Perioperative Complications After Aorto-iliac Stenting: Associated Factors and Impact on Follow-up Cardiovascular Prognosis

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WHAT THIS PAPER ADDS

Because of acceptable durability, low operative mortality, device improvement, and increased operator experience, stent-supported endovascular therapy is widely used and considered first-line therapy for patients with aorto-iliac occlusive disease in clinical practice. In light of the association between perioperative complications (POC) occurrence and clinical outcomes documented in this study, stratification based on number of risk factors for POC occurrence plays an important role in decision making in this therapeutic modality.

Objectives: To investigate factors associated with 30-day perioperative complications (POC) after aorto-iliac (AI) stenting, and to compare follow-up cardiovascular prognosis between patients with and without POC.

Materials and methods: This was a retrospective multicenter study. We used a multicenter database of 2012 consecutive patients who successfully underwent AI stenting for peripheral arterial disease in 18 centers in Japan from January 2005 to December 2009 to analyze independent predictors of POC and impact of POC on prognosis by logistic regression and a Cox proportional hazard regression model, respectively.

Results: Mean age was 71 $\pm$ 9 years (median: 72 years; range: 37—98 years), and 1,636 patients (81%) were men. POC occurred in 126 patients (6.3%). In multivariate logistic regression analysis, old age ($\geq$80 years), critical limb ischemia (CLI), and Trans Atlantic Inter-Societal Consensus (TASC) II class C/D were independently associated with POC with adjusted odds ratios and 95% confidence intervals (CI) of 1.9 (1.3—2.9), 2.3 (1.5—3.4), and 2.4 (1.6—3.4), respectively. Out of 2012 patients, 1995 were followed up for more than 30 days (mean: 2.6 $\pm$ 1.5 years; range: 2—2,393 days). In a Cox hazard regression model adjusted for baseline clinical characteristics, POC was positively and independently associated with follow-up major adverse cardiac events (adjusted hazard ratio [HR]: 1.9; 95% CI: 1.3—2.8; $p = .002$), but not with major adverse limb events and target lesion revascularization (adjusted HR: 1.4; 95% CI: 0.7—2.7; $p = .25$; and adjusted HR: 1.2; 95% CI 0.6—2.6; $p = .568$), respectively.

Conclusions: Age >80 years, CLI, and TASC C/D lesion were positively associated with POC after AI stenting. Occurrence of POC appears to adversely affect follow-up cardiovascular, but not limb and vessel prognosis.

INTRODUCTION

For localized (Trans Atlantic Inter-Societal Consensus [TASC] A/B) aorto-iliac occlusive disease (AIOD), stenting is considered the treatment of choice with high technical success rate[1] and acceptable durability thanks to recent device improvements and increased operator experience.[2,3] Extensive (TASC C/D) AIOD also is treated with stent-supported endovascular therapy (EVT) depending on site and operator experience, and studies have documented encouraging durability and low procedural mortality rates.[4] Although in the latter setting the long-term primary patency rate cannot yet compete with that reported for open reconstruction surgery, primary patency loss is predominantly treated by repeat EVT achieving secondary patency rates of 80—90%, which appear comparable to those of surgical bypass therapy.[5,6] Moreover, from the recent covered versus balloon expandable stent trial (COBEST) trial, covered stents perform better for TASC C and D lesions than bare stents in terms of longer-term patency and clinical outcome.[7] Because a wide range has been reported for rates of perioperative complications (POC) after stent-based AIOD treatment likely secondary to heterogeneity in techniques, devices, study populations, and comorbidities, we investigated clinical factors associated with 30-day POC after aorto-iliac (AI) stenting and assessed impact of POC on mid-term cardiovascular outcomes.

METHODS

Study population

This study enrolled consecutive patients who underwent stent placement for de novo atherosclerotic AI lesions in 18 centers in Japan from January 2005 to December 2009. In all participating centers in this study, AI disease was defined as arterial lesions spanning from the juxtarenal aorta to the external iliac artery (Fig. 1). Exclusion criteria have been reported previously[7] as (1) asymptomatic or with unknown symptoms before procedure ($n = 53$); (2) treatment with angioplasty alone ($n = 161$); (3) restenotic lesions ($n = 125$); (4) lesions secondary to radiation or dissection ($n = 0$); (5) history of lower extremity bypass surgery or EVT ($n = 169$); (6) acute onset limb ischemia ($n = 0$); (7) failed endovascular revascularization ($n = 51$); or (8) inadequate data ($n = 84$). Clinical factors associated with 30-day POC after AI stenting and impact of POC on follow-up prognosis were assessed in an overall population of 2012 consecutive patients who successfully underwent AI stenting and completed 30-day POC assessment. The study protocol was designed in accordance with the Declaration of Helsinki, approved by the ethics committee of each participating hospital, and registered with the University Hospital Medical Information Network-Clinical Trial Registry (UMIN000006032). All patients provided written informed consent.

Interventional procedure

Indication and strategy for endovascular procedure were decided by consensus among consulting vascular specialists, including vascular surgeons and interventional radiologists, based on findings in computed tomography or duplex ultrasound prior to diagnostic angiography of the lower limb. EVT was performed by an interventional radiologist at all centers but one, which reflects the fact that the vast majority of cardiac and peripheral vascular procedures in Japan are done by interventional cardiologists and radiologists. Indication of revascularization for AIOD included lesions with >50% diameter stenosis assessed by angiography and mean pressure gradient >10 mmHg evaluated by a 4-Fr diagnostic catheter. The EVT approach and stent selection were decided by the operators based on anatomical features. In general, for AIOD stenotic lesions, a 6-F sheath was inserted retrogradely through a femoral access, and 5,000 units of unfractionated heparin were injected intra-arterially. A 0.035- or 0.014-inch wire was advanced into the lesion, and the stent was directly deployed followed by dilation of an optimally sized balloon for 60 seconds. For totally occlusive lesions, a bi-directional approach, namely antegradely from brachial artery and retrogradely from ipsilateral femoral artery, was regularly used for recanalization and the intraluminal approach was generally used, with the subintimal approach with the wire loop technique being reserved for cases of failed wire-crossing. Re-entry devices were not approved for use in Japan at the time of the study. After successful wire-crossing of chronic total occlusion (CTO) lesions, direct stenting with encouraging angioplasty was done for prevention of distal embolization and vessel perforation based on each individual site's interventional experience. Post-procedure, the Angioseal STS PLUS (St. Jude Medical, St Paul, MN, USA) closure device was employed whenever possible. Iso-osmolar contrast medium was used during procedures with inconsistent use among centers of low osmolarity contrast medium. Dual antiplatelet therapy (aspirin 100 mg/d and cilostazol 200 mg/d, or ticlopidine 200 mg/d) was started at least 1 week prior to EVT and continued until follow up completion; clopidogrel was not approved for use in Japan at the time of study onset. All patients were followed up at 1 and 4 weeks, and every 3 months thereafter. Duplex ultrasound and ankle-brachial index (ABI) assessment for restenosis were routinely conducted at follow-up. The decision for target lesion revascularization (TLR) was clinically driven by recurrent symptoms and by angiographic assessment.

Figure 1. Representative case of aorto-iliac (AI) disease before and after stenting. Upper panel shows Trans Atlantic Inter-Societal Consensus (TASC) A common iliac artery (CIA) stenosis. Balloon-expandable stent was deployed. Lower panel shows TASC D AI occlusion. Balloon-expandable stents were implanted from aorta to CIA and self-expandable stents were implanted from CIA to external iliac artery.

Definitions

The definitions of lower limb severity and the criteria for diagnosis of atherosclerosis risk factors have been reported previously.[7] Worsening of renal function was defined as recurring transient hemodialysis or increase in creatinine level >0.2 (mg/dL). Coronary artery disease (CAD) and cerebrovascular disease (CVD) was defined as presence of symptoms or past history of infarction or history of any revascularization. Myocardial infarction (MI) was defined as significant elevation of levels of serum biomarkers (troponin T > 0.1 ng/ml or twice normal creatine kinase level) or new Q waves on electrocardiogram. Stroke was defined as cerebral stroke that persisted for at least 24 hours with neurological deficit. Critical limb ischemia (CLI) was defined as presence of chronic ischemic rest pain with ankle pressure <50 mmHg or toe pressure <30 mmHg, or ulcers or gangrene with ankle pressure <70 mmHg or toe systolic pressure <50 mmHg attributable to objectively proven chronically arterial occlusive disease in accordance with European Society for Vascular Surgery guidelines.[8] Major adverse cardiovascular events (MACE) included all-cause death, MI, and stroke. Major adverse limb events (MALE) were defined as major amputation or any major re-intervention during the study period. Major re-intervention included new bypass graft, jump, interposition graft revision, or the use of thrombectomy or thrombolysis in stents upon loss of primary assisted patency. Minor re-intervention was defined as endovascular procedures (percutaneous transluminal angioplasty, atherectomy, and stenting) without thrombectomy or thrombolysis, and minor surgical revisions (patch angioplasty). Major amputation was defined as above-ankle amputation. Any amputation at or distal to the Lisfranc level was not considered a limb salvage failure. Data on each event were obtained through outpatient clinic follow-up contact. Primary patency was defined as treated lesions without restenosis/reocclusion, as assessed by angiography or duplex ultrasound. TLR was defined as re-intervention for >50% diameter stenosis identified by angiography within 5 mm of the target lesion after documentation of recurrent clinical symptoms of peripheral artery disease (PAD).

Main outcomes

Main study outcomes were predictors of POC by logistic regression analysis. Additionally, a Cox proportional model was used to assess impact of POC on clinical outcomes, including MACE, cardiovascular events, all-cause death, MI, and stroke as patient-related outcomes; MALE and major

Table 1. Perioperative complications at 30 days.

Variables %, n	6.3 (126/2012)
Death	0.3 (7)
Myocardial infarction	0.2 (3)
Stroke	0.4 (7)
Worsening of renal function	0.9 (17)
Intestinal bleeding	0.2 (4)
Stent thrombosis	0.3 (6)
Pseudoaneurysm	0.3 (6)
Vessel perforation	0.2 (4)
Distal embolization	1.6 (32)
Puncture site hematoma	1.6 (33)
Others	0.3 (7)

amputation as limb-related outcomes; and TLR and primary patency as vessel-related outcomes.

Statistical analysis

Statistical analysis was performed using SPSS software (SPSS, Chicago, IL, USA). Data are shown as means and SD for continuous variables or as percentages for dichotomous variables, unless otherwise mentioned. Between-group differences in continuous or dichotomous variables were evaluated by the unpaired t test or Fisher's exact test, respectively. Statistical significance level was set at $p < .05$.

Independent POC predictors were determined by multivariate logistic regression analysis using two multivariate models for each outcome: one into which all significant explanatory variables in univariate models were entered (model 1), and another into which variables were entered using a stepwise method (model 2). Data are presented as odds ratios (OR) and their 95% confidence intervals (CI). Risk stratification of POC was based on groupings by number of risk factors. Impact of POC on prognostic outcomes was analyzed by the Kaplan–Meier method and the Cox proportional hazard regression model. Hazard ratios (HR) are reported with their 95% CI.

RESULTS

POC

Overall, POC within 30 days were documented in 6.3% (126/2012) of patients (Table 1). Death occurred in seven (0.3%) patients during the perioperative period. MI, stroke, and intestinal bleeding occurred in 0.2% (three), 0.4% (seven), and 0.2% (four), respectively. Post-procedural worsening of renal function was documented in seventeen (0.9%) patients. Distal embolism and vessel perforation, which are life- and limb-threatening complications during an endovascular procedure for AIOD lesions, were observed in 33 (1.6%) and four (0.2%) patients, respectively,

Table 2. Baseline characteristics.

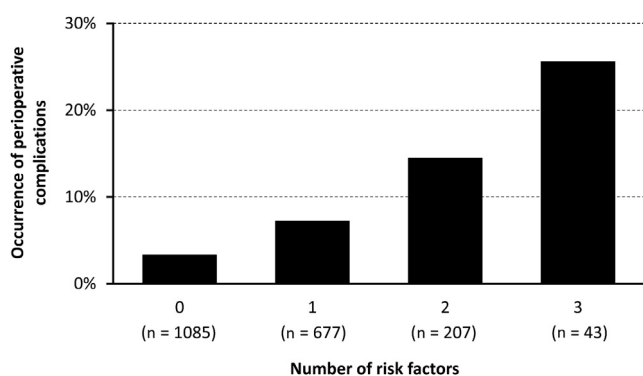| Variables %, n	POC (+), n = 126	POC (−), n = 1886	p
Patient characteristics			
Age, y	74 ± 9	71 ± 9	<.0001
Age > 80 y	30 (38)	14 (270)	<.0001
Male gender	79 (99)	81 (1537)	.42
BMI, kg/m²	21 ± 4	22 ± 3	.0057
BMI < 18.5	15 (19)	13 (241)	.46
Hypertension	81 (102)	81 (1524)	.97
Dyslipidemia	41 (52)	45 (843)	.45
Diabetes mellitus	52 (65)	48 (899)	.39
Regular dialysis	19 (24)	18 (333)	.69
CAD	46 (58)	51 (953)	.60
CVD	31 (39)	23 (428)	.03
Heart failure	14 (18)	12 (218)	.36
Ejection fraction <40%	10 (13)	9 (113)	.73
Lower limb characteristics			
Rutherford criteria (1/2/3/4/5/6)	6 (7)/19 (24)/41 (52)/19 (24)/13 (16)/2 (3)	8 (146)/30 (570)/47 (878)/7 (141)/6 (122)/2 (29)	<.0001
Critical limb ischemia	34 (43)	22 (407)	<.0001
ABI at baseline	0.53 ± 0.28	0.63 ± 0.23	<.0001
Lesion characteristics			
TASC classification (A/B/C/D)	28 (35)/27 (34)/17 (22)/28 (35)	50 (938)/27/(506)/10 (197)/13 (245)	<.0001
TASC C and D	45 (57)	23 (442)	<.0001
CTO	35 (44)	22 (407)	.0005
Lesion length, mm	60 ± 36	51 ± 40	.012
RVD, mm	7.9 ± 1.1	8.1 ± 2.4	.26
% diameter stenosis (pre-/post-)	90 ± 11 (50–100)/7 ± 12 (0–50)	87 ± 11 (25–100)/5 ± 11 (0–75)	.005/.06
Lesion calcification	59 (74)	51 (968)	.11
Femoral lesions	41 (52)	31 (585)	.02
Outflow lesions	48 (61)	35 (666)	.0030

Note. BMI = body mass index; CAD = coronary artery disease; CVD = cerebrovascular disease; ABI = ankle-brachial index; TASC = Trans Atlantic Inter-Societal Consensus; CTO = chronic total occlusion; RVD = reference vessel diameter.

Figure 2. Occurrence of perioperative complications according to the number of risk factors. Perioperative complications (POC) occurred in 126/2012 (6.3%) of patients. Risk factors for POC were old age (>80 years), critical limb ischemia, and Trans Atlantic Inter-Societal Consensus (TASC) C or D lesion (see Table 3). According to number of risk factors for POC, incidence of POC was higher in the higher score groups (0: 3% [36/1085]; 1: 7% [49/677]; 2: 14% [30/207]; 3: 26% [11/43]).

while residual stenosis >30% at completion angiogram was observed in 39/2012 (1.9%) patients. Of the 1.6% of patients who developed puncture site hematoma, all managed without surgical repair, but required transfusion. Pseudoaneurysm was observed in six (0.3%) patients. Within 30 days, stent thrombosis occurred in six (0.3%) patients.

Baseline characteristics of patients with and without POC

Comparison of baseline characteristics between patients with and without POC is shown in Table 2. Mean age was higher (74 ± 9 years vs. 71 ± 9 years; $p < .0001$) and body mass index was lower (21 ± 4 vs. 22 ± 3; $p < .0001$) in the POC (+) group than in the POC (−) group. In terms of risk factors and comorbidities, there were no significant differences except for frequency of patients with CVD (31% vs. 23%; $p = .03$). Compared with the POC (−) group, the POC (+) group had higher prevalence of patients with critical limb ischemia (34% vs. 22%: $p < .0001$), and lower ABI at baseline (0.53 ± 0.28% vs. 0.63 ± 0.23: $p < .0001$),

suggestive of more severe limb status. Regarding baseline lesion characteristics, there was a higher prevalence of TASC C/D lesions (45% vs. 23%: $p < .0001$), with longer mean lesion length (60 ± 36 mm vs. 51 ± 40 mm; $p = .012$), and higher prevalence of CTO (35% vs. 22%; $p = .0005$) and outflow lesions (48% vs. 35%; $p = .003$).

Independent predictors for POC and risk stratification

Predictors of POC by multivariable analysis using a logistic regression model are shown in Table 3. Age >80 years (OR, 1.9; 95% CI, 1.3–2.9; $p < .01$), critical limb ischemia (OR, 2.3; 95% CI, 1.5–3.4; $p < .01$), and TASC C/D (OR, 2.4; 95% CI, 1.6–3.4; $p < .01$) were positively associated with POC. Fig. 2 shows risk stratification of POC according to number of these risk factors. POC incidence was higher in the higher score groups.

Prognostic impact of POC on follow-up outcomes

Prognostic impact of POC on follow-up outcomes is shown in Table 4. Mean and median follow-up period was 2.6 ± 1.5 and 2.4 years (range, 2–2393 days), respectively. After multivariate Cox proportional hazard regression analysis, POC was positively and independently associated with follow-up MACE (adjusted HR, 1.9; 95% CI, 1.3–2.8; $p = .002$) and cardiovascular events (adjusted HR, 2.5; 95% CI, 1.6–4.0; $p < .001$). Fig. 3 shows the impact of POC on MACE up to 5 years. Freedom from MACE was higher in the POC (−) group than in the POC (+) group up to 5 years (56.8 ± 8.0% vs. 76.5 ± 1.7%, $p < .001$). In univariate Cox proportional hazard regression analysis, POC occurrence had the strongest impact on incidence of major amputation (adjusted HR, 5.6; 95% CI, 1.8–17.0; $p = .003$), but this was not entered into the multivariate model because of an insufficient number of events for multivariate analysis. Impact of POC on incidence of major amputation is shown in Fig. 4. Freedom from major amputation was higher in the POC (−) group than in the POC (+) group up to 5 years (96.3 ± 1.8% vs. 99.1 ± 0.3%; $p = .001$). The adjusted HR for MALE and TLR was 1.4 (0.7–2.7; $p = .254$) and 1.2 (0.6–2.6; $p = .568$), respectively. During follow-up, surgical

Table 3. Predictors of perioperative complications after multivariable analysis by logistic regression model.

	Univariate model Unadjusted OR (95% CI)	Multivariate model 1 Adjusted OR (95% CI)	Multivariate model 2 Adjusted OR (95% CI)
Age > 80 y	2.2 (1.5, 3.3)**	1.9 (1.3, 2.9)**	1.9 (1.3, 2.9)**
Male gender	0.8 (0.5, 1.3)	—	—
BMI < 18.5 kg/m^2	1.2 (0.7, 2.0)	—	—
Diabetes mellitus	1.2 (0.8, 1.7)	—	—
Hypertension	1.0 (0.6, 1.6)	—	—
Hyperlipidemia	0.8 (0.5, 1.1)	—	—
Regular dialysis	1.1 (0.7, 1.7)	—	—
Cardiovascular disease	1.2 (0.8, 1.7)	—	—
Critical limb ischemia	2.8 (1.9, 4.2)**	2.0 (1.3, 3.2)**	2.3 (1.5, 3.4)**
TASC C or D	2.7 (1.9, 3.9)**	2.4 (1.6, 3.4)**	2.4 (1.6, 3.4)**
Femoral lesion	1.6 (1.1, 2.3)*	1.1 (0.8, 1.7)	—
Below the knee lesion	1.9 (1.2, 3.1)**	1.3 (0.7, 2.2)	—

Note. Data are odds ratios (OR) and their 95% confidence intervals (CI). BMI = body mass index; TASC = Trans Atlantic Inter-Societal Consensus.*$p < .05$, **$p < .01$.

Table 4. Hazard ratio (HR) of perioperative complications for various future outcomes.

Outcome measure (number of observed events)	Univariate model Unadjusted HR [95% CI] (p)	Multivariate model 1[a] Adjusted HR [95% CI] (p)	Multivariate model 2[b] Adjusted HR [95% CI] (p)
Per patient			
MACE (285)	2.2 [1.5, 3.3] (<0.001)	2.0 [1.3, 2.9] (.001)	1.9 [1.3, 2.8] (.002)
Cardiovascular event (168)	3.0 [1.9, 4.6] (<.001)	2.7 [1.7, 4.2] (<.001)	2.5 [1.6, 4.0] (<.001)
All-cause death (224)	1.8 [1.1, 2.8] (.017)	1.5 [0.9, 2.4] (.105)	1.4 [0.9, 2.2] (.181)
Cardiovascular death (97)	2.4 [1.3, 4.6] (.005)	2.1 [1.1, 3.9] (.028)	—
Myocardial infarction (44)	3.5 [1.6, 7.9] (.002)	3.4 [1.5, 7.8] (.004)	—
Stroke (66)	3.5 [1.8, 6.8] (<.001)	3.3 [1.7, 6.6] (.001)	—
Per limb			
MALE (148)	1.5 [0.8, 2.8] (.186)	1.5 [0.8, 2.7] (.223)	1.4 [0.7, 2.7] (.254)
Major amputation (17)	5.6 [1.8, 17] (.003)	—	—
Per lesion			
Surgical re-intervention (28)	2.2 [0.7, 7.4] (.191)	—	—
Any re-intervention (133)	1.2 [0.6, 2.5] (.604)	1.2 [0.6, 2.5] (.581)	1.2 [0.6, 2.6] (.568)
Primary patency (306)	1.3 [0.9, 2.1] (.200)	1.3 [0.8, 2.1] (.266)	1.3 [0.8, 2.0] (.298)

Note. Data are adjusted HR and their 95% confidence intervals (CI). "—" indicates that multivariate analysis was not performed owing to an insufficient number of events (relative to the number of explanatory variables). MACE = major adverse cardiovascular events; MALE = major adverse limb events.*p < 0.05, **p < 0.01.
[a] Multivariate model 1: adjusted for age ≥80 y, critical limb ischemia (CLI), and Trans Atlantic Inter-Societal Consensus (TASC) C/D (risk factors for perioperative complications).
[b] Multivariate model 2: adjusted for age ≥80 y, CLI, and TASC C/D, as well as gender, body mass index <18.5 kg/m^2, diabetes mellitus, hypertension, hyperlipidemia, regular dialysis, history of cardiovascular disease, femoral lesion, and below-the-knee lesion.

revascularization was performed for 28 patients (1.3%), including 15 who received treatment for restenosis (re-obstruction), eight who underwent femoropopliteal bypass surgery as additional treatment to improve symptoms, two who received endoatherectomy, and three who received treatment for a new lesion. This a relatively low proportion of post-EVT surgical revascularization, thereby unlikely to sizably bias EVT outcome interpretation.

DISCUSSION

According to the latest 2013 American College of Cardiology/American Heart Association guidelines,[3] stenting is effective as the primary therapy for both stenosis and
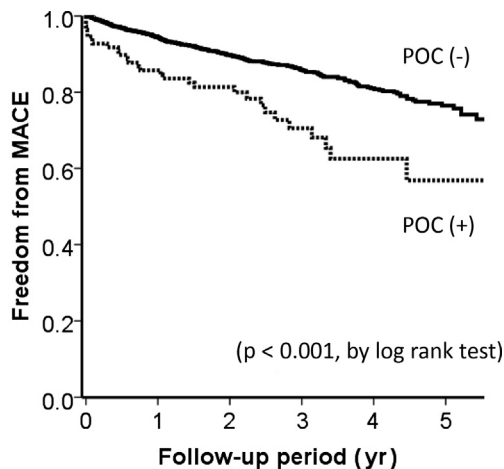
		0 yr	1 yr	2 yr	3 yr	4 yr	5 yr
No. at risk	POC (-)	1884	1605	1142	687	343	125
	POC (+)	111	80	56	30	16	5
Rate	POC (-)	100.0%	94.5%	89.8%	85.8%	81.0%	76.5%
	POC (+)	100.0%	85.7%	81.4%	70.5%	62.5%	56.8%
S.E.	POC (-)	0.0%	0.5%	0.7%	0.9%	1.3%	1.7%
	POC (+)	0.0%	3.4%	3.9%	5.4%	6.5%	8.0%

Figure 3. Impact of perioperative complications (POC) on major adverse cardiovascular events (MACE). Freedom from MACE was higher in the POC (−) group than in POC (+) group up to 5 years (56.8 ± 8.0% vs. 76.5 ± 1.7%; p < .001).
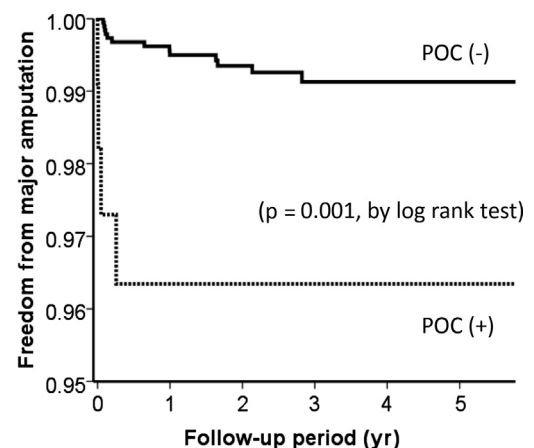
		0 yr	1 yr	2 yr	3 yr	4 yr	5 yr
No. at risk	POC (-)	1884	1617	1162	703	350	127
	POC (+)	111	84	60	32	17	6
Rate	POC (-)	100.0%	99.5%	99.4%	99.1%	99.1%	99.1%
	POC (+)	100.0%	96.3%	96.3%	96.3%	96.3%	96.3%
S.E.	POC (-)	0.0%	0.2%	0.2%	0.3%	0.3%	0.3%
	POC (+)	0.0%	1.8%	1.8%	1.8%	1.8%	1.8%

Figure 4. Impact of perioperative complications (POC) on incidence of major amputation. Freedom from major amputation was higher in the POC (−) group than in POC (+) group up to 5 years (96.3 ± 1.8% vs. 99.1 ± 0.3%; p = .001).

occlusions in common to the external iliac artery with evidence level 1 and class B. For severe AIOD, including TASC II C and D lesions, surgical bypass therapy has been used as a first-line therapy because of its reliable durability.[2,9] However, EVT with stenting is widely used for these lesions because of relatively acceptable durability, albeit lower than that for surgery, and low procedural mortality in the clinical setting. Although patency after AIOD stenting has been investigated as a primary outcome measure, POC rate, especially in this era of device and technique advances in endovascular therapy, has not been systematically examined. Therefore, it is clinically important to define future occurrence of POC and its clinical impact on outcomes to inform decision making on EVT strategy.

In this study, among PAD patients treated with AI stenting, incidence of POC increased with greater severity of patient, limb, and lesion status. This appears to be the case across vascular treatment options, including percutaneous coronary intervention (PCI) and major vascular surgery. For instance, in this era of elective PCI for patients with CAD, coronary perforation, a life-threatening complication, is associated with complex lesions leading to higher occurrence of acute and long-term major adverse cardiac events.[10] An adverse impact of perioperative bleeding on prognosis also has been reported in patients with acute coronary syndrome.[11] After major vascular surgery, patients with major complications have a higher mortality rate and prolonged hospitalization.[12,13] In contrast, risk stratification of POC and its clinical impact on prognosis after AI stenting has not been well examined. To the best of our knowledge this is the first study on risk factor-based stratification of POC occurrence and evaluation of association between POC and clinical outcomes following stent-supported EVT for patients with PAD presenting with AIOD. In earlier studies, heterogeneity in baseline characteristics of PAD patients with AIOD, endovascular devices used, and operator experience likely underlies the variation in complication rates reported. Our results are based on more homogeneous distributions of these variables and, consequently, should provide greater reliability to inform decision making of EVT strategy.

In terms of associations between POC and clinical outcomes, POC independently influenced incidence of MACE and cardiovascular events. However, MALE as limb-related endpoint, and TLR and primary patency as vessel-related endpoints were not independently associated with POC. However, in univariate analysis, POC showed a strong impact on follow-up occurrence of major amputation, especially during the early phase after EVT (Fig. 3). There was an insufficient number of patients with major amputation to perform multivariate analysis; however, POC would be expected to affect the major amputation rate after EVT in patients with AIOD. In terms of patient-related clinical outcomes, POC did not affect overall survival, even though it was associated with incidence of MACE, as well as cardiovascular events and cardiovascular death. To explain the latter observation, one might hypothesize that POC might lead to anemia or untoward hemodynamic changes,

in turn underlying cardiovascular ischemia that negatively affected only patients with CAD and CVD. The impact of a restrictive strategy of red cell transfusion on short-term mortality was reported for intensive care unit (ICU) patients with a hemoglobin concentration of no more than 9.0 g/dL within 72 hours of ICU admission;[14] however, further investigation is needed to assess the impact of anemia on clinical outcomes after AI stenting.

Because of acceptable durability, albeit not as high as that for open surgery,[9] low procedural mortality, device improvement, and increased operator experience, stent-supported EVT is widely used in clinical practice. In light of the association between POC occurrence and clinical outcomes documented in this study, stratification based on number of risk factors for POC occurrence plays an important role in decision making in this therapeutic modality. The findings of this study, however, are limited by the retrospective nature of the analysis of only endovascular procedural and clinical data, despite the inclusion of a large number of patients form multiple centers. Also, new-generation stents, especially covered stents were not used in this study population. A recent trial reported that covered stents play an important role in obtaining acceptable patency and low complication rates.[5,15] Therefore, further investigation is needed with covered stents and POC. Finally, there was not a universal protocol for antiplatelet therapy use among participating centers, which precludes appropriate analysis of the effect of adjunctive pharmacotherapy in the context of POC. In particular, the role of dual antiplatelet therapy (DAPT) should be studied because cardiovascular events regularly occur in patients with PAD; whether the benefits of DAPT supersede its risk remains unclear.

CONCLUSION

Age >80 years, CLI, and TASC C/D lesion were positively associated with POC after successful AI stenting. Occurrence of POC appears to adversely affect follow-up cardiovascular, but not limb and vessel, prognosis.

CONFLICT OF INTEREST

None.

FUNDING

None.

APPENDIX A. SUPPLEMENTARY DATA

Supplementary data related to this article can be found online at http://dx.doi.org/10.1016/j.ejvs.2013.09.024.

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