Objective: This study was designed to investigate our long-term experience with combined iliac endovascular therapy (EVT) and infrainguinal bypass to treat critical limb ischemia (CLI) and compare outcomes to those of patients who underwent surgery for aortoiliac lesions.

Materials and Methods: From April 2000 to June 2013, 57 patients (58 limbs) underwent an infrainguinal bypass combined with aortoiliac reconstruction to treat CLI. Eighteen limbs were treated by bypass alone and 8 limbs were treated by bypass with EVT for aortoiliac lesions (Bypass group). Thirty-two limbs were subjected to EVT alone for iliac lesions (EVT group).

Results: Preoperative limb ischemia was more severe in the EVT group. There were no significant differences in major procedure-related complications ($\chi^2$ test, $P = 0.853$), systemic complications ($P = 0.853$), and mortality ($P = 0.916$) between the 2 groups. The limb salvage rates were 92% at 1, 3, and 5 years in the Bypass group and 93% at 1, 3, and 5 years in the EVT group, with no significant difference observed between the groups (Kaplan-Meier, log-rank test, $P = 0.616$).

Conclusion: Infrainguinal surgical reconstruction combined with an iliac EVT is an acceptable strategy for managing patients with CLI.

Keywords: critical limb ischemia, hybrid procedure, endovascular treatment

Introduction

Atherosclerotic lesions in patients with critical limb ischemia (CLI) are diffuse and multilevel, featuring the involvement of both the iliac artery and infrainguinal outflow vessels. The therapeutic options in CLI with multisegmental lesions include endovascular therapy (EVT), surgical revascularization, or a combination of both.\(^1\)\(^2\) Adequate inflow must be established prior to improvement in the outflow. It is well recognized that inadequate runoff is an important risk factor for iliac arterial reconstruction failure, and relief of ischemic symptoms may be insufficient in some cases.\(^4\)\(^5\) Although synchronous surgical reconstruction of both the inflow and outflow lesions offers the best outcome and may be necessary for limb salvage in CLI, patients with multilevel lesions often exhibit many comorbidities including diabetes, end-stage renal disease, and coronary artery disease, and the extensive surgical procedures may result in high morbidity and mortality in such high-risk patients. Previous studies suggested that a combination of iliac EVT and distal surgical reconstruction may potentially be an advantageous method for reducing the operative risk and improving infrainguinal bypass graft patency.\(^6\)\(^7\) However, there are extremely few reports of the long-term results of the combined use of iliac endovascular and infrainguinal surgical procedures providing comparisons to those of combined iliac and infrainguinal surgical procedures, especially in patients with CLI.

The purpose of this study was to investigate our long-term experience of this combined iliac endovascular procedure and infrainguinal surgical revascularization to treat CLI, and these results were compared to those in a group of consecutive patients who underwent infrainguinal revascularization performed with suprarenal prosthetic inflow bypass operation for aortoiliac lesions during the same period.

Materials and Methods

1. Patients’ backgrounds

During a 13-year period covering April 2000 to June 2013, all patients with CLI who underwent arterial reconstruction at The Tokyo University Hospital were reviewed retrospectively. Among 241 patients (281 limbs) who
underwent arterial reconstruction to treat arteriosclerosis obliterans, 57 patients (58 limbs) underwent an infralingual bypass procedure combined with aortoiliac arterial reconstruction. The study population consisted of 42 men and 15 women with a mean age of 72.5 years (range: 43–89 years). One patient underwent bilateral procedures. Eighteen limbs were subjected to surgical reconstruction alone, and eight limbs were treated by surgical reconstruction compared with EVT for aortoiliac lesions (Bypass group). The surgical procedures underwent by the patients are described in Fig. 1. Thirty-two limbs were treated by EVT alone for aortoiliac lesions (EVT group). The patients' characteristics are listed in Table 1.

2. Aortoiliac procedure
All preoperative angiograms were reviewed to classify the patients' iliac occlusive lesions according to the TransAtlantic Inter-Society Consensus (TASC) classification. The basic indications for endovascular interventions were symptomatic focal stenosis with TASC type A or B lesions and high-risk patients with poor cerebrovascular or cardiopulmonary reserve. Stent implantation was preferentially performed in patients with a long-segment lesion, dissection, or recoiling after balloon dilatation. The remaining patients for whom these criteria did not apply were included in the indication for surgical revascularization.

Balloon angioplasty and stent implantation were performed with a coaxial balloon catheter through a vascular introducer placed in a retrograde manner into the arteriotomy intraoperatively in most patients or using the Seldinger method preoperatively in some patients. Balloon-expandable stents were used preferentially to treat focal lesions, severely calcified lesions, and all lesions adjacent to the aortic bifurcation. Self-expandable stents were preferentially placed in patients with long-segment disease or tortuous iliac arteries. Completion angiography was performed to ensure a satisfactory morphological result of angioplasty. Stent placement was deemed technically successful if there was less than 30% residual stenosis and the pressure gradient across the treated lesion was less than 5 mmHg.

3. Infrainguinal procedure
Following a successful aortoiliac endovascular or surgical procedure, distal surgical revascularization was performed. The bypass procedure was performed using Dacron or autologous vein grafts. The intraoperative assessment was performed by angiography using portable C-arm fluoroscopy once distal anastomosis was completed.

4. Postoperative management
Patients were usually seen within 2 weeks after discharge, and postoperative follow-up, including a clinical examination, serial duplex ultrasound, or both, was conducted every 3 months by one of the authors or surgical staff. Routine follow-up angiograms were not obtained unless indicated because of recurrent symptoms or suspected impending graft or angioplasty/stenting failure. The mean follow-up time was 39 months (range: 1–144 months). The indications for repeat intervention included stenosis greater than 60% and an intra-arterial pressure gradient across the lesion greater than 10 mmHg at rest, when an improvement of symptoms was not obtained. We routinely use anti-platelet agents as a post-operative medication. Perioperative morbidity and mortality were defined as events occurring within the first 30 days following surgery. Survival was established by telephone contact, but patency and limb salvage were determined at the most recent examination.

5. Statistical analysis
Univariate analyses of categorical variables were performed using the χ² test. Primary/secondary patency, overall survival, major adverse limb event + perioperative death (MALE + POD), and amputation-free survival (AFS) were determined by the Kaplan-Meier method. Comparisons of the patency curves were conducted by univariate analysis using the log-rank test. Data were considered significant at P <0.05. For statistical analysis, Microsoft Excel 2010 was used. All analyses were performed according to the intention-to-treat principle. This study was approved by the Institutional Review Board of the Tokyo University Hospital.

Results
1. EVT group
Endovascular procedures were performed for 12 (37.5%) TASC type A lesions and 20 (62.5%) type B lesions. In total, 1 femoral artery interposition, 13 femoropopliteal
bypass procedures, and 18 femorodistal bypass procedures were performed with iliac EVT in 31 patients (32 limbs). Thirty-one of these procedures were performed intraoperatively, and bypass with EVT for an iliac lesion was performed immediately before infrainguinal bypass in 1 patient (1 limb). All 11 above-knee bypasses were performed with prosthetic grafts, and all 21 below-knee bypasses were performed with autologous vein grafts.

2. Bypass group
Suprainguinal prosthetic inflow procedures, consisting of three aortofemoral bypasses, one iliofemoral bypass, five axillofemoral bypasses, nine crossover bypasses, two iliofemoral bypasses with EVT, and six crossover bypasses with EVT, were performed with Dacron grafts (Fig. 1). Regarding iliofemoral bypasses with EVT, bypass was performed at first and then we punctured the graft and EVT procedure was added to the upstream CIA lesion via the bypass graft. Regarding crossover bypassed with EVT, EVT procedure was performed to the donor-side iliac artery. These patients required downstream repairs concomitant with suprainguinal bypass. In total, three femoral artery interpositions, 18 femoropopliteal bypasses, three femorodistal bypasses, and two other bypasses were performed. Twenty four of these procedures were performed intraoperatively, and EVT was performed immediately before infrainguinal bypass in two patients (two limbs). All 22 above-knee bypasses were performed with prosthetic grafts, and all four below-knee bypasses were performed with autologous vein grafts.

3. Comparison of patients’ clinical characteristics (Table 1)
In the EVT group, the proportion of patients with end-stage renal disease was higher than that in the Bypass group. Although the iliac artery lesion was more extensive and multifocal in patients with TASC type C and D lesions in the Bypass group, preoperative limb ischemia was more severe in the EVT group.

4. Distal anastomotic level of revascularization (Table 2)
The distal anastomotic level of each revascularization is listed in Table 2. In the Bypass group, femoropopliteal bypass was performed in 73% of the procedures, whereas in the EVT group, crural or paramalleolar bypass was performed in 56% of the procedures. Distal bypass was required more often in the EVT group than in the Bypass group ($\chi^2$ test, $P = 0.001$).

5. Initial results
In the EVT group, initial technical success was obtained in all 32 iliac endovascular procedures (100%). No operative death occurred, and the overall morbidity rate was 9.3%. The only major procedure-related complication was one case of early distal graft occlusion. Two systemic complications occurred, consisting of one case each of cerebral infarction and ischemic colitis.

In the Bypass group, no operation was considered a failure for suprainguinal prosthetic inflow bypass. One perioperative death occurred (3.8%) as a result of non-occlusive mesenteric ischemia (NOMI). The overall morbidity rate was 11.5%. The major procedure-related complications were two cases of early distal graft occlusion. Two cases of systemic complications occurred, consisting of one case each of cerebral infarction and ischemic colitis.

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There was a trend toward higher morbidity and mortality in the Bypass group than in the EVT group, but no significant difference was observed between the groups regarding major procedure-related complications ($\chi^2$ test,
P = 0.853), systemic complications (P = 0.853), overall complications (P = 0.869), and mortality (P = 0.916).

6. Long-term results
In the long-term follow-up in the Bypass group, 1 case of restenosis and 2 cases of occlusion of the femoropopliteal bypass occurred, resulting in primary patency rates of 92, 92, and 76% at 1, 3, and 5 years, respectively (Fig. 2A). Secondary interventions were successfully performed in 2 cases of thrombectomies, giving a secondary patency rate of 100% at 5 years (Fig. 2B). In the long-term follow-up in the EVT group, 2 cases of occlusion of iliac lesion and 4 cases of occlusion of the femoropopliteal bypass occurred, resulting in primary patency rates of 83, 78, and 78% at 1, 3, and 5 years, respectively (Fig. 2A). Secondary interventions were successfully conducted for one case of thrombectomy, giving secondary patency rates of 86, 78, and 78% at 1, 3, and 5 years, respectively (Fig. 2B). There was a trend toward a higher patency rate of surgical reconstruction compared to endovascular procedures, but no significant difference was observed (Kaplan-Meier, log-rank test, primary patency, P = 0.370). The AFS rates were 84, 66, and 56% at 1, 3, and 5 years, respectively in the EVT group, and no significant difference was observed (Kaplan-Meier, log-rank test, P = 0.770).

Discussion
The most common pattern of peripheral artery disease is diffuse and multisegmental lesions. Most patients with such multilevel occlusive disease will experience symptom improvement after the aortoiliac procedure alone. However, in some patients, symptom relief will be insufficient, and these patients will require subsequent downstream reconstruction. Previous reports illustrated that poor runoff is an independent predictor of adverse outcome after iliac endovascular interventions. Inflow lesions will also have a determined effect on the long-term patency of infrainguinal surgical reconstruction. Therefore, the combined procedure would have a beneficial result concerning the patency of both iliac and infrainguinal lesions.

There are some conflicting opinions regarding the optimal timing of combined procedures. Separation of the endovascular and surgical procedures will permit the use of the strategy in patients with early complications or inadequate dilatation before distal surgery. However, some other authors successfully employed intraoperative angioplasty by surgically exposing the femoral artery and then proceeding directly to the distal surgical procedure. The advantages of performing both procedures simultaneously in the operating suite are expediency and convenience for the patient, as the patient undergoes a single procedure, in addition to possible cost savings as a result of shorter hospital stays. Several studies reported the results of iliac EVT combined with an infrainguinal procedure. In the two largest series to date, Brewster, et al. reported a 5-year cumulative patency rate of 68% for 55 ipsilateral infringuinal bypass grafts, whereas Peterkin, et al. reported a primary patency of 76% at 3 years in 23 patients. Our result compares favorably with these previous studies, and the follow-up protocols of their and our studies were similar, including the clinical examination, duplex ultrasound, and angiography, in addition to the usual follow-up interval of 6 months. A short follow-up interval is considered an important factor for long-term patency, as a
failure to repair endovascular lesions may subsequently result in acute occlusion of the distal bypass graft in the postoperative follow-up of combined procedures.

Although the iliac lesions were more extensive in patients with TASC type C and D lesions in the Bypass group in the present study, in line with defined our indications for the iliac endovascular procedure, and the preoperative limb ischemic symptoms were more severe and distal bypass was performed more often in the EVT group. Accordingly, the main targets for treatment were infrainguinal lesions in the EVT group, while aortoiliac lesions in the Bypass group. Since the TASC background of the two groups was different, we are not able to compare two groups and we can just say that bypass alone is superior to the combined procedure because no significant difference was observed regarding the patency and limb salvage rates between the Bypass group (performed for TASC type C/D) and the EVT group (performed for TASC type A/B). Importantly, although preoperative limb ischemia was more severe in the EVT group, there was no statistically significant difference in the patency and limb salvage rates between the two groups, suggesting that infrainguinal surgical reconstruction combined with iliac endovascular procedures is an acceptable strategy for
managing patients with CLI. In patients with CLI in the EVT group, crural or paramalleolar bypass was performed more often compared to the findings in the Bypass group, and therefore, distal bypass might contribute to symptom relief in patients with more severe limb ischemia. Careful follow-up of the EVT site could permit its use for the treatment of iliac lesions combined with infraringuinal reconstruction. Although there was no significant difference regarding morbidity or mortality between the two groups in this study, there were no perioperative deaths in the EVT group, and there was a trend toward lower morbidity in the EVT group than in the Bypass group. These results suggested that the combined endovascular and surgical procedure would be safe and less invasive. In patients with CLI for whom there is a choice of treatment or it is possible to perform a bypass procedure to treat infraringuinal lesions, our clear preference is for bypass procedures opposed to endovascular procedures, as the BASIL trial suggested that patients with CLI who are likely to live for more than 2 years are probably better served by a bypass-first strategy.22,23 The hybrid approach appears to be a valuable alternative to completely open or endovascular procedures. Recently, the treatment options of CLI have included the aggressive application of EVT to treat more widespread lesions of the iliac artery, superficial femoral artery (SFA), and infrapopliteal artery,1,2,4,13 in addition to hybrid procedures such as EVT of the SFA combined with distal or infraringuinal bypass and EVT of infrapopliteal lesions.24-26 Clarification of the efficacy of these strategies requires additional studies and experiences.

Our study had several potential limitations because it was a retrospective observational study. Although only a randomized clinical trial could assess the exact influence of the combined procedure, such a trial has not been performed and is unlikely to be conducted in the future.

In conclusion, infraringuinal surgical reconstruction combined with an iliac endovascular procedure represents an acceptable strategy for managing patients with CLI, and further, the long-term patency or limb salvage of the hybrid procedure was comparable to that of surgical reconstruction.

Disclosure Statement
The authors declare no conflicts of interest.

References
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