\%$ and $48 \pm 3.3\%$, respectively, in the intermittent claudication patient group and 43% and 30%, respectively, in the CLI patient group (46).

According to Hunink et al. (47), the 5-year patency rate was 45% for balloon angioplasty of the femoro-popliteal artery, 73% for bypass surgery using veins, and 49% for bypass surgery using polytetrafluoroethylene (PTFE), which is an artificial blood vessel. Therefore, the long-term patency rate of balloon angioplasty in the femoro-popliteal artery was lower compared to that of surgical bypass using veins. In particular, it was reported that the 1-year patency rate was much lower if the length of the lesion was greater than 10 cm. Furthermore, complete occlusive lesion and CLI patients had worse outcomes than simple stenosis and claudication patients. The incidence of restenosis was also high for diabetes patients as well as for those with renal failure and poor distal run off arteries (48).

Subintimal Balloon Angioplasty

In the meta-analysis of subintimal balloon angioplasty for the femoro-popliteal artery and arteries below the knee in 23 articles, the technical success rate was 80–90%, the clinical success rate was 50–70%, the occurrence rate of procedure-related complications was 8–17% (mild in most cases), the 1-year follow-up primary patency rate was

50%, and limb salvage rate was 80–90% (49). Therefore, there was no evidence that the patency rate of subintimal balloon angioplasty was better than that of intraluminal balloon angioplasty. There was a report that a stent was placed in subintimal space to improve the primary patency rate of subintimal balloon angioplasty, which showed good outcomes with a technical success rate of 91.4% and a 3-year limb salvage rate of 88.7%, However, subintimal stent placement could not increase the long-term patency rate significantly and the 1, 2, and 3-year patency rate were 80.1%, 42.3%, and 29%, respectively. In particular, long-term patency is not favorable in patients with multiple stenting (50). Although the patency rate of subintimal balloon angioplasty appears low, it is a useful technique in that it provides the opportunity to reopen blood vessels in occlusive lesions with long length. And as limb salvage rate appears relatively higher compared to patency, it has been accepted as a useful treatment for limb salvage in CLI patients.

Recommendation
1. Subintimal balloon angioplasty can be performed to improve limb salvage rate in patients who have limitations in surgical treatment and who also have occlusive lesions longer than 10 cm in the femoro-popliteal artery (Class IIb, Level C).

Stent Placement

Various types of stents have been used in femoro-popliteal artery lesions. Femoral-popliteal artery stents had a ground breaking improvement in patency rates during the switch from stainless steel stents to laser-cutting nitinol stents. In a retrospective study comparing 104 nitinol stent placements with 123 stainless steel stent placements among 175 patients with femoro-popliteal artery disease, there was a significance difference in patency rate between the two stents. The 1-year and 2-year patency rates in the nitinol stent group were 75% and 69%, respectively and those in the stainless steel stent group were 54% and 34%, respectively. However, there was no difference in patency rates between different types of nitinol stents (51). However, stent placement leaves a foreign body in a blood vessel and restenosis can occur due to neointimal hyperplasia caused by the stent. Furthermore, stent fracture or deformation is likely to occur because the femoral-popliteal artery tends to receive a large amount of stress constantly and this is accompanied by limb exercise such as walking, sitting, bending, and twisting.

Stents can be placed in the femoro-popliteal artery lesions either primarily or for a salvage purpose in the case of lesions that are not resolved by balloon angioplasty or when hemodynamic problems occur immediately after balloon angioplasty (1). However, there is no clear evidence on which femoro-popliteal artery lesions are suitable for primary stenting.

A number of randomized studies on primary stent placement have reported that primary stent placement is not necessary for short lesions, because there is no significant difference in terms of patency rate compared to balloon angioplasty during the long-term follow-up period. In a clinical trial involving 154 patients with intermittent claudication or CLI of less than 5 cm in lesion length randomized to balloon angioplasty or balloon-expandable stent placement, there was significant difference in technical success rates (84% vs. 99%) (52). However, there was no significant difference in patency rates and clinical success rates. The 1-year and 2-year patency rates were 63% and 53% in each group, and the 1-year and 2-year clinical success rates was 72% and 65% for balloon angioplasty and 77% and 65% for stents (52). Representative randomized controlled studies on comparison of balloon angioplasty and self-expandable nitinol stent placement for the femoro-popliteal artery are the Vienna-ABSOLUTE trial (53, 54), the FAST trial (55), the ASTRON trial (56), and the RESILIENT trial (57). Although the types of nitinol stent used in each study differed, only the FAST trial showed no difference in the two groups in terms of the 1-year restenosis rates. The other trials showed excellent results for the self-expandable nitinol stent group in terms of the 1-year restenosis rates (32–37% vs. 39–63%), 1-year primary patency rates (81.3% vs. 36.7%), free rates (87.3% vs. 45.1%) of 1-year target lesion revascularization (TLR) and increase in walking distance compared to balloon angioplasty (53, 54, 56, 57). Based on only these results, it can be said that primary stent placement is superior to simple balloon angioplasty, but there are different opinions about the interpretation of results and more research on long-term follow-up results is needed.

Recommendation
1. Primary stent placement is not recommended for short segments of the femoral-popliteal artery (Class III, Level A).
2. Bail-out stent placement is recommended when there

is residual stenosis of more than 30% or flow-limiting dissection after balloon angioplasty (Class IIa, Level C).

New Procedures

Drug Eluting Stent

Drug eluting stent placement has been studied for femoro-popliteal artery lesions in order to prevent stent restenosis caused by neointimal hyperplasia. Nevertheless, the SIROCCO I & II studies using Sirolimus eluting stents in the superficial femoral artery did not show significant differences in comparison results between the drug eluting stent and bare metal stents (58). However, in a randomized controlled trial of other types of paclitaxel-coated nitinol stent, the 2-year primary patency rate was 74.8% in the drug eluting stent group and 26.5% in the balloon angioplasty control group, so the outcome up to 2 years showed excellent results compared to balloon angioplasty (59).

Angioplasty with Drug Eluting Balloon

Angioplasty with drug eluting balloons was designed to reduce restenosis and improve the patency rate, which were considered as the disadvantages of plain old balloon angioplasty. It helps to minimize neointimal hyperplasia which is the main cause of restenosis. Its mechanism results from the effects of the drug coated onto the surface of the balloon catheter and it does not leave a foreign body in the blood vessel after the procedure unlike the stent, which can induce neointimal hyperplasia. The procedure is carried out in such a way that the drug is sufficiently instilled into the blood vessel wall by maintaining a state of expansion for about 30–80 seconds after the balloon catheter reaches the lesion.

The results of comparing the drug eluting balloon to plain old balloon angioplasty have been reported in the THUNDER trial (60), the FemPac trial (61), the LEVANT trial (62), and the PACIFIER trial (63). In all of these, the drug eluting balloon catheter group was significantly superior to plain old balloon angioplasty group during over 6-month follow-up observation. In the meta-analysis of 381 patients included in the randomized controlled trials of THUNDER, FemPac, LEVANT, and PACIFIER, TLR was 12.2% for the paclitaxel-coated balloon (PCB) and 27.7% for the uncoated balloon (UCB) while restenosis after angiography was 18.7% for PCB and 45.5% for UCB. Thus, all PCB results were better than those for UCB (64). However, there are no

long-term results yet. Although drug-eluting balloons can prevent neointimal hyperplasia by the effect of the drug, there is a disadvantage in that bail-out stent placement is necessary similarly to plain old balloon angioplasty because there is still a risk of flow-limiting intimal dissection from the expansion of the balloon catheter.

Stent Graft

The indications of stent graft in the femoro-popliteal artery are aneurysm, arteriovenous fistula, and arterial rupture, etc. However, e-PTFE constituting the inner wall of the stent graft can contribute to separating blood flow from the inflammation of the arterial wall after stent placement and has the effect of preventing the migration of smooth muscle cells which can cause neointimal hyperplasia. This has been attempted in patients with CLI in an effort to prevent restenosis caused by neointimal hyperplasia, which is the biggest drawback of femoro-popliteal artery stenting.

Published studies show that the outcome of stent graft compared to bare metal stents or balloon angioplasty was the same, but heparin-bounded Viabahn is a little better (VIASTAR trial) (65). However, there are no long-term results yet and there are also no recent comparative studies with surgical bypass, drug eluting stents or drug eluting balloons showing good results.

Atherectomy Device

Atherectomy devices were introduced in the late 1980s to reduce the damage caused by the expansion of blood vessel walls, elastic recoil, and dissection in balloon angioplasty by directly removing atheroma, and to prevent restenosis caused by smooth muscle cell proliferation at the blood vessel wall. However, the clinical outcome was not good.

The Silverhawk peripheral plaque excision system, introduced in 2003, is a device consisting of a monorail system using a 0.014-inch guide wire, and it removes atheroma while blades rotate at the speed of 8000 rpm. In a clinical study in which 84 infrainguinal artery lesions in 58 patients were randomized into Silverhawk atherectomy device and plain old balloon angioplasty, technical success rates were similar in the two groups and 1-year TLR was not significantly different in the two groups (11.1% vs. 16.7%) (66). However, the incidence of bailout stent placement was significantly higher in the plain old balloon angioplasty group (27.6% vs. 62.1%) (66). The occurrence of major complications was not significantly different between the two groups, but the occurrence of macroembolization was

significantly higher after atherectomy. The incidence of macroembolization was 64.7% and 0%, respectively, when using an embolization protection filter device.

There have been no reports yet of the superiority of atherectomy in the long-term compared to plain old balloon angioplasty or stent placement. Therefore, the application of atherectomy requires care because distal embolism occurs frequently.

Cutting Balloon Angioplasty

Restenosis is closely related to unpredictable vascular injury caused by angioplasty. Thus, cutting balloon angioplasty was introduced as a way to prevent restenosis by adding controlled vascular injury during balloon angioplasty. The results of various clinical trials showed that cutting balloon angioplasty can be effective in reducing restenosis rate in only very short lesions, but this also requires long-term follow-up results.

Laser Therapy

Laser therapy is used to re-open the lumen by laser ablation of atheroma and thrombus obstructing the inner lumen of the blood vessel, but its superiority compared to other treatments has not been proven yet.

Recommendation
1. The efficacy of drug-eluting stent, atherectomy, cutting balloon angioplasty, and laser therapy in the interventional treatment of femoro-popliteal artery has not been established yet (Class IIb, Level A).
2. Angioplasty with drug eluting balloons had a good patency rate compared to plain old balloon angioplasty, but a clear clinical effect has not been proved yet with respect to the cost and risk of bail-out stent placement (Class IIb, Level A).

Infrapopliteal Artery Interventional Procedure

Passage of the Lesion

The most important part of the infrapopliteal artery procedure is the passage of a guide wire for the blood vessel at the lesion site. The passage of the guide wire is important not only in the infrapopliteal artery but also in the recanalization of arteries below the ankle. Its failure accounts for the largest portion of technical failure during angioplasty of the infrapopliteal artery and in arteries below the ankle.

Lesion sites can be divided into stenosis and occlusion sites, and stenotic lesions can be classified into non-calcified and calcified stenosis with an average length of 10 cm or more. But the feet of most diabetics have long and diffuse calcifications of the arterial wall, and stenosis in this recommendation is targeted to calcified stenosis. There are various types of occlusive lesions according to the starting point of occlusion, the length of occlusion, the degree of occlusion, the presence of concomitant occlusion of arteries below the ankle, and the presence and degree of calcification. However, in diabetic feet, complete occlusion with more than 10 cm in length is the most commonly observed, so this guideline targets the lesions of infrapopliteal arteries above the ankle showing complete calcified occlusion, with more than 10 cm and with the orifice of the infrapopliteal artery preserved.

Techniques involving passing a guide wire can be subdivided as follows based on the searched articles: 1) intraluminal guide wire passage for stenotic and occlusive lesion accompanied by calcification, 2) intraluminal guide wire passage initially for infrapopliteal artery above the ankle showing long calcified complete occlusion, and tandem subintimal guide wire passage in case of failure, and 3) routine subintimal guide wire passage for the entire occlusive artery.

The procedure is relatively easy for long stenotic lesions accompanied by calcification regardless of the length of the lesion. It is recommended that intraluminal guide wire passage is first attempted by combining various guide wires of 0.014–0.018-inch with long balloon catheters of more than 10 cm in length. In particular, a micro-guide wire that has a smooth floppy tip with a 0.014-inch diameter is recommended to reduce arterial spasm and rupture when intraluminal passage of the guide wire is attempted in arteries below the ankle. Occasionally it is difficult to advance the balloon catheter despite passage of the guide wire in arteries below the ankle because of the smaller diameter, tortuous course, and severe calcifications. In this situation, the wire should be replaced with a stiffer micro-guide wire, and balloon catheters with excellent trackability and pushability should be used (67).

The technique of guide wire passage for infrapopliteal arteries above the ankle with long calcified complete occlusion is more complicated. It is possible to use anything from a 4-Fr diagnostic curved catheter and 0.035-inch hydrophilic guide wire to a combination of 0.014–0.018-inch of various micro-guide wires. In particular, in

cases where the orifice of the target artery is relatively well preserved, trying intraluminal guide wire passage is recommended with a combination of 0.014–0.018-inch of various guide wire and long balloon catheters of more than 10 cm in length. Guide wire passage is possible in most cases if the true lumen of the blood vessel is preserved. However, in cases of long calcified complete occlusion, it is often difficult to determine whether to pass a guide wire into the true lumen and continue trying intraluminal passage, whether to try to pass a guide wire into the subintimal space where intraluminal passage failed, or whether to intentionally try subintimal guide wire passage from the beginning. Nevertheless, it should be taken into consideration that the most common cause of failure during infrapopliteal angioplasty is reentry failure from the occlusive artery to the true lumen of the distal patent artery, and reentry is more difficult in the arteries under the ankle. Thus, it is highly recommended to try intraluminal guide wire passage from the proximal part of the occlusive arteries, but in the case of failure, to try to pass a guide wire into the subintimal space and reenter a guide wire into the true lumen above the ankle if possible (67).

Recommendation

1. During infrapopliteal angioplasty, guide wire passage into the true lumen of the lesion is primarily attempted for stenotic lesions (Class IIb, Level A).
2. During infrapopliteal angioplasty, intraluminal guide wire passage at the proximal part of lesion is primarily attempted for calcified complete occlusion lesions, and if fails, tandem subintimal guide wire passage is attempted (Class IIb, Level B).

Balloon Angioplasty

Angioplasty using balloon catheter is a common treatment method for chronic stenotic or occlusive lesions in arteries below the knees. It has the advantage that low profile balloon catheters with a 0.014-inch or 0.018 inch guide wire system can be used during angioplasty of arteries below the knees in order to pass severe stenotic lesions with calcification.

The diameter of the balloon catheter is determined according to the diameter of target arteries and it is desirable not to exceed 3 mm because of the risk of arterial rupture. If it is not possible to properly expand the diameter of the artery with angioplasty using balloon catheter due to calcified lesions, a cutting balloon catheter can be

used with low pressure. The length of the balloon should sufficiently include the lesion site, but should not contain too much of the normal artery. Changes in the arterial wall that can occur during angioplasty include intimal rupture, increase in the inner diameter of the artery resulting from rearrangement or stretching of the elastic fiber in the subintimal layer and compression of the atheroma. However, intimal dissection can occur in the normal arterial wall to expose the substrates of the subintimal layer, which can result in adhesion and aggregation of platelets and fibrin.

Angioplasty using a long balloon catheter for long and multiple lesions has several advantages in that the inner surface of the artery can be flattened to shorten the procedure time and reduce unnecessary radiation exposure. When using a long balloon catheter, tapered balloon catheters in which the distal diameter of the balloon is thinner than the proximal diameter can be used. Typically, a long balloon catheter has poor pushability and the diameter of the device is larger than a short balloon catheter. If advancement of the balloon catheter or the supporting catheter after guide wire passage is difficult due to severe calcified stenosis, a short balloon catheter with 2 cm in length that has good pushability and a small profile is necessary for easy entry.

Stent Placement

There are a variety of self-expandable stents and balloon expandable stents that are available for the infrapopliteal artery but primary use of these stents is not recommended yet. This is because lesions are often long at more than 100 mm, there are often multiple lesions, and infrapopliteal arteries are typically thin at less than 3 mm and blood flow is slow, as a result, stenosis and occlusion of stents occur easily. However, secondary use of the stents can be considered for lesions where patency cannot be obtained by balloon angioplasty alone such as with flow-limiting dissection (68).

Recently, there has been a high level of interest in drug-eluting stents. Several studies such as the recent DESTINY, YUKON, and ACHILLES have proven that drug-eluting stents have a lower restenosis rate compared to plain old balloon angioplasty or bare metal stents (69). However, there was no significant difference between the rate of amputation and mortality, and also the average length of the applicable lesion was approximately 15–45 mm. Thus, application is limited to patients with CLI whose lesions mostly exceed 100 mm.

Recommendation

1. Primary stent placement in infrapopliteal arteries is not desirable, but it can be considered as a bail-out method after balloon angioplasty (Class IIa, Level A).

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