



# Balloon Test Occlusion of the Carotid Artery: Internal Validation of Predictive Results

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## ABSTRACT

**AIM:** To develop a protocol of balloon test occlusion (BTO) to perform single-photon emission computed tomography (SPECT) only in cases that require it by using mean stump pressure (MSTP).

**MATERIAL and METHODS:** BTO was performed in 52 consecutive patients (derivation group). Using the derivation group data, a protocol was created and applied to 55 consecutive patients (validation group).

**RESULTS:** In the derivation group, all patients with MSTP  $\geq 65$  mmHg had an ischemic tolerance, whereas those with MSTP  $\leq 45$  mmHg were considered ischemic intolerant. Based on these results, we developed a protocol wherein MSTP between 45 mmHg and 65 mmHg was defined as "ischemic borderzone" and SPECT was performed in these cases. Using this protocol, BTO was performed in the validation group and 19 patients were treated with parent artery occlusion with or without bypass. In two cases that did not follow the protocol, the occurrence of hypoperfusion caused cerebral infarction after treatment. However, if this protocol had been followed for all cases, no false-negative cases of BTO would have occurred.

**CONCLUSION:** By measuring MSTP and identifying the approximate ischemic tolerability, the current protocol can identify cases requiring SPECT, which is particularly reliable but complicated. Moreover, this protocol would be especially useful for reducing false-negative cases of BTO.

**KEYWORDS:** Balloon test occlusion, Carotid artery sacrifice, Ischemic tolerance, Mean stump pressure, Cerebral blood flow

**ABBREVIATIONS:** **ACA:** Anterior cerebral artery, **BTO:** Balloon test occlusion, **CBF:** Cerebral blood flow, **CCA:** Common carotid artery, **CT:** Computed tomography, **EEG:** Electroencephalography, **HFB:** High flow bypass, **ICA:** Internal carotid artery, **LFB:** Low flow bypass, **MCA:** Middle cerebral artery, **MSTP:** Mean stump pressure, **PAO:** Parent artery occlusion, **rCBF:** Regional cerebral blood flow, **ROIs:** Regions of interest, **SPECT:** Single-photon emission computed tomography, **SSEPs:** Short latency somatosensory evoked potentials, **STA:** Superficial temporal artery, **STP:** Stump pressure, <sup>99m</sup>Tc-HMPAO: Technetium-99m hexamethylpropylene amine oxime

## INTRODUCTION

Carotid artery sacrifice can be a strategy for the treatment of large or giant aneurysms of the internal carotid artery (ICA), tumors invading the ICA or common carotid artery

(CCA) at the neck, skull base tumors, and traumatic lesions involving the ICA or CCA (31). However, 26% of patients who underwent a nonselective and abrupt sacrifice of the carotid artery experienced infarction (23,36). Pretherapeutic

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knowledge of carotid artery dependence is essential in these patients, because vascular bypass or alternative surgical approaches may be necessary for patients unable to tolerate carotid artery sacrifice (11,31). Balloon test occlusion (BTO) of the ICA or CCA has been used to evaluate the ischemic tolerability of permanent parent artery occlusion (PAO). However, the BTO procedure and the assessment of the ischemic tolerability based on its results are not standardized. Previous reports of BTO have proposed various methods to predict the ischemic tolerability (33), such as angiographically synchronous venous filling (1,35), stump pressure (STP) (12), monitoring of short latency somatosensory evoked potentials (SSEPs) and electroencephalography (EEG) (13,21), and direct or indirect measurements of cerebral blood flow (CBF). Various methods of measurements of CBF such as xenon-enhanced computed tomography (CT) (8), positron emission tomography (3), single-photon emission computed tomography (SPECT) (24), perfusion magnetic resonance imaging (18), regional cerebral oxygen saturation monitoring (9), and X-ray angiography perfusion have been reported (2,30). Among these assessment modalities, the measurement of CBF is particularly useful to reduce the number of false-negative BTO cases (14,19,28). However, CBF measurement is not recommended for all cases because they are extremely complicated and expensive. Therefore, we developed a protocol for the procedure and assessment of BTO such that approximate ischemic tolerability is predicted using MSTP, which is easily measured and SPECT is performed only for cases that essentially require CBF measurement. Subsequently, we internally validated the accuracy and reliability of this protocol.

## ■ MATERIAL and METHODS

### Study Design and Ethics

Between 1993 and 2001, BTO of the ICA or CCA was performed in 52 consecutive patients (derivation group). A protocol was created using the derivation group BTO data and results of treatment. Based on this acquired protocol, between 2002 and 2018, BTO of the ICA or CCA was performed in 55 consecutive patients (validation group). The accuracy and reliability of this protocol were evaluated.

We conducted a retrospective observational study approved by the Nagoya City University Hospital Institutional Review Board (IRB 60-18-0217). All patients provided written informed consent.

### BTO Procedure

BTO was generally performed under local anesthesia without using sedatives. At first, a 6-F sheath was inserted in the femoral artery and 2000 IU of heparin was systemically administered. Diagnostic cerebral angiography, including Matas and Allcock maneuvers, was performed using a 4-F catheter. After an additional administration of 2000–3000 IU of heparin, a 5.5-F triple-lumen balloon catheter (Endeavor or Sentry; Boston Scientific, Fremont, CA) was mainly used and placed in the cervical portion of the ICA. While maintaining the activated clotting time between 250 and 300 seconds, the

balloon was carefully inflated under fluoroscopic observation and the ICA remained occluded for up to 15 minutes. In cases of BTO of the CCA, a 5F-guide catheter was also placed in the CCA in addition to the 5.5-F balloon catheter placed in the ICA. The ICA was occluded using the 5.5-F balloon catheter and ECA was occluded using a compliant balloon or PercuSurge GuardWire (Medtronic, Minneapolis, MN, USA) from the 5F-guide catheter. The patients were neurologically examined during the carotid artery occlusion. The stump pressure was measured using an arterial line and monitored continuously for the 15 minutes. Systemic blood pressure was monitored at 1-minute intervals using an automatic sphygmomanometer. During BTO, we maintained systemic blood pressure in the range of the patient's baseline pressure at rest, if necessary, by intravenously injecting nicardipine. Also, in the derivation group, SSEPs and EEG monitoring were performed. If any neurological symptoms, or abnormality of SSEPs or EEG were observed, the balloon was immediately deflated.

### CBF Measurements

CBF was measured using  $^{15}\text{O}\text{-H}_2\text{O}$  positron emission tomography (PET) (9 patients), and Xenon CT (5 patients) in the derivation group. When CBF was measured, the parent artery on the affected side was manually occluded in four of the nine patients using  $^{15}\text{O}\text{-H}_2\text{O}$ , and occluded by the balloon catheter in the other 10 patients. The derivation group was analyzed using the method of the CBF measurement that has been previously described (10). Regional CBF (rCBF) values were acquired from the average values of pixels in regions of interest (ROIs). ROIs were placed over the anterior cerebral artery (ACA) and middle cerebral artery (MCA) territories in the slice of the transaxial images, which were at the level of the basal ganglia. The CBF reduction rate was calculated as follows; CBF reduction rate (%) =  $100(1 - \text{rCBF during occlusion} / \text{rCBF at rest})$  (10).

In the validation group, the BTO procedure was similar, but CBF was measured using technetium-99m hexamethylpropylene amine oxime ( $^{99\text{m}}\text{Tc}\text{-HMPAO}$ ). The measurement method of  $^{99\text{m}}\text{Tc}\text{-HMPAO}$  SPECT has been previously reported (33). The noninvasive method used by Matsuda et al (16) (Patlak plot method) was used for the quantitative measurement rCBF with  $^{99\text{m}}\text{Tc}\text{-HMPAO}$  SPECT (33). An intravenous injection of 740 MBq of  $^{99\text{m}}\text{Tc}\text{-HMPAO}$  was performed five minutes after the balloon occlusion. After the balloon had been inflated for 15 minutes, the balloon catheter was deflated and removed, and the patient was transported to the nuclear medicine department. CBF data were acquired and analyzed with a three-dimensional stereotactic ROI template, which has fully automated ROI analysis software (29). The SPECT images were anatomically standardized using statistical parametric mapping 99, followed by quantification of 318 constant ROIs, grouped into 12 segments (1, callosomarginal; 2, precentral; 3, central; 4, parietal; 5, angular; 6, temporal; 7, posterior cerebral; 8, pericallosal; 9, lenticular nucleus; 10, thalamus; 11, hippocampus; 12, cerebellum) on each side (29). Segmental CBF can be calculated as the area-weighted mean value for each of the respective 12 segments based on the rCBF in each ROI (29). As CBF changes, the ratio of occluded-side CBF during BTO to ipsilateral CBF at rest is more reliable than the

ratio of occluded-side CBF to contralateral CBF during BTO (33). However, there was also a measurement error between the CBF during BTO and the CBF at rest. In order to reduce this error, the ratio of rCBF to CBF of ipsilateral cerebellum (R/CE ratio) was calculated (25,34). Therefore, for almost all patients, CBF at rest was measured before BTO and CBF changes were evaluated using the ratio of occluded-side R/CE ratio during BTO to ipsilateral R/CE ratio at rest. If not, CBF changes were evaluated by the ratio of occluded-side R/CE ratio to contralateral R/CE ratio during BTO.

**RESULTS**

In all, 107 patients were analyzed. Baseline characteristics are shown in Table I. The derivation group had 52 patients (mean age, 57.2 years; median age, 61 years; range, 21–74 years; female, 42%), while the validation group had 55 patients (mean age, 57.5 years; median age, 59 years; range, 33–80 years; female, 56%). In the derivation group, 52 BTO were performed for 52 patients (51 BTO of the ICA and 1 BTO of the CCA), and the diseases were internal carotid aneurysm in 15, cervical aneurysm in one, carotid artery stenosis in three, head and neck tumor in 30, and skull base tumor in three. In the validation group, 55 BTO were performed for 55 patients (53 BTO of the ICA and 2 BTO of the CCA), and the diseases were internal carotid aneurysm in 26, cervical aneurysm in two, head and neck tumor in 26, and skull base tumor in one.

**The Derivation Group**

Neurological symptoms were present in seven patients. There were abnormalities of SSEPs (low-frequency N20) or

EEG (slowing down) in eight patients; without neurological symptoms in six patients. All patients with abnormalities of neurological findings, SSEPs, or EEG had MSTP  $\leq$ 64 mmHg (Table II).

Of the 52 patients, occlusion of the parent artery with or without bypass was performed in 10; “PAO alone” in six,

**Table I:** Clinical Characteristics of the Derivation and Validation Groups

	Derivation (n=52)	Validation (n=55)
<b>Age, years</b>		
Median (IQR)	61 (48–65)	59 (52–65)
Female, n (%)	22 (42)	31 (56)
<b>Disease, n (%)</b>		
<b>Aneurysm</b>		
Internal carotid artery	15 (28.8)	26 (47.3)
Cervical	1 (1.9)	2 (3.6)
Carotid artery stenosis	3 (5.8)	0 (0)
<b>Tumor</b>		
Head and neck	30 (57.7)	26 (47.3)
Skull base	3 (5.8)	1 (1.8)

*IQR: Interquartile range.*

**Table II:** Summary of 13 Patients in the Derivation Group with Abnormalities of Neurological Findings, SSEPs, or EEG during BTO Procedure

Case No.	Age	Gender	Disease	Neurological symptoms	ECG change	SSEPs change	MSTP (mmHg)
7	66	Female	ICA aneurysm	+	NA	NA	<30
9	65	Male	Head and neck tumor	-	-	+	NA
15	67	Male	Head and neck tumor	-	+	NA	39
16	61	Male	Carotid artery stenosis	-	+	-	41
23	65	Female	ICA aneurysm	+	+	NA	59
30	25	Male	Head and neck tumor	+	-	NA	56
32	52	Female	Head and neck tumor	+	-	NA	54
39	72	Male	Head and neck tumor	+	+	NA	62
41	52	Male	Head and neck tumor	-	+	NA	59
43	74	Male	Head and neck tumor	+	+	NA	40
44	70	Female	Head and neck tumor	-	+	NA	64
47	65	Male	Head and neck tumor	+	NA	NA	NA
49	65	Male	Head and neck tumor	-	+	NA	49

**BTO:** Balloon test occlusion, **EEG:** Electroencephalography, **ICA:** Internal cervical artery, **MSTP:** Mean stump pressure, **NA:** Not available, **SSEPs:** somatosensory evoked potentials.

“PAO + high flow bypass (HFB)” in three, and “PAO + low flow bypass (LFB)” such as superficial temporal artery (STA) – MCA bypass in one. 35 patients were treated preserving the parent artery and seven patients were observed without treatment.

Of the six patients who underwent “PAO alone”, only one patient suffered from symptomatic ischemic complications which seemed to be due to hypoperfusion. The patient who had an unruptured carotid–ophthalmic aneurysm was treated by surgical clipping. After the operation, the aneurysm ruptured. In reoperative findings, the cause of the rupture was thought to be an aneurysmal neck laceration caused by postoperative slippage of an aneurysm clip, and in order to stop massive hemorrhage, the ICA was ligated without bypass. This patient had an MSTP 41 mmHg in BTO, while the other five patients without ischemic complication had an MSTP of 64.8 mmHg or more.

When MSTP was 65 mmHg or more, all patients of the derivation group had no abnormalities of neurological findings, SSEPs, or EEG during the BTO procedure. Also, no ischemic complications occurred after PAO without bypass. Hence, when MSTP is 65 mmHg or more, the patient can be considered to have an ischemic tolerance for PAO without any bypass.

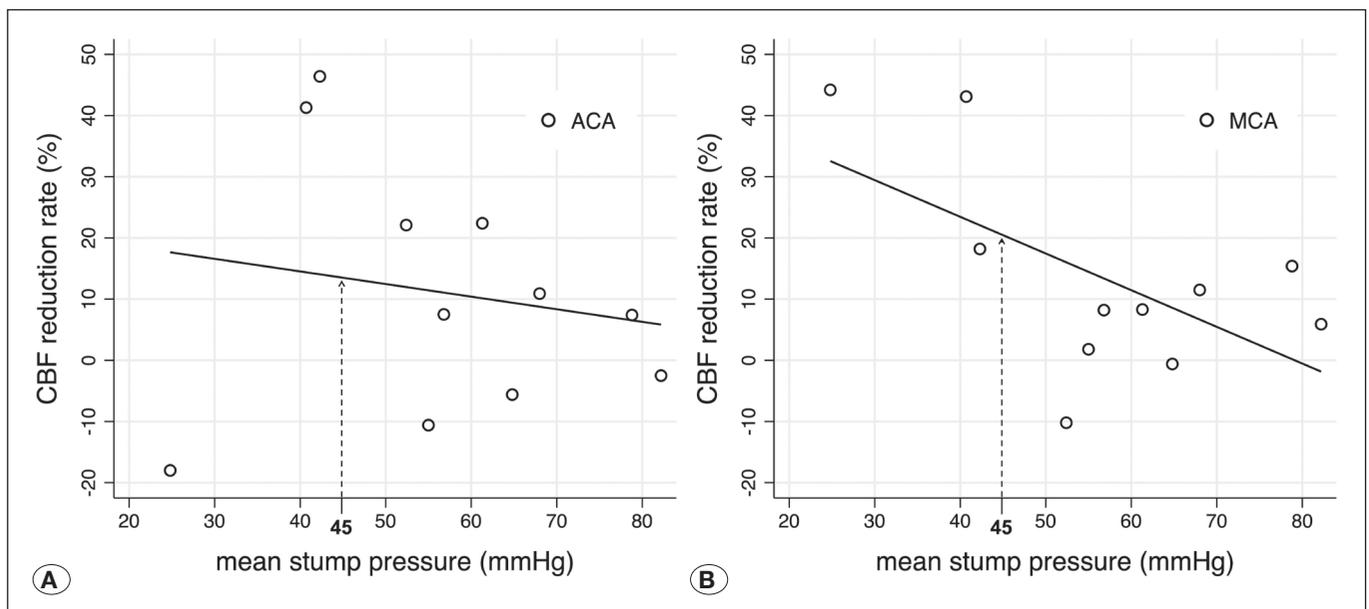
The measurement of CBF was performed in 14 patients. Nine patients were measured using <sup>15</sup>O-H<sub>2</sub>O PET and five patients using Xenon CT. In one of the 14 patients, CBF could not be measured because neurological symptoms appeared, and in two patients, MSTP could not be measured because of technical error. There was no significant correlation between MSTP and the rate of CBF decrease in each of the ACA and MCA territories. However, when MSTP was 45 mmHg or less,

the rate of CBF decrease should have greatly exceeded 10% in both the ACA and MCA territories (Figure 1A, B). Also, it has previously been reported that when the minimum STP is less than 40 mmHg, the rate of CBF decrease exceeds 20% (32), and our results were largely consistent with this, though STP was evaluated on mean, not minimum pressure.

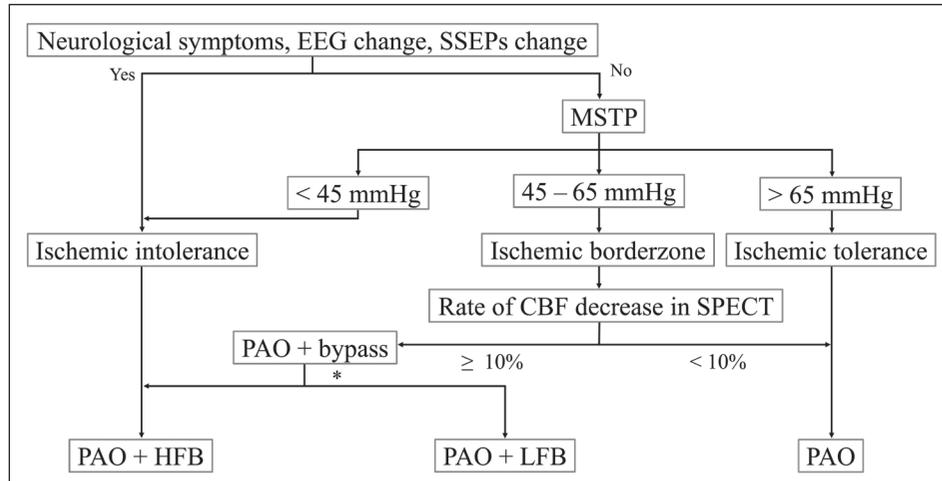
**Creation of Assessment Protocol for BTO**

As mentioned above, when MSTP was 65 mmHg or more, none of the patients of the derivation group had abnormalities of neurological findings, SSEPs, or EEG during the BTO procedure, and none of the seven patients undergoing PAO without bypass had any ischemic complications. Also, when MSTP was 45 mmHg or less, the rate of CBF decrease greatly exceeded 10%. Although there are no strict criteria to define hypoperfusion in BTO with SPECT, it is generally accepted that the abnormal areas are where the CBF is less than 90% of the baseline (19,28,33).

Therefore, a protocol was created from the above mentioned treatment results or measurement of CBF in the derivation group. We defined MSTP <45 mmHg as “ischemic intolerance,” MSTP >65 mmHg as “ischemic tolerance,” and MSTP between 45 mmHg and 65 mmHg as “ischemic borderzone.” The cases of “ischemic borderzone” were assessed for the ischemic tolerability using SPECT. If the rate of CBF decrease is less than 10%, PAO without bypass is possible and if it is 10% or more, a bypass is considered necessary when performing PAO. “PAO + LFB” was performed in cases of CBF decrease of local area where sufficient CBF was maintained only by a single or double STA-MCA bypass, while “PAO + HFB” was performed otherwise (Figure 2).



**Figure 1:** Relationship between mean stump pressure (MSTP) and CBF reduction rate in both the ACA and MCA territories. The measurement of CBF was performed on 14 patients, and data of both MSTP and CBF were acquired in 11 patients. Spearman rank correlation analysis between MSTP and the rate of CBF decrease in each of the ACA and MCA territory (A;  $r=-0.182$ ,  $p=0.597$ , B;  $r=-0.400$ ,  $p=0.223$  using Stata software, version 16.0 [StataCorp]). When MSTP is 45 mmHg or less, the rate of CBF decrease greatly exceeds 10% in both the ACA and MCA territory. **ACA:** anterior cerebral artery, **CBF:** cerebral blood flow, **MCA:** middle cerebral artery.



**Figure 2:** Algorithm for assessment of balloon test occlusion and treatment. \*: “PAO + LFB” is performed in cases of CBF decrease of local area in which sufficient CBF is maintained only by a single or double superficial temporal artery – middle cerebral artery bypass, while “PAO + HFB” is performed otherwise. **CBF:** cerebral blood flow, **EEG:** electroencephalography, **HFB:** high flow bypass, **LFB:** low flow bypass, **MSTP:** mean stump pressure, **PAO:** parent artery occlusion, **SPECT:** single-photon emission computed tomography, **SSEPs:** somatosensory evoked potentials.

Based on this protocol, BTO of the ICA or CCA was performed in the validation group, and all CBF measurements were performed using <sup>99m</sup>Tc-HMPAO SPECT.

**The Validation Group**

Using this protocol, it was judged that in 55 patients of the validation group, 11 patients were “ischemic tolerance,” 21 patients were “ischemic intolerance,” and 22 patients were “ischemic borderzone.” Complications caused by the BTO procedure itself occurred in two patients (3.6%) and in one patient, the ischemic tolerability could not be evaluated because of the complication. All complications were embolic with transient neurological symptoms.

Table III shows the evaluation from BTO and the results of treatment. In 11 patients judged to have “ischemic tolerance,” treatment was performed in eight patients. “PAO alone” was performed in three patients, and the parent artery was preserved in five patients. One patient undergoing “PAO alone” had ischemic complications caused by hypoperfusion. This patient had thyroid cancer encasing the ICA and underwent BTO of the ICA before operation by otolaryngologists. In the BTO, this patient was considered to have an ischemic tolerance for occlusion of the ICA. However, because the cancer was extended to the CCA, the CCA was sacrificed instead of the ICA during the operation. Consequently, the ischemic complication occurred. The other two patients undergoing “PAO alone” had no ischemic complications.

In 21 patients judged to have “ischemic intolerance,” treatment was performed in 19 patients. “PAO + HFB” was performed in eight patients, “PAO + LFB” in one patient, and the parent artery was preserved in ten patients. One patient undergoing “PAO + HFB” had ischemic complications caused by postoperative occlusion of the bypass graft. One patient undergoing “PAO + LFB” had ischemic complications due to hypoperfusion, though the patency of bypass graft was maintained. Following our protocol, it was considered that “PAO + HFB” was necessary for this patient. This patient had a recanalization after coil embolization of a partially thrombosed large aneurysm of the right ICA. She had a history of ipsilateral neck surgery and was taking an antiplatelet drug

after coil embolization. In addition, she was treated with an anticoagulant drug because a cerebral infarction had occurred due to dissection of the internal carotid artery during the BTO procedure. For these reasons, “PAO + HFB” was abandoned, and “PAO + LFB” was performed for this patient.

In 22 patients judged to have “ischemic borderzone,” 18 patients were treated. “PAO alone” was performed in one patient, because the MSTP was 60 mmHg and the rate of CBF decrease was <10% during BTO. “PAO + HFB” was performed in four patients, “PAO + LFB” in two patients, and the parent artery was preserved in 11 patients. One patient undergoing “PAO + HFB” had ischemic complications caused by postoperative occlusion of the bypass graft.

In all 19 patients of the validation group treated with PAO with or without bypass, except for four patients who had postoperative ischemic complications caused by hypoperfusion, there were no delayed ischemic complications during at least two years of observation.

**DISCUSSION**

In the BTO procedure, during the inflation of the balloon in the ICA, neurological monitoring and angiographic evaluation of collateral circulation is simple. However, with only these, the complication rate after ICA occlusion has been reported to be 16% (22). Therefore, a combination of procedures and modalities of BTO have been proposed to increase the positive predictive value, such as neurological monitoring after performing a hypotensive load (5,6,15,27), SSEPs, EEG, MSTP, left / right difference in venous return on cerebral angiography, and measurement of CBF.

For patients in the derivation group, we judged ischemic tolerability based on neurological findings, SSEPs, EEG, MSTP, and CBF measurement during BTO. Using the data of the derivation group, we developed a protocol that approximate ischemic tolerability was identified using MSTP and, only in patients with MSTP between 45 mmHg and 65 mmHg, ischemic tolerability was accurately determined by performing SPECT. Next, we applied this protocol to 55 patients in the validation group. As a modality of assessment,

**Table III:** Evaluation by BTO and Results of Treatment in the Validation Group

Evaluation by BTO	Modality of treatment (n)	Ischemic complications due to hypoperfusion (n)
Ischemic tolerance (n=11)		
	PAO+HFB	0
	PAO+LFB	0
	PAO	3
	preserved parent artery	5
Total	8	1. The CCA was sacrificed instead of the ICA.*
Ischemic intolerance (n=21)		
	PAO+HFB	8
	PAO+LFB	1
	PAO	0
	preserved parent artery	10
Total	19	1. The HFB was required in BTO but the LFB was performed.
Ischemic borderzone (n=22)		
	PAO+HFB	4
	PAO+LFB	2
	PAO	1
	preserved parent artery	11
Total	18	1. The HFB was occluded.

\*This patient was assessed to have ischemic tolerance for occlusion of the ICA; however, the CCA was sacrificed during operation.

**BTO:** Balloon test occlusion, **CCA:** Common carotid artery, **HFB:** High flow bypass, **ICA:** Internal carotid artery, **LFB:** Low flow bypass, **PAO:** parent artery occlusion.

the usefulness of measurement of CBF has particularly been reported (14,19,28). However, CBF-measuring examinations such as SPECT are cumbersome for a BTO procedure. In our BTO protocol, by measuring MSTP and identifying cases of "ischemic borderzone," it is possible to narrow down cases for which SPECT is needed.

Hypotensive challenge and venous phase delay assessment during BTO are useful to reduce false-negative cases (1,5,6,27,36). However, according to the previous report of BTO with hypotensive challenge, ischemic complications due to a hemodynamic mechanism can occur in up to 6% of cases (15). Hypotensive challenge has a potential risk of ischemic complication, especially for cases of "ischemic borderzone." Moreover, reported false-negative rates of BTO with only hypotensive challenge may be as high as 15% (4,5). CBF-measuring examinations are generally considered more reliable than hypotensive challenge or venous phase delay assessment. In this study, SPECT was performed for cases of "ischemic borderzone" and ischemic tolerability was strictly determined. For these reasons, hypotensive challenge and venous phase delay assessment were not performed.

In the validation group, complications of the BTO procedure itself occurred in two (3.6%) of 55 patients. The complications were all embolic ischemic events, and the neurological deficits were transient. One patient could not be evaluated because of embolic ischemic complication while navigating the balloon catheter. Previous studies have reported the incidence of all complications of the BTO procedure itself to range from 3.2 to 8.0% (15,17,31). In this study, the complication rates of BTO procedure were similar to those of the previous reports.

In 55 patients of the validation group, based on the BTO results, 45 patients were treated, and PAO with or without bypass was performed in 19 patients. There were four cases in which the postoperative occurrence of hypoperfusion caused cerebral infarction. In one patient, although this patient was assessed as "ischemic tolerance" for occlusion of the ICA, the CCA was sacrificed instead of the ICA. In two cases including this patient, the protocol was not complied with, and in other two cases, the bypass was obstructed. If the protocol had been followed, there would have been no false-negative cases in which ischemic complications due to hypoperfusion were observed.

In previous reports, an MSTP of around 40–50 mmHg was generally considered as a borderzone of ischemic tolerability (7,15,32,33). However, in this study, neurological abnormalities were found at an MSTP of approximately 60 mmHg (Table II Case 23, 39). Even an MSTP of 60 mmHg was not necessarily a safe pressure. Therefore, even if the MSTP is around 60 mmHg, CBF should be evaluated to decrease false-negative cases. Because MSTP is affected by systemic blood pressure, there are reports that the ratio of MSTP to systemic blood pressure should be evaluated, rather than the absolute value of MSTP (12,20,36). We controlled the range of systemic blood pressure at rest in the patient during the BTO procedure and evaluated only the absolute value of MSTP. No cases showed abnormally low or high blood pressure during the BTO procedure, with occasional use of nicardipine. By avoiding abnormal hypotension and hypertension during the BTO procedure, the ischemic tolerability can be approximately determined using only the MSTP value.

As for BTO of the CCA, BTO was performed for one and two patients in the derivation and validation groups, respectively. All of them were preoperative evaluations for patients with head and neck tumor, which may require CCA sacrifice during tumor removal. However, in all patients, the carotid artery was preserved during operation, regardless of the patient's ischemic tolerability. Furthermore, for one patient who was considered to have an ischemic tolerance for occlusion of the ICA, ischemic complication occurred after CCA sacrifice. Therefore, BTO of the CCA should also be performed if the CCA could be sacrificed in operation.

There are some limitations to this study. It was conducted in a single center, and the number of patients who underwent the BTO procedure and were treated with PAO with or without bypass was small. The CBF was measured using  $^{15}\text{O}$ - $\text{H}_2\text{O}$  PET or Xenon CT in the derivation group, whereas it was measured using  $^{99\text{m}}\text{Tc}$ -HMPAO in the validation group.  $^{99\text{m}}\text{Tc}$ -HMPAO SPECT can be advantageously performed using readily available technology and offers regional information (19). Therefore, at present,  $^{99\text{m}}\text{Tc}$ -HMPAO SPECT has been primarily used to assess CBF during the BTO procedure. In our study, based on the CBF data from the derivation group, CBF of the validation group was evaluated using  $^{99\text{m}}\text{Tc}$ -HMPAO SPECT, which is currently the most used technique. Although the CBF-measuring method differed between the derivation and validation groups, this protocol could be useful for the validation group without any discrepancies. In our protocol, the threshold of the ischemic tolerance may be generally considered to be high, however, this prevented false-negative cases. Regarding treatments, operative complications would increase in the order of "PAO alone", "PAO + LFB, and "PAO + HFB (26). In this protocol, since the threshold of the ischemic tolerance is high, cases, that were determined to need the bypass, increased. Therefore, based on operative complications, this protocol might not always be useful and further studies are needed. Also, given the use of flow diverters for aneurysms of the ICA such as large or giant aneurysms, it is necessary to compare with the outcomes of flow diverters.

Even in this era, when flow diverters are available for aneurysm treatment, BTO remains an important examination (30). Moreover, especially for tumors invading the ICA or CCA at the neck, skull base tumors, and traumatic lesions involving the ICA or CCA, treatment based on BTO results should still be considered as a requirement.

## CONCLUSION

In BTO, the patient with MSTP of approximately 60 mmHg did not necessarily have an ischemic tolerance. Therefore, even in cases with MSTP of approximately 60 mmHg, the CBF should be measured. In this BTO protocol, by measuring MSTP and identifying cases of "ischemic borderzone," it is possible to narrow down cases requiring SPECT which is particularly reliable but complicated. Moreover, this protocol can be very useful for reducing false-negative cases of BTO and predicting the ischemic tolerability of PAO.

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