11 Complications of Aneurysm Embolization and Their Management: Basic and Practical Considerations

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Abstract

This chapter discusses the periprocedural complications of coil embolization for cerebral aneurysms and their management. Moreover, an explanation on delayed leukoencephalopathy after coil embolization has been included. The most important complications are hemorrhagic and ischemic events. The associated factors include type of aneurysm (ruptured or unruptured); aneurysm location, size, and morphology; and its relationship with the parent vessels. Five hundred and seventy ruptured cerebral aneurysms embolizations were performed, in total, 29 (5.1%) patients presented with perioperative hemorrhagic complications. Moreover, 1178 patients with unruptured cerebral aneurysms underwent embolization. Among them, 22 (1.9%) presented with perioperative hemorrhagic complications. The risk factors for perioperative bleeding include aneurysms with an anterior communicating artery, small-size aneurysms, and ruptured aneurysms. By contrast, local thrombus formation is a periprocedural ischemic complication and is correlated to aneurysm neck size, use of stents (particularly for ruptured aneurysms), aneurysm angle relative to the parent artery, and duration of the procedure. The endovascular outcomes of aneurysm embolization were presented and systematically compared with those of previous reports. Moreover, the pathophysiology and management of complications and methods associated with a decreased risk of catastrophic events were discussed. In all cases, the initial treatment is important, and a multidisciplinary team who can respond to emergency situations should be established.

Keywords

Intracranial aneurysm · Complications · Coil embolization

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11.1 Introduction

This chapter discusses the complications of coil embolization for cerebral aneurysms and their management. In 1991, Guglielmi et al. first reported the use of coil embolization for cerebral aneurysms [1]. Compared with clipping, which is the standard treatment for cerebral aneurysms, the technique is minimally invasive. Hence, it was considered a breakthrough in the history of cerebral aneurysm therapy. In particular, the indications for aneurysms located at the vertebral basilar artery system, which are challenging to manage with clipping, were expanded to facilitate safer interventions. The International Subarachnoid Hemorrhage Trial [2] and the Barrow Ruptured Aneurysm Trial [3] have a significant impact, particularly in the treatment of ruptured aneurysms, to communities in this field worldwide. Endovascular coiling involves the replacement of surgical clipping, and it is the preferred option for treating not only ruptured but unruptured aneurysms in the USA [4]. A previous research has compared the complication rates between coiling and clipping [5]. Intraoperative bleeding (IOB) is common among patients undergoing surgical clipping for ruptured aneurysms. Moreover, some studies showed that the incidence rate of IOB with new disability was similar between the endovascular and surgical treatment groups [2, 3, 5].

The important complications of coiling are hemorrhagic and ischemic events [6–12]. Three general perspectives should be considered when discussing complications. First, the concept of "risk factors," including the demographic patient's data and aneurysmal morphology was used if the risk of developing complications is significantly high. Whether postoperative complications can be predicted or prevented remains to be elucidated. This can be addressed by acknowledging the existence of risk factors first. Second, technical issues as well as problems and pre-cautionary measures in handling devices, such as micro-guidewire, microcatheter, microballoon, and coil, must be examined. Third, treatment measures for complications should be planned. That is, simulation is useful in ensuring that all members of a team can take appropriate and prompt actions when managing crisis [13]. Moreover, one wrong procedure can worsen the situation, resulting in devastating consequences.

Delayed leukoencephalopathy, a complication of unruptured aneurysmal embolization, is also explained in this study. Delayed encephalopathy, which occurs several months after treatment, has been attributed to contrast-induced encephalopathy [14], nickel allergy [15], and plugging due to the use of hydrophilic catheter coated with polyvinylpyrrolidone (PVP) [16]. PVP is a coating material widely used on catheters and guidewires, and it has been considered a causative agent [17, 18]. Although this complication is rare and not observed perioperatively, it should be considered by all neurointerventionists because it is unique in endovascular management [17].

Some of our results are presented in this chapter. Factors associated with complications, including incidence, mechanism, and prognosis, have been discussed. However, each case is unique, and there is no general principle that can be used because the situations are multifactorial, unpredictable, and specific [5, 7–9]. In this chapter, complications from the perspective of what should be the focus in performing coil embolization for cerebral aneurysm were discussed.

11.2 Hemorrhagic Complications

11.2.1 Incidence, Risk Factors, and Mechanisms of IOB

This section aimed to present the incidence, mechanism, management, and outcome of hemorrhagic complications in endovascular coil embolization for cerebral aneurysms. Hemorrhagic complications are among the most serious complications [6–8], and they affect prognosis. We addressed some complications based on risk factors and technical problems. Hemorrhagic complications in endovascular coiling include procedural aneurysmal perforations caused by the use of devices such as microcatheter, micro-guidewire, microballoon, and coil. IOB is defined as the first radiographic sign of a

perforation caused by a breach of any device out of the aneurysmal boundary on a road-map image [13]. This breach is followed by an increase in blood pressure and pulse rate. Contrast material that does not wash out in the venous phase indicates blood in the extravascular space. Decreasing the risk of mortality and permanent neurologic disability caused by IOB is dependent on immediate and appropriate treatment measures after a perforation occurs. Hence, IOB should be immediately recognized.

The complication rate was first described in a multicenter study. Results showed that the aneurysm perforation rate was 2.7% among patients (n = 403) admitted in eight centers [6]. Doerfler et al. [19] reported that the rupture rate was 3% in a series of 164 patients with acute rupture of aneurysm. In the study of Ricolfi [20], Cognard et al. [21], and Raymond et al. [22], the iatrogenic rupture rates were 4.4%, 4%, and 5.8%, respectively. The IOB rates vary from 1% to 5%. Regardless of whether the procedure is performed for ruptured or unruptured aneurysms, the prognosis of IOB is generally poor, with a mortality rate of up to 40% [8, 23, 24]. However, the severity of IOB may vary, ranging from a slight leakage of contrast material into the subarachnoid space to a massive hemorrhage with severe intracranial hypertension.

Several studies have assessed the risk factors of IOB. A meta-analysis showed that the risk of aneurysm perforation in coil embolization was significantly higher in patients with previous ruptured aneurysms than in those with unruptured ones [8]. Ruptured differ from unruptured aneurysms due to the presence of a rupture point and bleb. Moreover, a history of SAH may stimulate blood vessel walls and aneurysms with blood filling the subarachnoid space, resulting in an increased susceptibility to aneurysm rupture [8]. Although IOB is less common in unruptured than in ruptured aneurysms [25, 26], it is associated with increased morbidity and mortality rates [11, 27–29]. The other risk factors of IOB are small-size aneurysms and those with an anterior communicating artery (Acom) aneurysm [25]. A high risk of rupture in small-size aneurysms is attributed to the increased restriction of microcatheter movement within the aneurysm, resulting in greater stress within the aneurysm sac, particularly in cases of Acom aneurysms [30]. The risk factors of IBO may include unfavorable dome-neck ratio, acute angle between the internal carotid artery and the anterior cerebral artery, and morphological complexities of Acom [31]. Coronary artery disease, hyperlipidemia, race, chronic obstructive pulmonary disease (COPD), and low Hunt and Hess grade were associated with a greater risk of IOB, thereby indicating differences in vessel fragility requiring further confirmation [5]. For patients undergoing coiling, the independent predictors of IOB were Asian and black race, COPD, and lower initial Hunt and Hess grade [5]. Since the complication rate is low, the identification of these risk factors becomes challenging.

Regarding procedural issues, the balloon-assisted technique is similar to the use of temporary clips for the treatment of aneurysms. However, some studies showed that the use of balloons is a risk factor for IOB [32]. However, others have contrasting results [33–35]. In a retrospective study on subarachnoid hemorrhage (SAH), the incidence rate of IOB was significantly higher in patients who received local anesthesia than in those who received general anesthesia [36]. The high incidence rate of IOBs is attributed to unexpected movements, which can displace micro-instruments, during local anesthesia administration. The hemorrhagic complications of endovascular coiling include procedural aneurysmal perforations caused by devices including microcatheter, micro-guidewire, microballoon, or coil. Although these complications can occur, they are unexpected, complex and can have devastating outcomes [9]. Cloft et al. reported that the morbidity and mortality rates of perforations caused by coils (39%) and microcatheters (33%) were similar, and the morbidity and mortality rates of IOBs caused by micro-guidewires were considerably lower than those caused by coils or microcatheters [8]. Kawabata et al. showed that the clinical outcomes depend on the cause of IOB, and patients who experience aneurysmal rupture caused by microcatheter present with worst outcomes. Moreover,

the rates of good clinical outcomes associated with the use of coils, micro-guidewires, and microcatheters were 90%, 100%, and 57%, respectively [37]. Over-packing of the aneurysm, oversized coils, and use of stiff three-dimensional coils and inappropriate devices are associated with IOBs [33].

Decreasing the risk of mortality and permanent neurologic disability caused by IOB is dependent on immediate and proper treatment after a perforation occurs [8]. The immediate identification of IOB is extremely important. The first radiographic sign of a perforation is breakage caused by any tool used beyond the anatomic boundary on a road-map image. This is followed by increased blood pressure and pulse rate. Occasionally, false breaching can appear due to a patient's feeble movement, partially thrombosed aneurysm, or superimposed parent artery [9, 13]. Moreover, blood pressure quickly increases without an IOB when manipulation of devices stimulates the endothelium of a cerebral artery or in the event of diminished anesthesia [13].

11.2.2 Comparison Between the Outcomes of Coiling and Clipping

The incidence rates of IOB caused by coiling range from 1% to 2% for unruptured aneurysms and from 4% to 5% for ruptured aneurysms. The rate has been discussed and compared with that of IOB caused by clipping, which is the standard treatment for cerebral aneurysms. Several retrospective case series conducted in single institutions showed that the incidence rates of IOB vary from 2% to 4.5% for coiling and from 7.6% to 34.9% for clipping [3, 19, 26, 38–43]. CARAT is an ambidirectional cohort study of 1010 unselected patients with ruptured intracranial aneurysms who were treated by coil embolization or surgical clipping at 9 high volume centers in the United States from 1996 to 1998 and who were followed-up for more than 5 years. Moreover, it is an important prospective study as it revealed the complication rates between clipping versus coiling [5]. According to the study, IOB occurred in 148 (14.6%) patients, and ruptures during coiling (5%) or clipping (19%) increased the risk of periprocedural mortality/disability by four- and two-fold, respectively. The complications, risks, and morbidity and mortality of ruptured cerebral aneurysms are significantly low in coil embolization. Moreover, race and lower initial Hunt and Hess grade were associated with IOB based on a univariate analysis. The relationship between lower Hunt and Hess grade and a higher risk of IOB is perplexing probably because data were not collected prospectively and patients were not randomized to treatment type. The risk of IOB with COPD may be lower with clipping because vessels are not approached intraluminally or simply because the risk is predicted based on other unidentified factors that obscure an association with COPD.

However, the technical challenges between clipping and coil embolization are challenging to compare in terms of SAH severity and location of the targeted aneurysm because both are completely different treatment modalities. In the BRAT study [3], a policy of intent to treat favoring coil embolization, rather than clip occlusion, resulted in a low incidence of poor outcomes. Hence, a substantial number of treatments were switched from endovascular coiling to surgical clipping. Therefore, high-quality surgical clipping should be used as an alternative treatment modality. In summary, whether coiling is superior to clipping has not been validated in real-world settings, and performing either coiling or clipping should be based on the protocols of each institution.

11.2.3 Results

Data on IOB are described in this section. This retrospective study aimed to investigate the prevalence, risk factors, and management of complications among patients admitted to our institutions.

11.2.3.1 Material and Methods

Between April 2007 and October 2020, 570 ruptured cerebral aneurysm embolization procedures

Table 11.1 Total number of coiling procedures for ruptured and unruptured aneurysms and incidence of intraoperative bleeding (IOB) and mortality. The overall incidence rate of IOB was 2.9%, and the incidence of IOB and mortality was high in ruptured aneurysms

	Total number of interventions	Proportion of patients with IOB	%	No. of deaths	Mortality rate
Ruptured	570	29	5.1%	8	1.4%
Unruptured	1178	22	1.9%	3	0.3%
Total	1748	51	2.9%	11	0.6%

were performed at our institution and affiliated hospitals. Then, 29 (5.1%) patients presented with perioperative hemorrhagic complications, and 1178 patients with unruptured cerebral aneurysms underwent embolization. Moreover, 22 (1.9%) had perioperative hemorrhagic complications (Table 11.1). Next, we examined the location, shape, size, and severity of aneurysms and SAH in patients with intraoperative hemorrhage.

Our interventions have been reported in a previous study [44]. In brief, patients with unruptured aneurysms received two types of antiplatelet treatment (ticlopidine and aspirin or clopidogrel and aspirin) 1 week before surgery. Those treated with antiplatelet drugs received oral aspirin 100 mg daily and ticlopidine 100 mg twice a day. Heparin was administered intravenously (50 IU/kg) after the placement of a vascular sheath in the common femoral artery. In patients with ruptured aneurysms, treatment with systemic heparin was delayed until the guiding catheter was successfully placed. Anticoagulation therapy aimed to maintain the activating clotting time (ACT) at 1.5–2 times above the control level. The guiding catheters were continuously flushed with saline, and the sheaths were not continuously flushed. In all cases, systemic heparin was not reversed, and the patient was transferred to the stroke intensive care unit.

11.2.3.2 Results

Ruptured aneurysm: In total, 29 (5.1%) patients presented with perioperative hemorrhagic complications. Acom is the affected site in 16 (9.7%) of 165 patients. Intraoperative rupture was fatal in eight (50%) patients. Intraoperative hemorrhagic and other cases are presented below, followed by middle cerebral artery aneurysms in 2 (6.3%) of 32 patients and paraclinoid aneurysms of the internal carotid artery in 1 [5.0%] of 20 patients. IC-posterior communicating artery (Pcom) aneurysms (3 [1.9%] of 156) and basilar top aneurysms (0/48) were less common (Table 11.2). The total aneurysm size was smaller in the IOB group than in the non-IOB group (5.1 vs 6.3 mm), and the VER was higher in the IOB group than in the non-IOB group (44.4% and 33.1%, respectively) (Table 11.3). Intraoperative hemorrhage was characterized by neck outpouching (NOP) in four (26.7%) patients with Acom aneurysms.

Table 11.2 Proportion of patients with and location and incidence rate of IOB in embolization for ruptured aneurysms

Location	No.	IOB	%
Acom	165	16	9.7
ICPC	159	3	1.9
BA-top	48	0	0
ICaca	36	2	5.6
MCA	32	2	6.3
BASCA	23	0	0
ICpara	20	1	5.0
VAPICA	17	2	7.1
BA trunk	12	0	0

Acom is the most common site of IOB. By contrast, there is no IOB on BA-top. In addition, the incidence rate of IOB in MCs is high. However, the number of cases is small. *Acom* anterior communicating artery; *ICPC* internal carotid–posterior communicating artery; *ICaca* internal carotid–anterior choroidal artery; *MCA* middle cerebral artery; *BASCA* basilar artery–superior cerebellar artery aneurysms; *ICpara* paraclinoid aneurysms of the internal carotid artery; *VAPICA* vertebral–posterior inferior cerebellar artery aneurysms

Unruptured aneurysms: Perioperative hemorrhagic complications occurred in 22 (1.9%) of 1178 patients, of which three (0.3%) resulted in death (Table 11.1) and residual disability with a

modified Rankin scale (mRS) score 4 or greater in 2 (0.1%) patients. Then, 15 patients were discharged from the hospital with an mRS score 0 or 1 without any disability. Four (0.3%) patients underwent clipping. In 5 (4.6%) of 107 patients, the middle cerebral aneurysm (MCA) was the site of intraoperative hemorrhage. Intraoperative hemorrhage and other cases are presented below, followed by IC–Pcom aneurysms in 6 (3.7%) of 163 cases and Acom aneurysms in 4 (2.8%) of 140 cases. IC–paraclinoid aneurysms (4 [1.0%] of 402) and basilar top aneurysms (0/64) were less common (Table 11.4). IOB was most common in MCA aneurysms in unruptured aneurysms than in ruptured aneurysms. The total aneurysm size was smaller in the IOB group (5.7 mm) than in the non-IOB group (6.4 mm), and the VER was high in the hemorrhagic group (44.1% and 35.4%, respectively) (Table 11.5).

Intraoperative rupture caused by different devices was observed (Table 11.6). Intraoperative rupture during filling is common in ruptured cerebral aneurysms. However, poor prognosis is somewhat less common. Patients with intraoperative rupture with microcatheters and framing coils had a poor prognosis. There were no complications with the use of micro-guidewires or microballoons in ruptured cerebral aneurysms. Two patients with unruptured cerebral aneurysms presented with microballoon-induced vessel cracking, which is a fatal complication. In several intraoperative rupture cases, the cause was unknown. Thus, disease onset is difficult to predict.

Table 11.3 Size of the neck, long axis, and volume of embolization (VER) for ruptured aneurysms between the IOB and non-IOB groups. In the IOB group, endovascular obliterated aneurysms have a small neck and long axis size, and the volume embolization rate was high

	IOB group (n = 29)	Non-IOB group (n = 541)	Total number of patients (n = 570)
Age	66.5	64.7	64.8
Neck (mm)	3.1	3.8	3.8
Long axis (mm)	5.1	6.3	6.3
VER (%)	44.4%	33.1%	33.8%

11.2.3.3 Case Presentations

Case 1 (Fig. 11.1). A 69-year-old woman was unconscious and admitted to our institution. The preoperative WFNS grade was 4. The patient was diagnosed with ruptured aneurysm at Acom. Thus, coil embolization was performed. In particular, the angle from A1 to the axis of the mass was acute. Thus, the approach used was challenging. Moreover, there was neck outpouching (NOP). When the fifth coil was embolized, extravascular leakage of the contrast agent was observed. Two coils were subsequently embolized and hemostasis was achieved. However, the patient died due to severe SAH.

Table 11.4 Location of unruptured aneurysm, number of interventions, and proportion of patients with IOB. In unruptured aneurysms, IOB is more common in MCA and ICPC and is less common in BA-top and ICpara

Location	No. of interventions	Proportion of patients with IOB	%
ICpara	402	4	1.0
ICPC	163	6	3.7
Acom	140	4	2.8
MCA	107	5	4.6
BA-top	64	0	0
ICaca	46	0	0
BASCA	40	1	2.5
AC distal	27	0	0
IC others	26	0	0

Acom anterior communicating artery; *ICPC* internal carotid–posterior communicating artery; *ICaca* internal carotid–anterior choroidal artery; *MCA* middle cerebral artery; *BASCA* basilar artery–superior cerebellar artery aneurysms; *ICpara* paraclinoid aneurysms of the internal carotid artery; *VAPICA* vertebral–posterior inferior cerebellar artery aneurysms

Case 2 (Fig. 11.2). A 66-year-old man presented with grade 3 SAH. The patient was diagnosed with ruptured aneurysm in Acom. Moreover, NOP was observed. Axelguide 6F (Medikit), Fubuki 4.2F (Asahi Intec.), Neurodeo 10 (Medicos Hirata), Chikai14 (Asahi Intec.), first coil: Galaxy 3.5 mm 9 cm (J&J), one loop of the first coil was applied to the NOP, and the framing was good. After deploying the second coil, the loop deviated outside the coil mass at a slightly distant site from NOP, thereby indicating intraoperative rupture. Further embolization of the coils was performed to achieve hemostasis.

Case 3 (Fig. 11.3). A 67-year-old woman was admitted to the hospital for the endovascular treatment of right ICPC aneurysm without neurological deficits. Coil embolization was performed, and blood vessel cracking was observed during the third coil insertion. The aneurysm neck size was 4.0 mm; depth, 4.4 mm; width, 4.2 mm; and thickness, 3.8 mm. Axelguide 5F (Medikit), Hyperform 7 mm:7 mm (Medtronics), Neurodeo10 (Medicos Hirata), Chikai14 (Asahi Intec.), first coil: Galaxy 3.5 mm 5 cm (J&J), second coil: Target 360 nano 2 mm 4 cm (Striker), third coil: Target 360 nano 2 mm 4 cm. Balloon-assisted coil embolization was performed. The Hyperform 7*7 mm balloon caused cracks in the internal carotid artery, resulting in fatal vascular injury. The recommended infusion volume for Hyperform 7*7 mm is 0.27 mL. Visibility was not an issue in the use of this balloon, and the recommended infusion volume was maintained.

Table 11.5 Aneurysm neck and size and volume of embolization (VER) for unruptured aneurysms. The characteristics were similar to those of ruptured lesions (long axis size and high volume embolization rate)

	IOB group (n = 22)	Non-IOB group (n = 1156)	Total number of patients (n = 1178)
Age	60.8	61.4	61.4
Neck size (mm)	3.9	4.0	4.0
Long axis (mm)	5.7	6.4	6.4
VER (%)	44.1	35.4	35.6

11.2.3.4 Discussion

In this study, the incidence of IOB was similar to that of previous reports: 5.1% and 1.9% for ruptured and unruptured aneurysms, respectively. Compared with unruptured aneurysms, ruptured ones are associated with a higher incidence of IOB, and risk factors such as aneurysmal rupture, small-size aneurysms, and location in Acom have been reported previously. Moreover, a significantly high proportion of patients with IOB presented with neurologic deterioration at discharge and last follow-up. However, the proportion of functionally independent patients with an mRS score of 0–2 did not differ between the two cohorts. This result indicated that the degree of disability caused by IOB among patients with

Table 11.6 Devices that could cause intraoperative bleeding. Patients with intraoperative rupture caused by microballoon, framing coil, or microcatheter had a poor prognosis, whereas those with intraoperative rupture caused by filling coil had a better prognosis

	Number of ruptured cases	Mortality in ruptured cases	Number of unruptured cases	Mortality in unruptured cases
Microcatheter	1	1	1	0
Micro-guidewire	0	0	1	0
Microballoon	0	0	2	2
Coil				
Framing	2	2	1	0
Filling	10	1	6	0
Finishing	1	0	5	0
Increase in hematoma size	3	3	(−)	(−)
Unknown	10	2	6	1

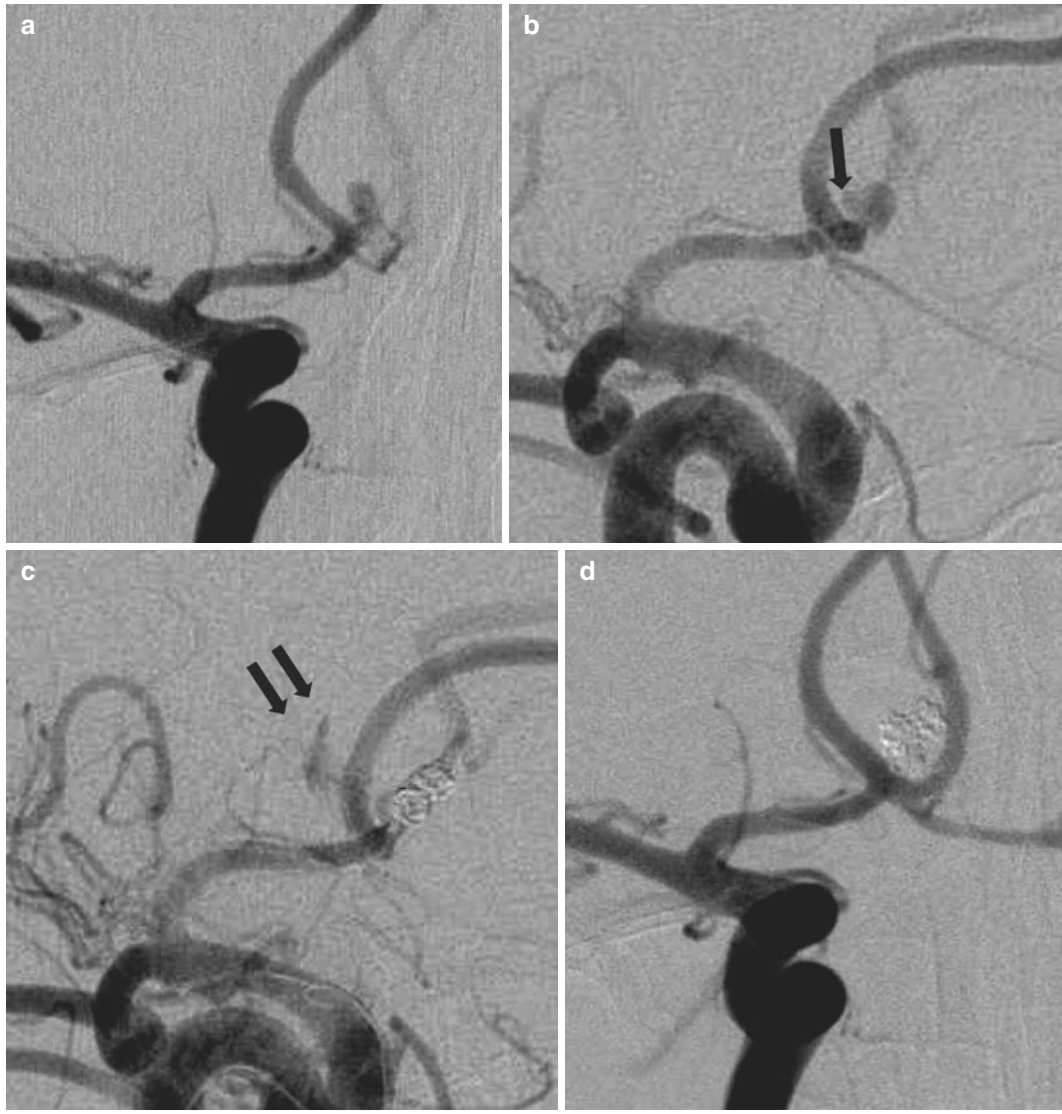

Fig. 11.1 Case 1. See text for full details. (**a**) Preoperative left carotid artery angiogram, neck view. (**b**) Other view on left carotid angiogram. A small basal neck outpouching was observed (arrow). (**c**) After five coils were embolized, extravasation of the contrast material was noted (double arrow). (**d**) Two coils were embolized and intraoperative bleeding was controlled

unruptured aneurysms was not severe. Notably, none of the patients in the IOB cohort with an aneurysm in Acom, which was the most common location of IOB in the ruptured aneurysms group, experienced neurological deterioration. By contrast, the IOB cohort with BA aneurysm had a high risk of neurological deterioration (two [66.7%] of three cases) [45]. There is a high incidence of IOB in Acom in our institution. However, no cases of intraoperative rupture of basilar artery aneurysms, which vary per institution, were observed.

Most cases of aneurysm intraoperative breach during filling were caused by microcatheter perforation and vascular damage caused by a microballoon in unruptured aneurysm treatment. There are only few reports on complications caused by microballoon as the Case 3. This complication is

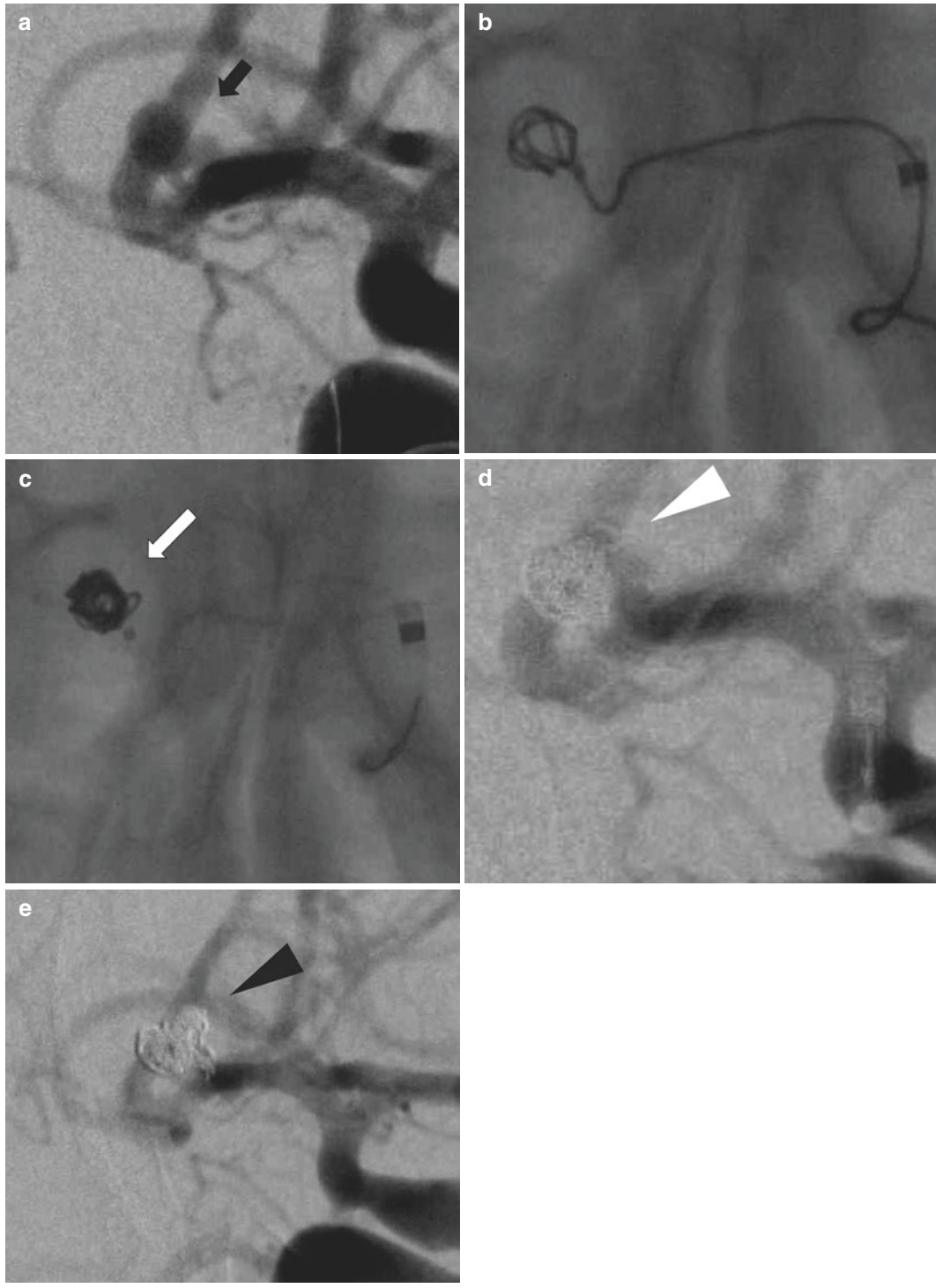

Fig. 11.2 Case 2. See text for full details. A 68-year-old man with grade 3 SAH. See text for full detail. A diagnosis of ruptured Acom was made. (**a**) There was a basal neck outpouching (NOP: black arrow). (**b**) Framing was in progress. (**c**) A coil loop was placed on the NOP and a good frame was made. (**d**) Coil protrusion outside the aneurysm during the second coil embolization. The loop was observed at site slightly distant to NOP (white arrowhead), resulting in an intraoperative rupture. (**e**) Hemostasis is complete and extravascular leakage has stopped (black arrowhead)

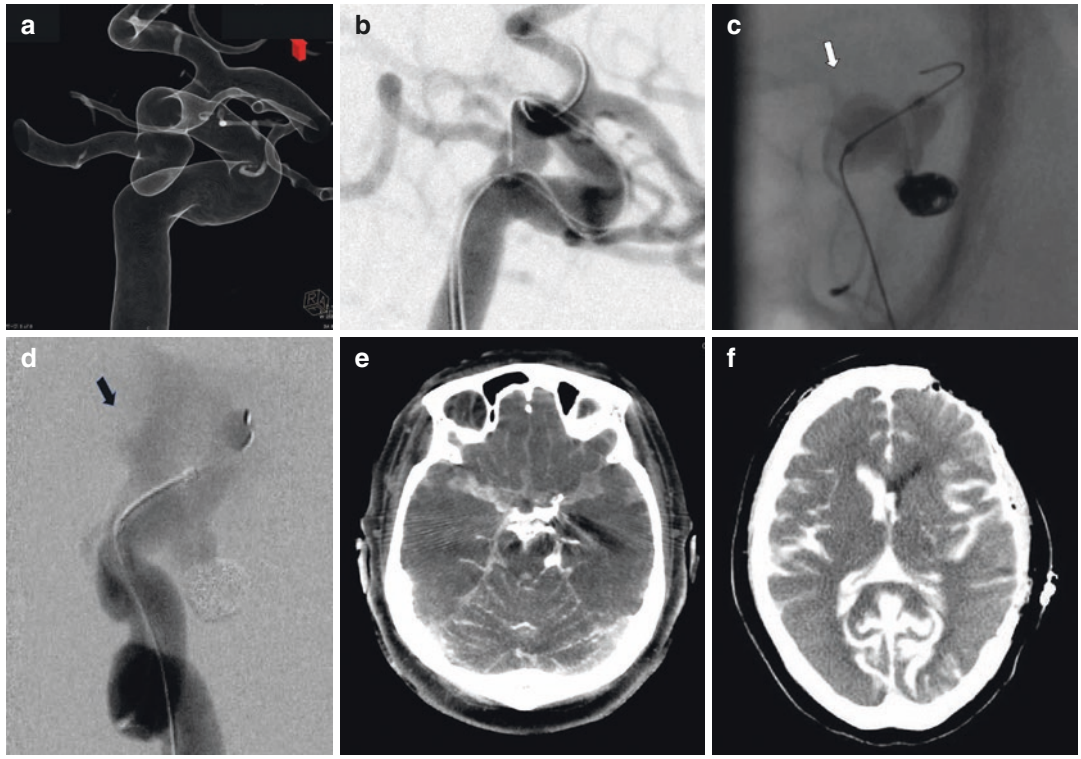

Fig. 11.3 Case 3. Fatal rupture with the use of microballoon. See text for full detail. Size of the neck 4.0 mm, aneurysmal dome size 4.4 mm. Broad neck and relatively small-size aneurysm. In placing the third coil the vessel laceration occurred. (**a**, **b**) ICPC aneurysm was observed on three-dimensional angiogram. Pcom branched from the neck. Although the dome-to-neck ratio was low, balloon-assisted coil embolization could be feasible. (**c**) The Hyperform balloon 7*7 mm was tearing the vessel wall. (**d**) Intraoperative rupture occurred. Balloon bursting was suspected. Local hemostasis was unsuccessful, and the patient died after external decompression. (**e**, **f**) The procedures were performed at the interventional room combined with multidetector computed tomography (CT). (**e**) Hemorrhagic complication was found in plain CT scan immediately after the rupture. (**f**) The patient underwent immediate decompressive craniotomy, the CT scan revealed diffuse swelling of the whole brain parenchyma and the cortico-medullary boundary was obscured

often fatal. Local hemostasis with balloons is no longer feasible, and parent vessel occlusion may be performed, or, alternatively, a liquid embolic material can be used. Middle cerebral and small-size aneurysms were associated with IOB in unruptured cases in the series. Most patients had a good prognosis due to rapid response to microballoons. Preoperative planning was considered important, and this management should consider the structure of the blebs and masses as well as microcatheter movement and coil embolization.

The presence of NOP, as shown in Figs. 11.1 and 11.2, is another issue. Although intracranial saccular aneurysms invariably rupture in the dome area, the wall of the aneurysm base can be the point of rupture. This finding has been reported for quite some time. In terms of incidence [44], the rate was 2% according to an autopsy study by Crompton [46]. Nonetheless, the recognition of such a basal rupture on angiographic evaluation is crucial for optimal treatment [47]. In a patient with an aneurysmal subarachnoid hemorrhage, the basal outpouching may be the point of rupture. These so-called basal ruptures are often accompanied by an angiographically identified blister at the neck region of the aneurysm [48]. In this series, the rupture site is the basal outpouching observed along with

Table 11.7 Risk factors of intraoperative bleeding in coiling based on previous studies

History of aneurysmal rupture [8, 25, 26]
Location (e.g., Acom [25, 30, 31] & BA-top [45])
Neck basal outpouching [47–49]
Small size [5, 8, 25]
History of chronic obstructive pulmonary disease [5]
Race (Asian, black [5])

ruptured aneurysms in approximately 33% of patients with surgically explored aneurysms with this pathoanatomic feature [49]. This finding was correlated with coil perforation of the ruptured basal outpouching or coil compaction into the dome, which exposes the basal rupture site. Hence, NOP is important and can be considered a risk factor.

Table 11.7 summarizes the risk factors for IOB in conjunction with the related previous reports. These include factors for which consensus has not yet been established. However, there is a consensus that at least ruptured aneurysms, small aneurysms, Acom, and the presence of NOP should be treated with full awareness.

11.2.4 Management of Hemorrhagic Complications

Angiogram can be performed to confirm the presence of IOB. Contrast material staying in the venous phase indicates blood in the subarachnoid space. Cone-beam computed tomography (CT) can be conducted to assess for this condition. If aneurysmal perforations are detected during the procedure, prompt treatments are critical. That is, blood pressure should be controlled, and anticoagulants must be immediately reversed. However, in some cases, we do not recommend protamine administration if rapid mechanical hemostasis can be achieved. Antiplatelet medications such as aspirin and clopidogrel can also be reversed [50].

Perforation caused by micro-guidewire may be minimal, and embolization can be continuously performed. However, caution should be taken. When perforation caused by devices such as coil and microcatheter is observed, the instrument should not be removed to prevent further injury to the structures. Laceration caused by a coil can be mitigated by leaving the perforating coil in place. Hence, the part of the coil outside of the aneurysm should be deployed, and the microcatheter tip must be withdrawn from the proximity of the aneurysm wall. Upon positioning the microcatheter tip, the rest of the coil should be delivered into the aneurysm. With the use of a second microcatheter, the aneurysm must be packed with coils, thereby temporarily leaving the first microcatheter in place. This multiple microcatheter technique is more advantageous than a single microcatheter technique for the immediate and accurate management of IOB [51]. In addition, hemorrhage can be immediately and effectively controlled with the application of a balloon, which is considered as temporary clipping, across the aneurysmal neck at the time of rupture. However, caution must be taken when using balloons because it may increase the risk of secondary procedural complications. In such circumstances, n-butyl cyanoacrylate can be considered in the closure of aneurysmal ruptures [52]. McDougall et al. reported that uncontrolled advancement of microcatheters can be a factor for IOB. The incidence of microcatheter perforation can be decreased by ensuring that no forward pressure is exerted on the microcatheter before the micro-guidewire is removed and by withdrawing the micro-guidewire very slowly while under fluoroscopy [39].

All endovascular devices placed into the aneurysm lumen can cause perforation. Moreover, neurointerventionists should be aware that microcatheters have a radiolucent distal segment with a length of approximately 0.5–1 mm between the distal marker visible on fluoroscopy and the actual microcatheter tip [53]. However, the incidence of wire perforations is underreported. The size of the perforation was correlated with the device size. Because of the small number of perforations in unruptured aneurysms, performing a statistical comparison is not practical.

11.3 Ischemic Complications

11.3.1 General Considerations

A thromboembolic event is defined as any event with complete or partial occlusion of arteries at the site of the parent vessel and aneurysm distal to the vascular territory where the endovascular procedure was performed and/or in other vascular territories. The mechanisms and management of thromboembolic complications are described in this section. Ischemic complications are important factors influencing prognosis after endovascular therapy for intracranial aneurysms. The incidence rates of symptomatic ischemic complications among individuals receiving this therapy range from 2% to 3% [54–56]. Furthermore, about 10%–60% of patients present with small high-intensity signals on diffusion-weighted images [57, 58]. Thromboembolic complications may begin with the emergence of a small thrombus in a vessel. First, a small thrombus develops in a vessel [9]. This can lead to vascular occlusion due to thrombosis. In addition, a thrombus may develop in the catheter when DAC is used, and the thrombus may somehow flow distally, causing an infarction. Although thromboembolic complications are more common and are associated with higher morbidity rates than intraprocedural ruptures, identifying a thromboembolism is more challenging than confirming the presence of aneurysmal perforations [9]. Appropriate response is still essential at an early stage. Heparinization and preoperative coagulation therapy can prevent complications. Oral clopidogrel and/or aspirin decreased the symptomatic thromboembolic complication rate of elective coil embolization for unruptured aneurysms [58]. This result indicates that the treatment of unruptured cerebral aneurysms begins with preoperative preparation.

Thromboembolic complications start with the formation of microthrombus in the local vessels. First, the pathogenesis of microthrombus was discussed. This condition might be attributed to the administration of antiplatelet therapy preoperatively. GP inhibitors [59, 60] might be more effective than fibrinolysis because acute thrombi are rich in platelets (white clot). Although it is used for the treatment of thromboembolic complication during procedures, there might be a higher risk of complication at the vascular access site, hemorrhage if emergency surgery is needed, thrombocytopenia, and intracranial hemorrhage, and the effects are not easily reversed. We administered aspirin 200 mg via a stomach tube, and systemic hypertension was controlled. In case of flow disturbance, tPA and GP1 inhibitors combined with fibrinolysis using urokinase were recommended. In recent years, the usefulness of prasugrel has been reported and it is being widely used in clinical practice [61]. In any opinion, thrombus formation in the parent vessels initially occurs in thromboembolic complications. Therefore, knowledge on the mild effects of contrast agents is important.

11.3.2 Local Thrombus Formation: Angiographic Classifications of Appearance and Management

Intraprocedural thrombus that forms at the boundary between the parent vessel and the aneurysm neck during coil embolization can be successfully treated if detected at an early stage [62–65]. The sources of these emboli vary, thereby indicating a potential risk of frequent thrombus formation during coil placement. In this procedure, particularly at the late stage, a minute thrombus appears around the parent vessel at the aneurysm neck with coil mass [65]. Intraprocedural thrombus that forms at the boundary between the parent vessel and the aneurysm neck during coil embolization can be successfully treated if detected at an early stage [63–65]. The following are some points regarding angiographic findings.

The coil–parent artery interface is the surface of the coil mass that interacts with the inflow and/or outflow of blood stream and is located at the parent artery and coil mass. Moreover, it includes areas in the parent artery where turbulence or stasis of flow might occur during procedures. Fresh thrombus was defined as the presence of a small

volume of contrast material at the coil–parent artery interface zone in coil embolization. A grading system that was modified based on the TICI grading systems [66–68] was used:

- Grade 1: microthrombus formation with normal flow, no distal occlusion
- Grade 2: distal artery occlusion without normal filling in the distal branch with near-normal appearance
- Grade 3: thrombus formation with significant flow reduction, poor filling of the parent
- Grade 4: no flow, parent vessel occlusion (Fig. 11.4)

Therapy for microthrombi was started based on the physician's discretion. Aspirin 200 mg was administered via a stomach tube. Moderate perfusion was achieved immediately after control angiography. Patients with grade 2 thrombus on angiography received fibrinolytic therapy. Intra-arterial urokinase infusion was started via continuous manual injection. The infusion rate was about 5000 IU/min, and the infusion lasted for 15–30 min. Angiography was performed repeatedly. Even if perfusion was not achieved, treatment was discontinued at a maximum dose of 100,000 IU. ACT was conducted in all patients before starting fibrinolysis therapy. Cronqvist et al. reported the outcomes of super-selective intra-arterial fibrinolytic therapy for thromboembolic events occurring during endovascular aneurysm treatment in 19 patients. Results showed complete recanalization in 10 and partial recanalization in 9 patients, and 14 eventually presented with good outcomes [59]. However, three of six patients with ruptured aneurysms had intracranial bleeding. Hence, compared with rescue therapy

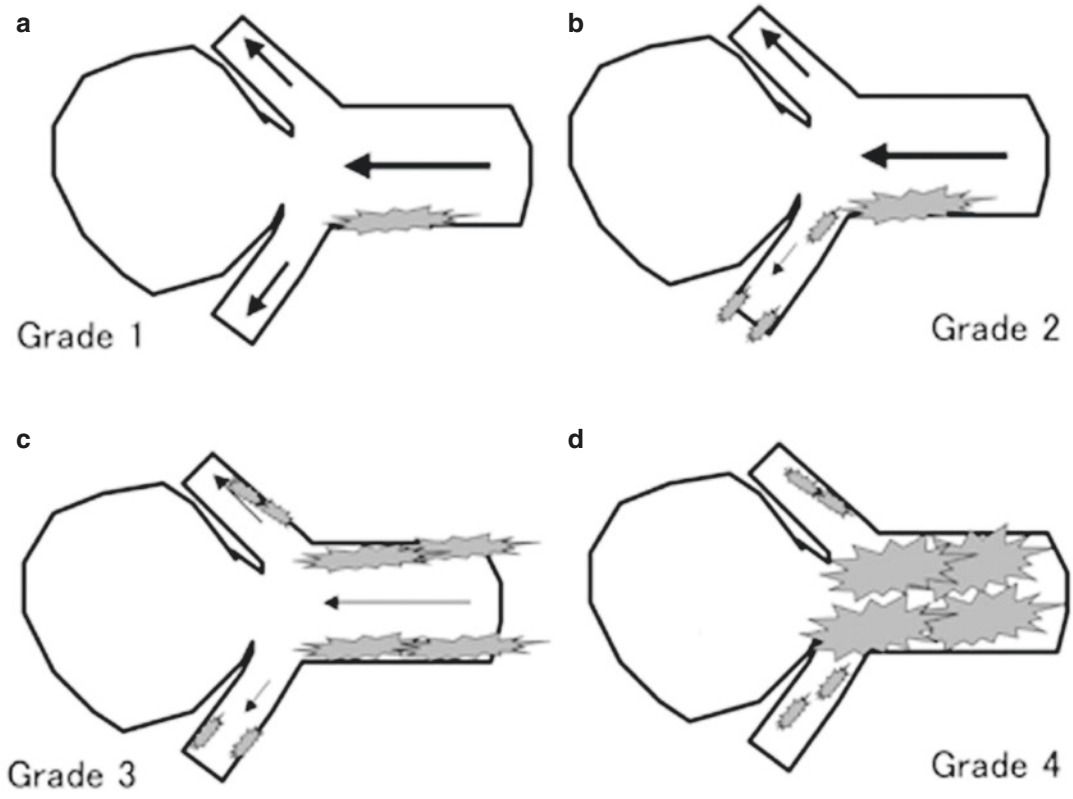

Fig. 11.4 Schematic representation of thrombus formation at the parent vessels. (**a**) Grade 1: Microthrombus formation with normal flow. (**b**) Grade 2: distal artery occlusion without normal filling in the distal branch. (**c**) Grade 3: thrombus formation with a significant flow reduction. (**d**) Grade 4: no flow, occlusion of the parent artery

with glycoprotein IIb/IIIa inhibitors, that with fibrinolytic agents for intraprocedural thromboembolic events is associated with significantly higher morbidity and mortality [69]. Therefore, urokinase and tPAs are no longer considered as the primary treatment for thrombi during coiling of aneurysms.

11.3.2.1 Case Presentation

Case 5 (Fig. 11.5)**. Grade 1: Microthrombus Formation**

A 67-year-old-woman underwent coil embolization for a ruptured Acom cerebral aneurysm (H&K grade 4, WFNS grade 4, and Fisher score of 3). The procedure was performed on day 0. The patient underwent elective coiling of the aneurysm. Embolization of the aneurysm was performed with a single catheter technique. A microthrombus appeared in the left A2 after the final stage of coil embolization. Aspirin 200 mg was administered immediately via a stomach tube. Serial angiography revealed diminished thrombus, and no distal artery emboli were observed. The thrombus soon disappeared.

Case 6 (Fig. 11.6)**. Grade 3: Thrombus Formation with Significant Decrease in Blood Flow**

A 63-year-old woman was admitted to our hospital due to altered mental status. CT scan revealed SAH (H&K grade 4, WFNS grade 4, and Fisher score of 3). The patient was diagnosed with ruptured cerebral aneurysm in Acom. Coil embolization was performed on day 0, with a simple catheter technique. A short time after catheter removal, a microthrombus was observed in the right A2. Then, there was a tendency for microthrombi to infiltrate toward the neck with significant decrease in blood flow in the parent artery. Aspirin 200 mg was administered immediately via a stomach tube, and serial angiography revealed diminished thrombus. No distal artery emboli were observed, and the microthrombus was resolved.

Case 7 (Fig. 11.7)**. Grade 1: Microthrombus Formation**

An unruptured basilar top aneurysm was detected on magnetic resonance imaging (MRI) in a 69-year-old female patient. She underwent elective coiling of the aneurysm. The longest aneurysms measured 8.84 mm, and the neck size was 6.20 mm. After the vascular sheath was placed, heparin 5000 IU was administered. Coil embolization of the aneurysm was performed using the balloon-assisted techniques. Coil treatment of the aneurysm was continued until a tight coil mass was achieved. The total coil length used was 133 cm, and the volume embolization ratio was 26.4%. When the last coil was placed and the balloon was removed, control angiography revealed

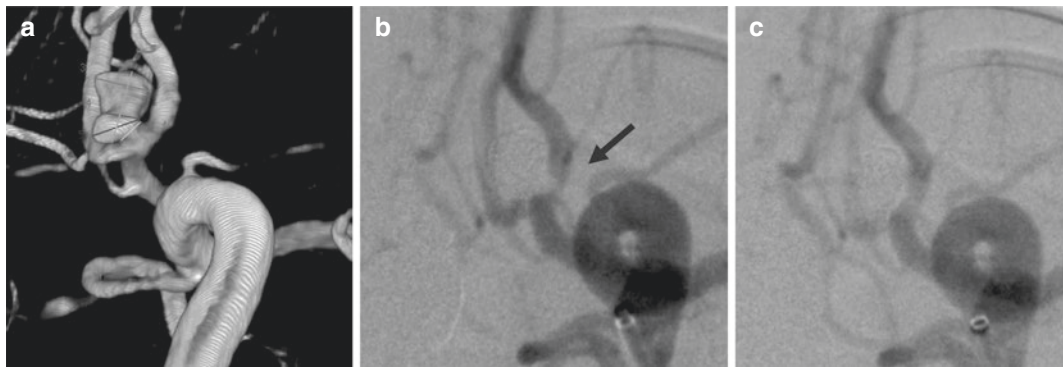

Fig. 11.5 Case 5. Grade 1 thrombus formation. (**a**) Ruptured aneurysm in Acom was observed on left internal carotid artery three-dimensional angiogram. (**b**) Left internal carotid artery angiogram revealed a small embolus at the left A2. (**c**) Complete recanalization of the vessel was achieved after the administration of aspirin 200 mg via a stomach tube

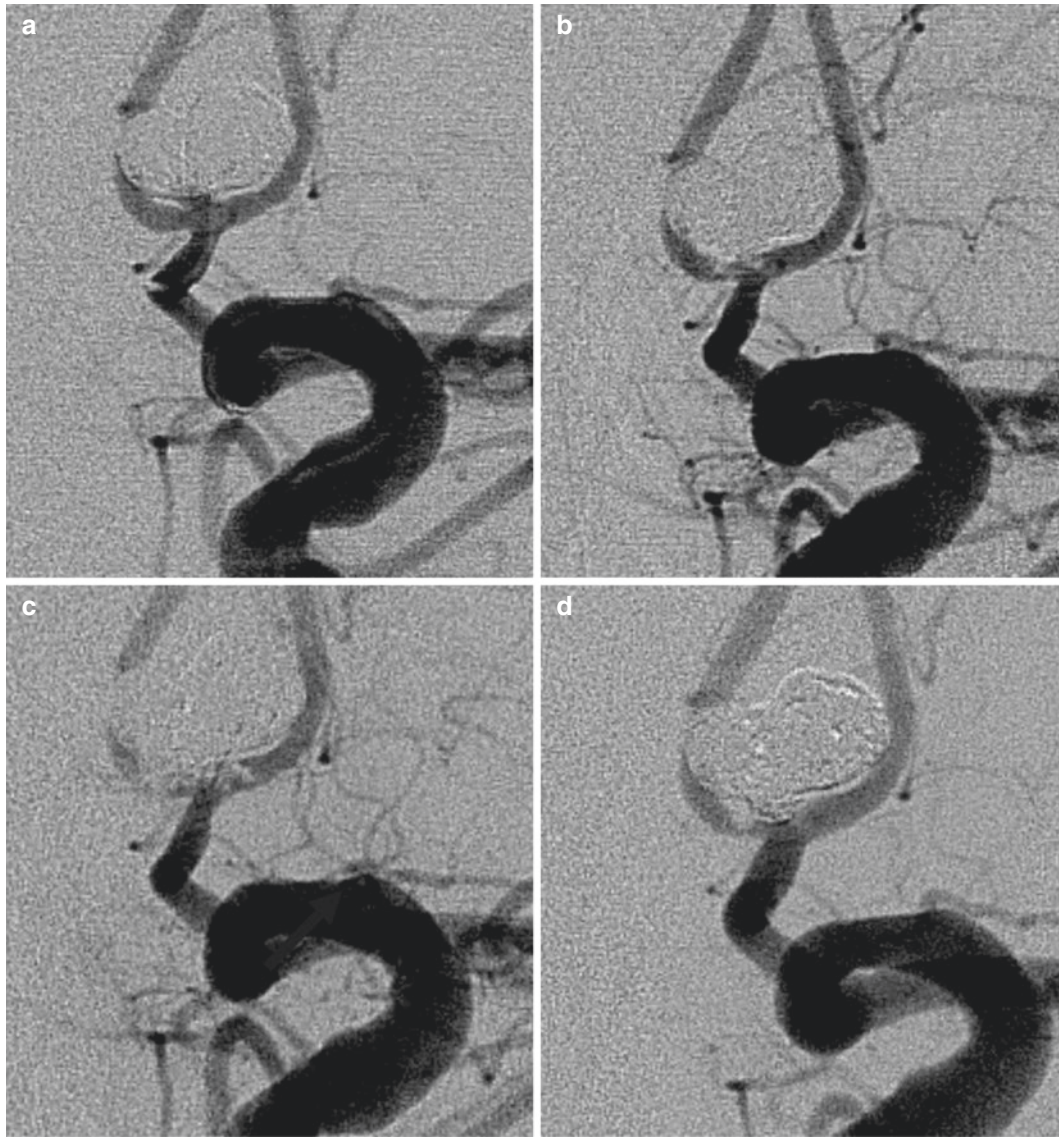

Fig. 11.6 Case 6. See text for full details. Grade 3 thrombus formation with significant reduction in blood flow. Left internal carotid angiogram revealed the following: aneurysm size, 9 mm; depth, 6.3 mm; and neck size, 2.9 mm. A simple technique of coil embolization. (**a**) Before microcatheter removal, complete embolization was achieved. (**b**) Twenty coils were used, one coil was added, and the microcatheter was removed at a VER of 26.9%. (**c**) After 10 min of waiting, there was further microthrombotic enhancement. (**d**) The microthrombus was stabilized by the drug (arrow), and the right A2 was well delineated, thereby completing the procedure

a small thrombus at the coil–parent artery interface. Aspirin 200 mg was administered immediately via a stomach tube, and serial angiography revealed diminished thrombus. No distal artery emboli were observed. After recovery from anesthesia, overnight heparinization and oral aspirin were started and continued for 3 months. The patient had no other morbidities.

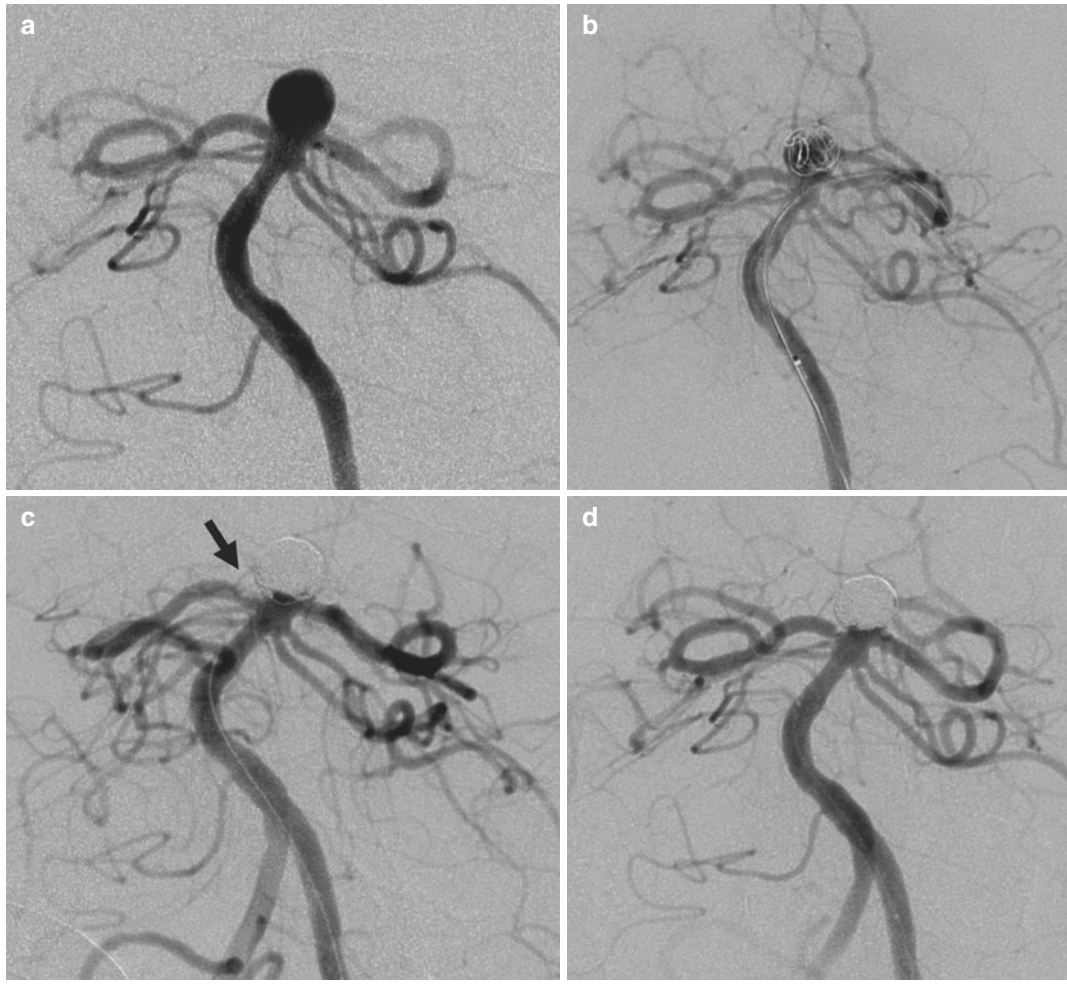

Fig. 11.7 Case 7. See text for full details. Acute thrombus formation: Grade 1. Microthrombus appeared at the right P1 of the coil–vessel border zone. (**a**) Left vertebral angiogram (frontal projection) before embolization. (**b**) Left vertebral angiogram revealed that the coil loop protruded into the parent artery, thereby maintaining normal flow in the vessel. (**c**) After balloon removal, the control angiogram showed a small volume of contrast material at the coil–parent artery interface, indicating grade 1 thrombus formation (arrow). (**d**) Angiogram after treatment. After the administration of aspirin 200 mg via a stomach tube, an almost complete resolution of thrombus at the coil surface line was observed

11.3.3 Risk Factors and Considerations

Thromboembolic complications may be caused by clot formation in the guiding catheter, on the coil mashes, or in parent vessels caused by induced vasospasm or coil mispositioning [70]. Prolapsed coil loops are the sites of platelet aggregation, leading to local thrombosis or distal thromboembolism [71]. Several reports have shown that embolic sources include air embolism, atheroma dislodgement during catheterization, thrombus formation from the device used during the procedure, and hydrophilic coating from catheters and wires [72, 73]. There are two types of factors for ischemic complications: procedure-related factors (procedure time and methods, number of coils inserted, extent of procedure manipulations, operator experience, etc.) and non-modifiable factors (patient age, aneu-

rysm size and location, presence of SAH, smoking, etc.). Regardless of the technique used, thromboembolic complications are more common in patients with a ruptured aneurysm than in those with an unruptured aneurysm [74]. A previous research showed that the other risk factor is a large aneurysm. In some studies, multivariate logistic analysis revealed that presence of SAH and procedure time were independent predictors of ischemic events during endovascular coiling of intracranial aneurysms [65, 75].

Recent advancements in vascular reconstruction devices and coils have facilitated the application of coil embolization even for aneurysms with a relatively wide neck. Despite tight coil packing, protrusion of coil segments out of the aneurysm and into the parent artery still occurs. Coil protrusions were sub-grouped according to form, degree of protrusion into the parent vessel, and position in the vessel. Coil protrusions did not increase the incidence of high-intensity lesions (infarcts) on diffusion-weighted MRI (33.3% vs 29% in cases without coil protrusion) [75]. A longer operative time increased the risk of infarct, and lesions were more commonly observed in the cortical area than in the perforating area [70, 75]. Coil protrusion was more likely to occur in cases of wide-neck aneurysms with loose neck framing. Moderate and less coil protrusion carries no additional thromboembolic risk if blood flow is maintained, which can be facilitated by additional postoperative antiplatelet therapy. Whether coil protrusion into the parent artery increases the risk of thromboembolic events is still a cause of debate. However, coil retrieval [76, 77] or parent artery stent deployment is commonly recommended for severe protrusion.

Some reports showed that stent-assisted coiling (SAC) was associated with a higher rate of thromboembolic complications than non-SAC [78]. However, if antiplatelets and anticoagulants are used appropriately, SAC is not likely associated with an increased risk of thromboembolic events, which are more common in coiling for acutely ruptured aneurysms [79, 80]. In the case of ischemic complications, there are many reports of risk factors, but no consensus has been reached by authors. This may be due to variation in treatment protocols, i.e. use of antithrombotic agents, timing and volume of their administrations in each institution. For ischemic complications, it may be difficult to compile a list similar to that for hemorrhagic complications.

11.4 Delayed Encephalopathy

11.4.1 General Considerations

Delayed leukoencephalopathy is a rare complication of coil embolization for unruptured cerebral aneurysms, and it occurs several months after treatment [17, 81]. Histologically, foreign body embolization is caused by catheter hydrophilic polymers resulting in distal embolization [16]. The cause can be hydrophilic polymer reactions, which may present as various lesions, including those in encephalopathy, chemical meningitis, and hydrocephalus. Because of insufficient data regarding this disease, a multicenter study should be conducted to elucidate its pathogenesis and prevention. Lesion biopsy suggests that device-associated PVP can cause distal embolization and granulomatous response [18]. Moreover, hydrophilic coating inside the catheter may detach during the insertion and removal of coils, which then leads to the formation of a distal embolus, resulting in granuloma at that site. In general, this condition has been reported in numerous cases of large cerebral aneurysms in which multiple coils have been used. However, in some case reports, it occurs after the implantation of flow diverters [73].

The characteristic imaging findings of multiple dots on gadolinium-enhanced T1-weighted images are granulomatous changes. These conditions are highly responsive to steroid treatment. The imaging findings are highly distinctive and have diagnostic significance. Thus, symptoms of relatively sudden neurologic deteriorations appeared several months after aneurysm coil embolization or pipeline implantation for unruptured aneurysm, in such a case, this is the first step to suspect this disease. Diagnosis is rela-

tively easy by MRI findings and is based on the following three points.

1. Multiple lesions with small patchy enhancement consistent with the access route of a cerebral aneurysm to appear after a few months later of the operation.
2. Only a slight change was observed on diffusion-weighted image in the white matter in the same area on fluid-attenuated inversion recovery with a wide range of high-signal area.
3. A low signal on magnetic susceptibility-weighted image.

It was associated with marked edema in the white matter, which might be caused by headache. The protein levels in the CSF fluid were elevated. However, no other findings were noted. Corticosteroid improved both symptoms and imaging findings and, in some cases, therapeutic diagnosis. Moreover, it has been used for treatment and found to improve both symptoms and imaging findings. Treatment with corticosteroids significantly improved both symptoms based on MRI findings.

11.4.2 Case Presentation

Case 8 (Fig. 11.8). A 62-year-old woman underwent stent-assisted coil embolization for a large unruptured left basilar artery–superior cerebellar artery aneurysm. 20.7 mm 16 mm 14.9 mm. Envoy 6F (J&J) placed at RT VA, two SL-10 (Stryker) jailed, LT VA: dominant, FUBUKI 6F (Asahi Intec), Headway17 (TERUMO), LVIS Jr. 2.5 mm 17 mm (TERUMO), 32 coils deployed, 762 cm; 819.9 mm^3, VER: 32.3%. The patient was discharged without new postoperative complications. She often complained of severe headaches. One month after coil embolization, the

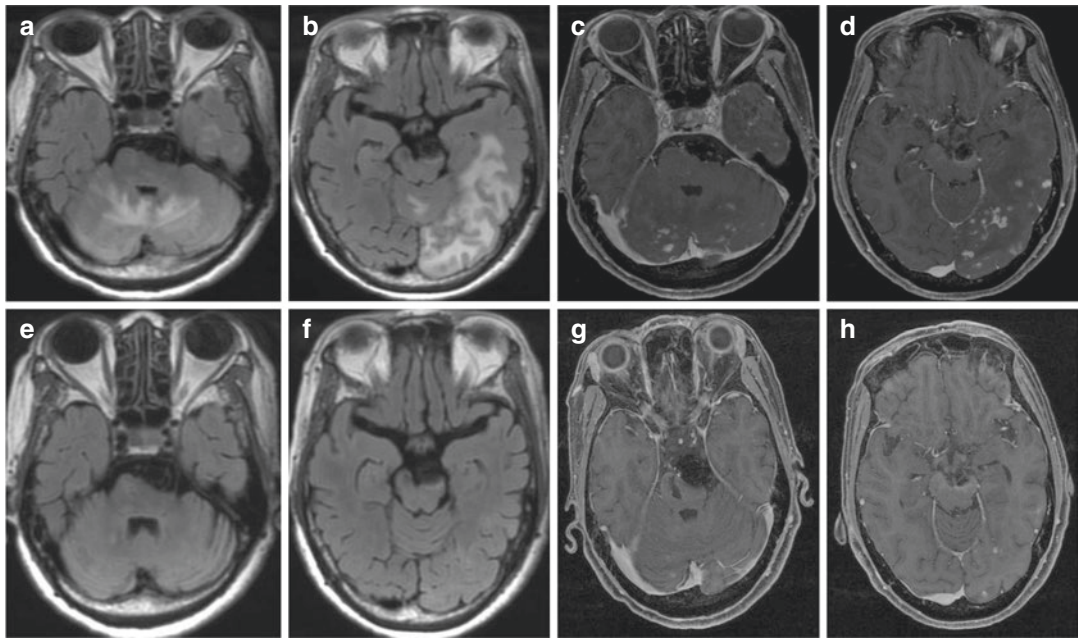

Fig. 11.8 Delayed encephalopathy. (**a**–**d**) Magnetic resonance imaging (MRI) at admission to our hospital about 1 month after coil embolization. (**a**, **b**) Fluid-attenuated inversion recovery (FLAIR) images. (**c**, **d**) Contrast-enhanced T1-weighted images. (**e**–**h**) MRI conducted 6 weeks after steroid pulse therapy. (**e**, **f**) FLAIR images, (**g**, **h**) Contrast-enhanced T1-weighted images. In the FLAIR image, there were high-signal areas in the bilateral cerebellum, left thalamus, and left temporal to the occipital lobes. On contrast-enhanced T1-weighted images, the same area had multiple punctate lesions. Six weeks after steroid pulse therapy, the high-signal range of the FLAIR images and the structures that should be assessed with contrast enhancement disappeared

patient was admitted to the hospital due to disorientation, behavioral abnormality, slurred speech, and aphasia. Fluid-attenuated inversion recovery magnetic resonance imaging revealed a high-signal intensity in the interventional perfusion areas. Multiple lesions were observed on contrast-enhanced imaging. The patient's symptoms improved with steroid pulse therapy after 6 weeks, and abnormal imaging findings disappeared.

11.5 Conclusion

The development of complications is challenging to predict and investigate using statistical methods because of their low incidence. The risk factors of IOB include ruptured, Acom, and small-size aneurysms and anatomical, morphological difficulties including NOP. Thus, these should be considered by neurointerventionists. The life-threatening factors associated with thromboembolism include large-size aneurysms, wide neck, long procedure time, and use of stent. However, this finding is controversial. To prevent thromboembolic complications, the early detection of a thrombus is important. While these risk factors are controversial, those are well known. Therefore, they should be cautiously considered in preoperative planning. When complications occur, a prompt response is important to reduce damage.

Disclosure None of the authors declared any conflict of interest.

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