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REVIEW

Secondary coiling after incomplete surgical clipping of cerebral aneurysms: a rescue strategy or a treatment option for complex cases? Institutional series and systematic review

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Abstract

Residual and recurrent intracranial aneurysms after surgical clipping present a persistent risk of bleeding. Secondary coiling after incomplete clipping represents a strategy to occlude the residual sac: feasibility, bleeding risk and outcome were evaluated through a systematic review of literature along with the series of two tertiary referral neurovascular centres. Demographics, ruptured status, aneurysm morphology, topography, exclusion at surgery, timing of secondary coiling, complications, occlusion rate and outcome were analysed. Percentage of incidence and 95% CI were calculated for all variables. *T* test was used for continue variables, whereas Fisher's test (two-sided) is for categorical ones. Overall, 102 patients (92 cases from literature and 10 cases from institutional series) were included. Mean age at diagnosis was 52.94 ± 12.17 years, and male/female ratio 0.5; 3/4 of aneurysms involved the anterior circulation, whereas ¼ the posterior circulation. An aneurysmal *neck remnant* was described in 58.43% of cases, an aneurysmal *sac remnant* in 29.21% and a *regrowth* in 12.36%. Residual aneurysm rupture was reported in 22% of cases. Complete/near-complete occlusion after secondary coiling was observed in 70% of cases, a partial in 25.56% and a failure in 4.44%. Only one case of perforation was reported. Complications were comparable to standard endovascular procedures. Aneurysms remnants after clipping are often observed in cases difficult anatomical locations. Their bleeding risk is not negligible. Secondary coiling is a rescue strategy to effectively and safely secure the aneurysm remnant. Only in a minority of cases, it is a staged treatment after 'remodelling' of the aneurysm neck.

Keywords Failed aneurysm clipping · Coiling · Secondary coiling · Aneurysm residual · Aneurysm regrowth

Introduction

Residual and recurrent intracranial aneurysms can occur after surgical clipping, leading a persistent risk of regrowth and rupture or re-rupture. Several authors have emphasised the potential for these remnants to grow and to cause subarachnoid haemorrhage (SAH) in a delayed fashion [3, 8, 26]. Until the advent of the GDC, surgical reintervention was the only available treatment, but it was associated with higher risk than the first operation [13, 25]. During the past two decades, however, advances in endovascular coiling techniques and technology have allowed some of these remnants to be treated safely with no open surgery [3, 34].

The steady improvement in microsurgical technique has greatly enhanced the surgeons' ability to successfully occlude also complex intracranial aneurysms in a single clipping procedure. Anyway, in the setting of complex cases, secondary

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coiling after clipping could be an elective preoperatively planned option, as both microsurgical and endovascular techniques continue to have their limitations, and certain aneurysm morphologies and locations remain exceedingly difficult to treat with a single modality [1, 7, 15]. In other contexts, a secondary coiling may represent a solution to obtain a complete aneurysm exclusion when it was not possible, for some reasons, at first surgery [2, 6].

The aim of this study is to systematically review the pertinent literature concerning cases of secondary coiling after incomplete clipping along with the institutional experience on this topic of two Italian tertiary referral centres for neurovascular surgery, in order to identify its indications, efficacy, feasibility and limitations.

Methods

Literature review

A comprehensive review of the literature was performed with the following keywords '((intracranial OR cerebral OR brain) AND aneurysm AND clipping AND coiling)' to search in PubMed and Scopus databases.

The search strategy followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement where applicable, and this checklist was used in designing and reporting our review.

The last search was launched in December 2016.

All studies reporting patients who underwent a surgical clipping followed by a secondary coiling for the treatment of the residual aneurysm were first included. Case reports were not included in the analysis. Cases treated with flow diverter devices were not included in the study as we focused on coiling techniques.

Two reviewers (G.M.D.P. and F.B.) independently collected data from the included articles. Any differences were resolved by consensus discussing with a third author (C.L.S.).

Then, English studies reporting detailed information regarding operative procedures (both surgical and endovascular), perioperative and postoperative complications, and aneurysm occlusion rates were included in the following analysis.

We evaluated the following variables: demographics, ruptured status, aneurysm morphology, topography and size, percentage of exclusion at first surgery, the entity of neck reduction after clipping, timing and modality (coiling, stent-assisted coiling and spontaneous thrombosis) of the secondary endovascular treatment, complications, final occlusion rate and clinical status at follow-up. We also explored, when reported, the prediction by the authors of an incomplete treatment at first surgery, in order to differentiate secondary coiling performed as a rescue strategies or as intentional treatments.

Periprocedural complications studied were the occurrence of intraprocedural thrombosis (with or without transient hemiparesis), stroke (with permanent hemiparesis) and intraoperative rupture, and slippage of the clip.

With regards to localization, we distinguished the aneurysms according to the vessel involved. Aneurysms were also divided in small (< 1 cm), large (> 1 cm < 2.5 cm) and giant (> 2.5 cm) according to what reported by the investigators.

The percentage of exclusion at first surgery was categorised, according the Sindou classification, with reference to presence of residual at the aneurismal neck or at the sac [32]. We identified the following four categories:

Neck remnant, corresponding to the Sindou grades I and II, when the remnant is only at the aneurysmal neck;
Sac remnant, corresponding to the Sindou grades III and IV, when it is present a residual lobe from a multilobulated sac, or the residual portion of the sac is less than 75% of the initial aneurysmal size;
Failed, corresponding to the Sindou grade V, when clipping did not produce significant change in aneurysmal sac filling with the residual aneurism > 75% of the initial size;
Regrown aneurysms, when a fully occluded aneurysm at postoperative digital subtraction angiography (DSA) appeared to be regrown and increased in size at controls.

Radiologic outcomes for surgery or endovascular procedures were stratified into three levels on the basis of the degree of angiographic aneurysm obliteration, evaluated immediately after the secondary endovascular procedure and stratified according the Raymond–Roy classification [31]: *grade 1*, complete/near-complete occlusion, defined as a lack of angiographic filling of the sac and the neck; *grade 2*, partial occlusion, defined as persistent angiographic filling at the aneurismal neck and *grade 3*, incomplete occlusion, defined as a persistent angiographic filling of a significant portion of the sac. Finally, clinical outcome was assessed both through the modified Rankin scale (mRS) and Glasgow Outcome Scale (GOS).

Statistical analysis

Data were individually extracted for each patient. Percentage of incidence and 95% of confidence intervals (CI) were calculated for all considered variables and outcomes.

Quantitative variables were expressed as mean ± standard deviation and Student's *t* test was used to compare their means. Fisher's exact test (two-sided) was instead used to compare categorical variables. The associations were considered significant when $P < 0.05$.

Results

Institutional series

Two institutional series was retrieved from the databases of two Italian tertiary referral centres for neurovascular surgery in Rome: seven cases (three males and four females with a mean age of 58.3 ± SD 8.0 years) from the 'Catholic University of Rome School of Medicine, A. Gemelli Hospital' and 3 cases (1 male and 2 females with a mean age of 55.6 ± SD 5.9 years) from the 'San Camillo Forlanini Hospital'.

Data from the two institutional series was pooled with those retrieved from literature in order to provide a homogenous analysis (Table 1).

Systematic review: study selection and characteristics

Demographic, angiographic and clinical features of the studies that met our inclusion criteria are summarised in Table 1.

According to our search strategy, articles in English language were retrieved through the electronic literature search. From the first search, 698 articles were available in literature. Among these, 110 were reviews without original series, 13 were animal studies, 90 papers were case reports and 36 were not in English language.

Among the 449 articles left, 397 were primarily excluded by abstract reading and 52 were assessed for eligibility and analysed in detail. After full-text reading and a forward search from the bibliography of the selected papers, 11 articles published between 1998 and 2016 and reporting patients endovascularly treated for aneurysms incompletely clipped at first surgery were finally included in the review [2, 3, 6, 7, 16, 20, 22, 25, 27, 30]; 92 patients were retrieved from literature analysis. Pooling these with the institutional series, an overall of 102 patients were included in this study **(**Fig. 1**).**

The pooled analysis of the main outcomes reported in the 11 included studies and institutional series is reported in Table 2.

Demographics

Age was reported in 70/102 patients (68.6%), and the mean age at diagnosis was 52.94 ± 12.17 years (range 29–80). Sex was reported in 71 out of 102 patients (69.6%) and the male/female ratio was 25/46 (35.21 vs 64.79%).

Localization, size and ruptured status of the aneurysms

Localization of the aneurysms was reported in 93 out of 102 patients (91.17%). The most common location of aneurysms that needs a secondary endovascular treatment was represented by the anterior circulation. In particular, 37.63% originated from the anterior communicating artery (ACoA) and about 31% originated from the internal carotid artery (ICA) distinguished in paraclinoid, Pcom origin, SHA origin, Acho origin and bifurcation segments. ACA was involved overall in about 3% of cases and MCA in 4%. Finally, about 24% of aneurysms treated with a secondary coiling involved the posterior circulation, especially the basilar artery (about 13% of cases).

Ruptured status was reported in 81 out of 102 patients (79.41%). Among them, 63/81 (77.78%; 95% CI 67.58–85.46) had an onset with subarachnoid haemorrhage (Table 1).

Size was instead reported only in little more than half of cases (63/102; 61.76%), with about the same percentage of small and large + giant aneurysms.

Percentage of exclusion and neck reduction at first surgery

The percentage of exclusion at first surgery was reported in 89 out of 102 patients (87.25%). Among them, a neck remnant (the Sindou grades I and II) was described in more than 50% of cases and a sac remnant (the Sindou grades III and IV) in about 29%, while a regrowth was observed in a little more than 12% of cases. No report of secondary coiling after a failed surgical procedure (the Sindou grade V) was observed, for which reoperation is generally indicated.

Only in about half of patients included in this systematic review (50 out of 102 cases) was described by the authors the size of the neck reduction after the first clipping. In particular, in 48/50 out of them (96%; 95% CI 86.54–98.9) was reported a neck reduction larger than 50%.

Data concerning postoperative DSA after the initial surgical treatment is reported in 89/102 cases (87.25% CI 79.41–92.40); data about postoperative controls cannot be retrieved from literature in 13/102 cases (12.75% CI 7.60–20.59). Postoperative DSA after surgery was reported in 87/89 patients (97.75% CI 92.17–99.38); in 2/89 cases (2.25% CI 0.62–7.83) it was performed no postoperative DSA or other radiological exam.

Secondary endovascular treatment and timing

A secondary selective coiling was reported in large majority of cases (95.1%; 95% CI 89.03–97.89), while a coiling procedure with adjuncts was described only in about 3% of cases (95% CI 1.01–8.29). In 2 cases, the incomplete exclusion after clipping was followed by a spontaneous thrombosis of the remnant.

Radiologic outcomes for endovascular procedures was a Raymond–Roy grade 1 in 70% of cases (95% CI 59.87–78.49), grade 2 in 25.56% (95% CI 17.67–35.44), while a failed procedure (grade 3) with a persistent angiographic filling of a significant portion of the sac in 4.44% of cases (95% CI 1.74–10.88).

The timing of the secondary endovascular treatment was reported in 79/102 out of patients (77.4.%). In 25 cases

Table 1 Demographic, angiographic, and clinical features of the studies that met inclusion criteria + institutional series

Author/ year	No. of cases	Mean age in years (± SD)	Sex	Arterial segment involved	Aneurysm size	Aneurysm morphology	Ruptured status	Result of First surgery	Predicted incomplete first surgery	Type of coiling	Occlusion rate after coiling (the Raymond–Roy occlusion classification)	Residual aneurysm rupture	Coiling compli-cations	GOS and mRS
Alobaid et al. [2]	4	50.25 (14.9)	F 2; M 2	ACA 2 ACoA 1 SHA 1	Small 1 Large 1 nr 2	Sacc 4	R 3 UR 1	SAC REMN 1 NECK REMN 3	N 4	Sel Coiling 4	Raymond–Roy 1: 3 Raymond–Roy 3: 1	1	None 4	MD (mRS 3–4) 1 SD (mRS 5) 1 D (mRS 6) 1 nr 1
Bendok et al. [3]	5	56 (6.0)	F 1; M 4	ACoA 1 BA 1 ICA (paraclinoid) 1 PICA 2	Small 1 Large 4	Sacc 4 Fus 1	R 3 UR 2	SAC REMN 1 NECK REMN 3 Regrowth 1	N 4 Y 1	Sel Coiling 5	Raymond–Roy 1: 5	1	None 5	GR (mRS 0–2) 2 SD (mRS 5) 1 D (mRS 6) 1 nr 1
Choudhri et al. [6]	6	66 (−)	F 1; nr 5	ACoA 2 ICA (paraclinoid) 2 MCA 1 Pcom 6	Giant 1 nr 5	Sacc 1 nr5	UR 1 nr 5	NECK REMN 1 Regrowth 1 nr 4	N 1 nr 5	Sel Coiling 6	Raymond–Roy 1: 1 nr 5	2	None 6	GR (mRS 0–2) 1 nr 5
Cockroft et al. [7]	3	40.33 (10.3)	F 1; M 2	BA 1 ICA (paraclinoid) 1 VA 1	Small 1 Large 2	Sacc 3	R 2 UR 1	SAC REMN 1 NECK REMN 2	Y 3	Sel Coiling 3	Raymond–Roy 1: 3		None 3	GR (mRS 0–2) 2 MD (mRS 3–4) 1
Hacein-Bey et al. [15]	5	50.4 (11.8)	F 4; M 1	ACoA 2 BA 2 ICA (paraclinoid) 1	Small 2 Large 3	nr 5	R 5	SAC REMN 3 NECK REMN 2	N 5	Sel Coiling 5	Raymond–Roy 1: 5		None 5	GR (mRS 0–2) 5
Hoh et al. [16]	11	59 (−)	F 2; nr 9	Pcom 1 VA 1 nr 9	Large 2 nr 9	Fus 2 nr 9	R 1 nr 10	NECK REMN 2 nr 9	N 2 nr 9	Sel Coiling 11	Raymond–Roy 1: 5 Raymond–Roy 2: 6	1	None 1 nr 10	GR (mRS 0–2) 1 D (mRS 6) 1 nr 9
Kang et al. [20]	13	65 (−)	F 1; nr 1-2	ACoA 6 BA 2 ICA (paraclinoid) 2 MCA 1 Pcom 1 PICA 1	nr 13	Sacc 1 nr 12	R 10 UR 3	SAC REMN 10 NECK REMN 3	N 13	Sel Coiling 13	Raymond–Roy 1: 4 Raymond–Roy 2: 9	4	nr 13	GR (mRS 0–2) 5 MD (mRS 3–4) 1 SD (mRS 5) 1
Lawton et al. [22]	6	34 (−)	F 1; nr 5	BA 2 ICA (paraclinoid) 1 Pcom 2 VA 1	Large 1 nr 5	Fus 1 nr 5	nr 6	SAC REMN 5 Regrowth 1		Sel Coiling 6	Raymond–Roy 1: 1 Raymond–Roy 2: 1 Raymond–Roy 3: 1 nr 3		None 1 nr 5	MD (mRS 3–4) 1 nr 5
Lim et al. [25]	6	54 (11.6)	F 5; M 1	Acho 1 ACoA 2 ICA (paraclinoid) 2	Small 1 Large 1 nr 4	nr 6	R 6	NECK REMN 4 Regrowth 2	nr 6	Sel Coiling 6	Raymond–Roy 1: 2 nr –4	2	None 6	MD (mRS 3–4) 1 nr 5

Table 1 (continued)

Author/ year	No. of cases	Mean age in years (±SD)	Sex	Arterial segment involved	Aneurysm size	Aneurysm morphology	Ruptured status	Result of First surgery	Predicted incomplete first surgery	Type of coiling	Occlusion rate after coiling (the Raymond–Roy occlusion classification)	Residual aneurysm rupture	Coiling compli-cations	GOS and mRS
Mangiafico et al. [27]	12	55.58 (14.0)	F 9; M 3	PCom 1 ACoA 8 ICA (paraclinoid) 1 MCA 1 Pcom 2	Small 6 Large 6	Sacc 2 nr 10	R 12	SAC REMN 2 NECK REMN 9 Regrowth 1	N 12	Sel Coiling 10 Stent ass coil 2	Raymond–Roy 1: 10 Raymond–Roy 3: 2	3	None 11 Perforation 1	D (mRS 6) 1 nr 11
Rabinstein and Nichols [30]	21	50.57 (13.5)	F 13; M 8	ACoA 8 BA 4 ICA (paraclinoid) 5 Pcom 1 PICA 1 VA 1	Small 12 Large 7 Giant 1 nr 1	nr 21	R 13 UR 8	NECK REMN 17 Regrowth 4	N 21	Sel Coiling 21 Coil + sp. thromb 2	Raymond–Roy 1: 15 Raymond–Roy 3: 6	4	None 21	GR (mRS 0–2) 15 MD (mRS 3–4) 1 SD (mRS 5) 2 D (mRS 6) 3
Institutional Series 'Gemelli' Hospital	7	58.28 (8.0)	F 4; M 3	MCA 1 ACoA 5 PCom 1	Small 6 Large 1	Sacc 7	R 5 UR 2	SAC REMN 1 NECK REMN 5 Regrowth 1	N 7	Sel Coiling 7	Raymond–Roy 1: 7		None 7	GR (mRS 0–2) 5 MD (mRS 3–4) 1 SD (mRS 5) 1
Institutional Series 'San Camillo' Hospital	3	55.66 (5.9)	F 2; M 1	A1A2 1 ICA (bifurcation) 1 PICA 1	Small 3	Sacc 3	R 3	SAC REMN 2 NECK REMN 1	N 3	Sel Coiling 2 Stent ass coil 1	Raymond–Roy 1: 2 Raymond–Roy 2: 1		None 3	GR (mRS 0–2) 2 MD (mRS 3–4) 1
Overall	102	52.94 (12.2)	F 46; M 2-5; nr 3-1	A1A2 1 ACA 2 ACho 1 MCA 4 ACoA 35 BA 12 ICA (bifurcation) 1 ICA (paraclinoid) 16 PCom 10 PICA 5 SHA 1 VA 5 nr 9	Small 33 Large 28 Giant 2 nr 39	Sacc 25 Fus 4 Diss 0 nr 73	R 63 UR 18 nr 21	SAC REMN 26 NECK REMN 52 Regrowth 11 nr 13	N 78 Y 4 nr 20	Sel Coiling 99 Stent ass coil 3 Coil + sp. thromb 2	Raymond–Roy 1: 63 Raymond–Roy 2: 23 Raymond–Roy 3: 4 nr 12	18	None 73 Perforation 1 nr 28	GR (mRS 0–2) 51 MD (mRS 3–4) 10 SD (mRS 5) 7 D (mRS 6) 7 nr 38

ACA anterior cerebral artery, *ACho* anterior choroidal artery, *MCA* middle cerebral artery, *ACoA* anterior communicating artery, *BA* basilar artery, *ICA* internal carotid artery, *PCom* posterior communicating artery, *PICA* postero-inferior cerebellar artery, *SHA* superior hypophiseal artery, *VA* vertebral artery, *Sacc* saccular, *Fus* fusiform, *Diss* dissecting, *R* ruptured, *UR* unruptured, *NECK REMN* neck remnant (the Sindou I and II), *SAC REMN* sac remnant (the Sindou III and IV), *Sel Coiling* selective coiling, *Stent ass coil* stent-assisted coiling, *Coil + sp. thromb* coiling + spontaneous thrombosis, *GR* 51, *GOS* Glasgow Outcome Scale, *MD* moderate disability, *SD* severe disability, *D* death, *nr* not reported

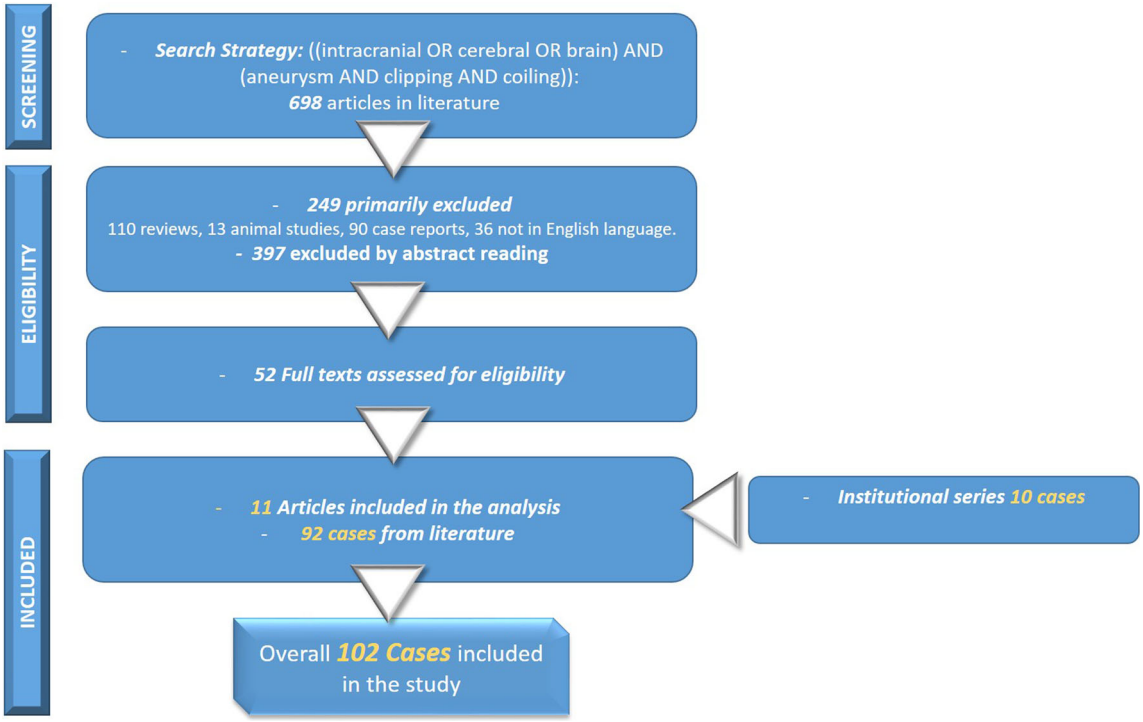

Fig. 1 Flow chart of search strategy

(31.65%; 95% CI 22.45–42.55), the secondary treatment was immediate after surgery (during the same hospitalisation), while in 68.35% (95% CI 57.45–77.55), it was delayed from 1 week to 26 years.

Rebleeding risk and risk of aneurysm regrowth from incompletely clipped aneurysms

Of the aneurysm residual after incomplete clipping, 18/83 cases (15.66%; 95% CI 9.39–24.98) presented a bleeding from the rupture of the remnant. Among the 26 patients with incomplete clipping with neck remnant (the Sindou grades I and II), two (7.69%; 95% CI 2.14–24.14) presented bleeding; among the 52 patients with partial clipping with sac remnant (the Sindou grades III and IV), 11 (21.15%; 95% CI 12.24–34.03) presented bleeding and among the 11 with aneurysmal regrowth, 5 (45.45%; 95% CI 21.27–71.99) presented bleeding. Re-bled aneurysms were treated with standard coiling in 17/18 cases (94.44%; 95% CI 74.24–99.01) and in a single case with a stent-assisted procedure (5.56%; 95% CI 0.99–25.76).

Complications of first surgery and secondary coiling and clinical outcome

The occurrence of complications after surgery was reported in 83 out of 102 patients (81.37%). A transient ischemia and a permanent stroke were reported in about 2.5% out of cases, respectively. An intraoperative aneurysm rupture was instead reported only in one case as well as the evidence of clip slippage in the postoperative imaging. Finally, a residual aneurysm rupture was reported in about 22% out of cases.

Only one case of aneurysm perforation was reported during the secondary coiling procedure (1.35%; 95% CI 0.24–7.27).

Clinical outcome was reported in 69/102 out of cases (67.64%). A GR was reported in about 67% out of cases, a MD in 13% and a SD in about 10%. The rate of mortality was overall 10.14% (7/69 out of patients; 95% CI 5–19.49). Clinical deterioration after the second (endovascular) procedure was reported in 1/62 cases (1.61%; 95% CI 0.29–8.59) and occurred after aneurysmal perforation during coiling.

Outcome comparison between patients with ruptured and unruptured aneurysms, small versus large + giant aneurysms and aneurysms of the anterior and posterior circulation

No statistically significant differences were observed in any outcomes comparison group (supplementary Tables 1, 2 and 3).

Discussion

The rate of incomplete aneurysm exclusion after microsurgical clipping has been estimated in literature to be as high as 4% [7, 29, 35].

From our analysis, it appears that insufficient surgical clipping resulted in a remnant at the aneurysmal neck (the Sindou

Table 2 Pooled analysis of the main outcomes reported in the 11 included studies + institutional series, grouped as reported in the first column

Outcome measured		Cumulative		
		Raw number	Percentage	95% CI
Demographics	Mean age ± SD	70/102	52.94 ± 12.17	
	Male sex	25/71	35.21	25.12–46.82
Subarachnoid haemorrhage		63/81	77.78	67.58–85.46
Localization	ICA paraclinoid	16/93	17.2	10.88–26.13
	ICA bifurcation	1/93	1.08	0.19–5.84
	Basilar artery	12/93	12.9	7.54–21.21
	Vertebral artery	5/93	5.38	2.32–11.97
	ACoA	35/93	37.63	28.46–47.79
	ACA	2/93	2.15	0.59–7.51
	SHA	1/93	1.08	0.19–5.84
	PICA	5/93	5.38	2.32–11.97
	MCA	4/93	4.3	1.69–10.54
	Pcom	10/93	10.75	5.95–18.67
	A1A2	1/93	1.08	0.19–5.84
	Acho	1/93	1.08	0.19–5.84
Size	Small	33/63	52.38	40.27–64.22
	Large	28/63	44.44	32.85–56.68
	Giant	2/63	3.17	0.87–10.86
Exclusion at first surgery	Neck Remnant (Sindou I–II)	52/89	58.43	48.05–68.11
	Sac Remnant (Sindou III–IV)	26/89	29.21	20.78–39.36
	Regrowth	11/89	12.36	7.04–20.79
Neck reduction > 50% at surgery		48/50	96	86.54–98.9
preoperative prediction of incomplete treatment		4/82	4.88	1.91–11.88
Timing of secondary coiling	Immediate	25/79	31.65	22.45–42.55
	Delayed	54/79	68.35	57.45–77.55
Secondary treatment	Selective coiling	97/102	95.1	89.03–97.89
	Stent-assisted coiling	3/102	2.94	1.01–8.29
	Spontaneous thrombosis	2/102	1.96	0.54–6.87
Angiographic Outcome after secondary coiling	Raymond–Roy 1	63/90	70	59.87–78.49
	Raymond–Roy 2	1	25.56	17.67–35.44
	Raymond–Roy 3	4/90	4.44	1.74–10.88
Complications of surgery	Transient ischemia	2/83	2.41	0.66–8.37
	residual aneurysm rupture	18/83	21.69	14.18–31.7
	Stroke	2/83	2.41	0.66–8.37
	Intraoperative rupture	1/83	1.2	0.21–6.51
	Slippage of the clip	1/83	1.2	0.21–6.51
Complications of secondary coiling	Perforation	1/74	1.35	0.24–7.27
Clinical outcome (GOS and mRS) at discharge	GR (mRS 0–2)	46/69	66.67	54.93–75.65
	MD (mRS 3–4)	9/69	13.04	7.02–22.97
	SD (mRS 5)	7/69	10.14	5–19.49
	VS	0/69	0	0–5.27
	D (mRS 6)	7/69	10.14	5–19.49

grades I and II) in 52/89 cases (58.82%), in a remnant at the aneurysm sac (the Sindou grades III and IV) in 26/89 cases (29.21%) and of a regrowth (complete clipping at first surgery, confirmed by a postoperative DSA and appearance of a newly formed aneurysm at follow-up) in 11/89 cases (12.36%). Illustrative cases are showed in Figs. 2, 3, 4 and 5.

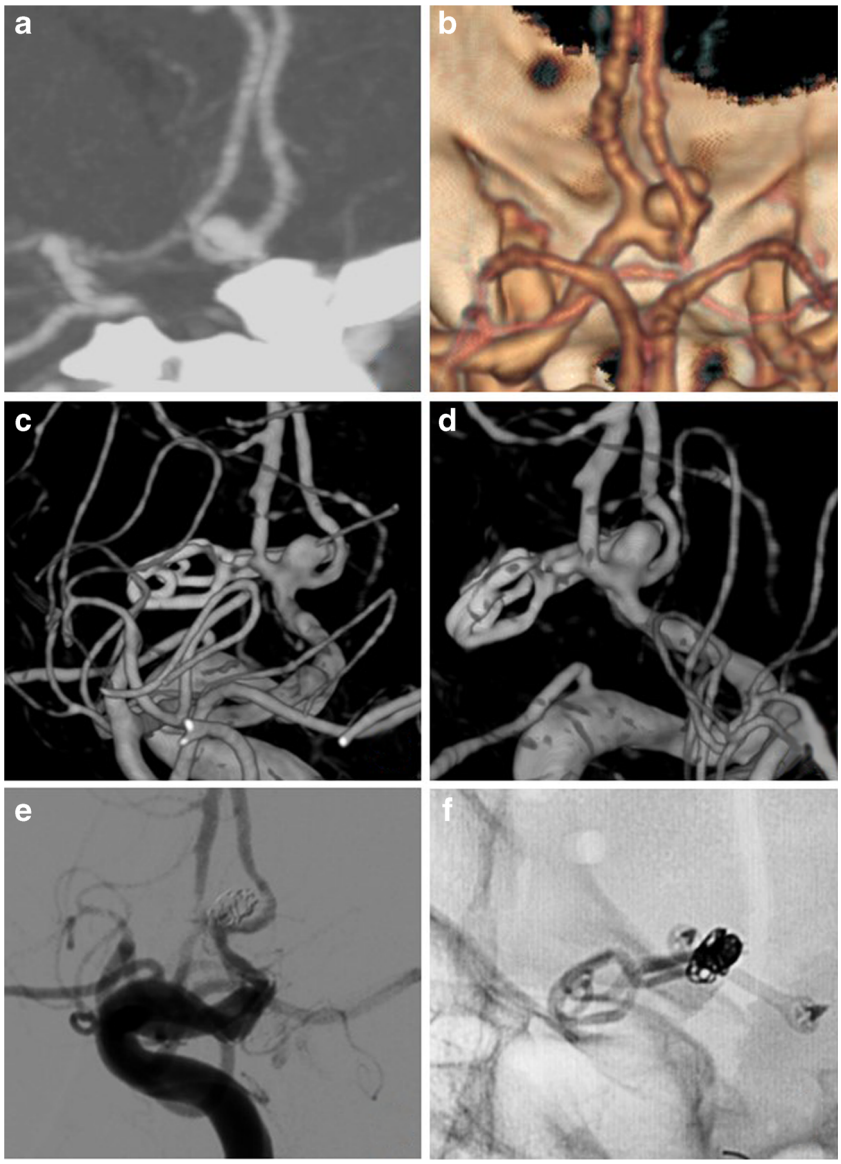

Fig. 2 Illustrative case 1: a 50-year-old man presenting with intense nuchal headache. Radiological examination showed SAH (HH4) secondary to ACoA aneurysm (**a**, **b**). Microsurgical clipping was attempted but early angiographic control enlightened a residual aneurysm due to partial clipping (**c**, **d**) with sac residual. Aneurysm residual was then completely coiled (**e**, **f**). The patient was discharged in good clinical and neurological condition

Risk of bleeding and regrowth of the residual aneurysm

The haemorrhagic risk associated with aneurysm remnants after incomplete clipping has been documented in literature by several studies [30]. Feuerberg et al. reported a 3.7% of incidence of rebleeding from residual aneurysms with rupture rate of up to 0.79%/year [11]. In the series by Drake and Vanderlinden, a significant number of patients with large aneurysm remnants experienced re-haemorrhage within 7 years of incomplete treatment and showed that remnants can increase in size and change morphology over time [9, 10]. Other experiences in literature displayed that the risk was not limited to large remnants but includes also neck remnants (the Sindou grades I and II) as small as 1 to 2 mm [26].

Important is to notice that the rate of bleeding from aneurysm remnants and from aneurysmal regrowth is not negligible. Our data, in fact, showed that 18 out of 83 cases (21.69%) of aneurysm residual after incomplete clipping presented a bleeding from the rupture of the remnant (Table 3). In particular, it is interesting to know that among the 11 patients who showed an aneurysmal regrowth, 5 presented a bleeding (45.45%); however, it should be acknowledged the selection bias behind this figure as most of the regrown aneurysms are discovered primarily because of bleeding.

Recent studies showed a 1.5% incidence of recurrent aneurysms in cases in which there was no residual after clipping [8, 36]. Regrowth of aneurysm after clipping (with an initial negative postoperative DSA) may have several explanations: for example, a highly calcified neck or a nearly complete neck exclusion, with clip blades almost reaching the neck edge, might favour aneurysm slow fill even after clip placement and over time cause aneurysmal recanalization [16, 17, 21].

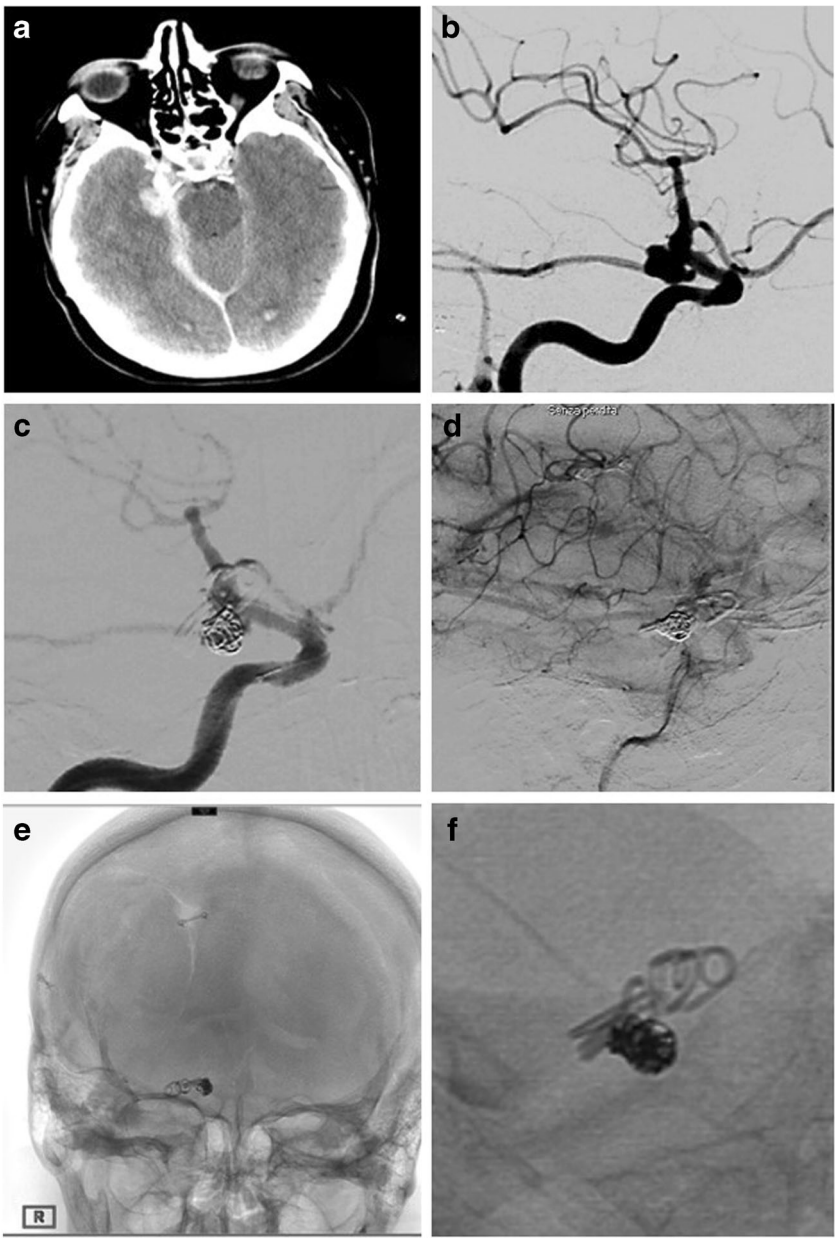

Fig. 3 Illustrative case 2: a 59-year-old woman presenting with SAH due to secondary to ACoP aneurysm (**a**, **b**). Microsurgical clipping was performed. Angiographic follow-up showed a partial clipping (**c**, **d**), with a portion of the aneurysmal sac still perfused. Aneurysm that was then completely coiled (**e**, **f**)

About timing, from data analyses, it appears that remnants can bleed also several years after treatment. In fact, bleeding from a residual has been reported up to 26 years after initial treatment [30].

Partial clipping that corresponds to a remnant at the aneurysmal neck only (the Sindou I–II) is generally not amenable to reoperation without creating stenosis of the parent artery. In these cases, most common attitude in literature is angiographic follow-up observation by means of DSA or angio-CT. Retreatment is generally considered if there is aneurysm morphological modification at follow-up.

Whereas, incomplete clipping with remnants of the aneurysmal sac (the Sindou III–IV) are generally considered for additional treatment in an early stage [19, 32].

DSA is the standard control after surgical clipping as reported in the majority of papers. Most of authors recommend late angiographic follow-up review for incompletely obliterated aneurysms, while for completely clipped aneurysms such follow-up studies are not routinely performed. There is still no consensus about the required duration of angiographic follow-up after aneurysm incomplete clipping [19].

Rescue strategy or staged treatment?

Complex, broad-necked aneurysms that may be difficult to treat with a single mode of therapy can be safely and successfully treated with a combination of endovascular and microsurgical techniques [2, 10]. For patients with broad-based

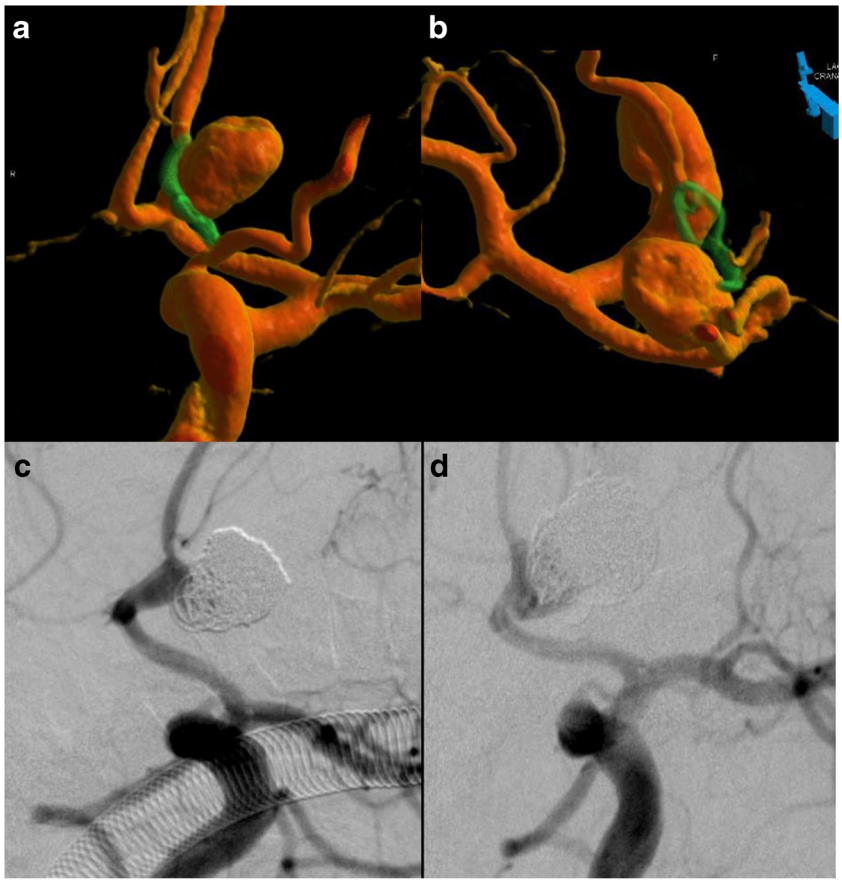

Fig. 4 Illustrative case 3: incomplete neck clipping of left A2 ruptured aneurysm (**a**, **b**). The residual aneurysm was endovascularly coiled (**c**, **d**)

aneurysms that are difficult to access surgically without incurring significant morbidity, microsurgical clipping may be used as the initial procedure to create a smaller neck [3]. As suggested by Cockroft [7], a planned dual-modality approach allows for a safer treatment of complex lesions and reduces the need for an exceedingly aggressive single-modality treatment [7]. Conversely, when an aneurysm seems both unfavourable for direct coiling (e.g too broad-based) and structurally unfavourable for microsurgical clipping, a planned approach of microsurgical partial clipping to reduce the size of the neck, followed by endovascular coiling, may be a safe and effective alternative to a single modality [3]. When planning is made in advance, the patient may be taken directly to the angiography suite, and the combined procedure can be performed without delay [3, 7].

However, this is true only in a minority of reports [3, 7], and, as shown from literature data, in the majority of cases, the incomplete clipping is not an expected result and the secondary coiling is considered a rescue strategy in order to secure the aneurysm. In fact, a preoperative prediction of incomplete

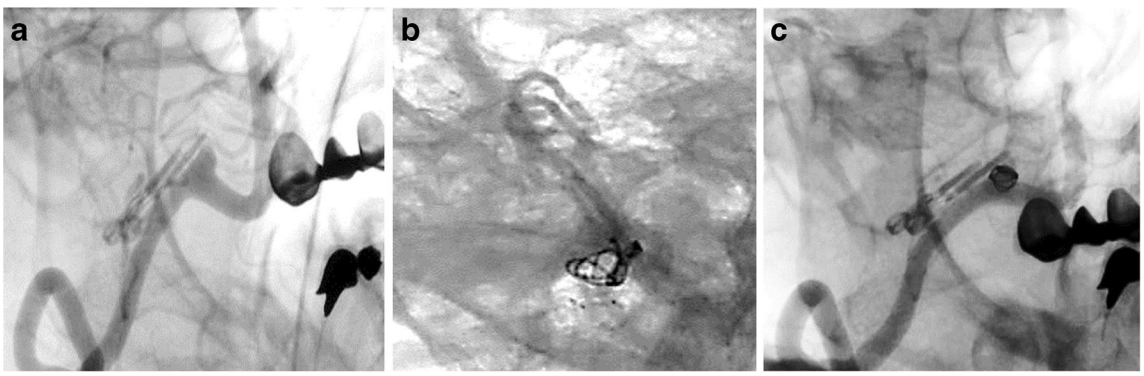

Fig. 5 Illustrative case 4: right vertebral artery angiography showing a clipped ruptured PICA aneurysm with a neck residual and partial exclusion of the sac (**a**). Stent-assisted embolization with coils. Stent markers, coils and clips are clearly visible (**b**). Post-procedural DSA showing the complete exclusion of the aneurysm and a patent vertebral artery (**c**)

Table 3 Residual aneurysm rupture according to different failed surgical clipping

Aneurysm exclusion at first surgery	No. of cases	No. ruptures of residuals	% ruptures of residuals
Sac remnant	26	2	8
Neck remnant	52	11	21
Regrowth	11	5	45
Total	89	18	20

treatment was reported only in a minority of cases included in this systematic review (less than 5%). Moreover, only in about 1/3 of the reported cases the residual aneurysm is suspected at surgery and immediately treated with a secondary coiling; on the other hand, in about 70% of cases, the presence of an unexcluded part of the sac is identified later on the follow-up imaging and then the secondary coiling is delayed after the first surgery.

If an experienced surgeon leaves a remnant because of anatomic constraints, reoperation is unlikely to be beneficial [6]. In addition, to repeat surgery for aneurysms that develop in a patient with a prior craniotomy is often challenging due to scar tissue, and cerebral spinal fluid (CSF) leaks might make a harder clear view of the aneurysm site; the clip applied during the previous surgery can be an obstacle at subsequent operation; often, it may be difficult or impossible to remove the clip when it is necessary, and aneurysm rupture and bleeding may occur during clip mobilisation [3, 28]. In other words, the presence of residual aneurysm reflects technical or anatomical difficulties of the prior operation, and the previously placed clips are often an additional problem [3].

Coiling seems to offer a solution for some aneurysm remnants [5, 28]. From a technical standpoint, remnant coiling usually is possible if the remnant is at least as deep as it is wide and if it is at least 2 mm in diameter [3].

Efficacy and safety

Secondary endovascular coil embolization resulted in complete aneurysmal occlusion (the Raymond–Roy grade 1) in 70% of cases, whereas a persistent partial occlusion (the Raymond–Roy grade 2) was still evident in about 25% of cases after the secondary procedure. In about 4.5% of cases, an incomplete occlusion or the failure of the procedure (the Raymond–Roy grade 3) was reported. There were no serious complications related to endovascular treatment and only one case of perforation was reported with associated clinical deterioration.

Clinical outcomes are generally favourable and there was no reported worsening of clinical status after procedure. Poor outcomes were significantly associated with a history of subarachnoid haemorrhage due to the rupture of the remnant.

The overall complication rate of the secondary coiling from our data is in fact little more than 1%, which is comparable to the rate of complications reported in literature for the endovascular treatment of previously untreated aneurysms [4]. This data is particularly interesting as it underlines that previous surgery does not constitute an extra risk for endovascular coiling. Partial clipping also reduces the size of the neck, making compaction of the coil mass less complex and, above all, safer. The phase of coils compaction is the stage where lies the greatest risk; the metal clip at the base provides a reliable rigid support on which to build the cast.

Other advantages to this approach involve the information provided by the surgeon regarding the peri-aneurysmal environment, such as the presence of perforators [15].

Timing of the secondary coiling

No clear data exists in literature on this topic [27]. However, this study discovered that in about 32% of cases, the secondary coiling was immediate after surgery (during the same hospitalisation), while in about 68% was delayed in a time lapse ranging from 1 week to 26 years.

Anyway, only in a minority of patients that were immediately re-treated, it had been forecasted before the clipping attempt (4/82; 4.9%), which was firstly aimed to remodel the aneurysm neck. In the majority of cases, instead, an incomplete clipping was demonstrated at postoperative angiographic studies, and an immediate endovascular treatment was then offered to the patients.

Our institutional experience, backed by many authors in literature [2, 7, 14, 27, 28], supports the idea that an incomplete clipping with neck narrowing it can alter flow dynamics with a higher flow jet toward the aneurysm dome increasing likelihood of rupture in some cases. Therefore, second-stage coiling should be completed soon after clip reconstruction or as soon as residual/regrowth is identified.

Complex aneurysm?

From our data, the majority of cases of secondary coiling after incomplete clipping concerns small saccular aneurysms [33/63 cases—52.38%]. This finding might seem surprising; however, if we carefully analyse that most cases are surgical failures, with a residual not expected or planned, this finding makes sense as large or giant aneurysms, as expected, are managed ‘a priori’ with combined therapies, often with extracranial–intracranial bypass followed by surgical trapping or endovascular obliteration of the aneurysm and the parent vessel. Conversely, larger aneurysms or fusiform or located in the posterior circulation are generally treated with endovascular intervention as primary treatment [33]. Thus, the aneurysm that most frequently undergoes a secondary coiling after clipping is the ‘common’ small-sized sacciform aneurysm (that

from our data represent more than a half of cases, and along with large ones, 93% of cases) for which a combined approach is not planned ab initio and surgery is expected to exclude aneurysm one shot.

Conditions favouring aneurysm residual after clipping

From literature analysis, it emerges that some anatomical locations are much more frequent than others. In particular, ICA paraclinoid, basilar artery (BA) and ACoA aneurysms are the most frequent sites for secondary coiling. Due to a limited surgical corridor and anatomical restraints, clips might not completely exclude the aneurysm. This scenario is encountered in carotid cave and paraclinoid aneurysms where part of the aneurysm extends beyond the dural ring and often the correct visualisation of aneurysmal neck might result difficult [24]. Moreover, in this anatomy often prevents the correct visualisation of the tips of the microsurgical clip and as a result a part of the aneurysm may still continue to fill. Similarly, in ACoA aneurysms, the rotation of the 'A1-ACoA-A2 complex' in the sagittal plane, associated to an elevated anatomical variability associated with this location (azygos A1/A2, duplications of ACoA, vascular hypotrophy or aplasia) can make difficult to fully control portions of aneurysm, especially if posteriorly projecting or embedded in brain parenchyma, resulting in a partial or incomplete clipping [12, 23]. As in paraclinoid and ACoA, also BA aneurysm represent an anatomically challenging position as operative filed is narrow and deep and the aneurysm can be partially hidden by prominent perforators that may preclude adequate circumferential dissection, or be embedded in eloquent brain parenchyma [12].

These observations are confirmed by our institutional data that, according meta-analytic data from literature, places these three anatomical sites as the more at risk of incomplete clipping.

Our data show also that residual aneurysm after clipping is more frequent if operated after SAH (63/81–77.8% cases in ruptured status versus 18/81–22.2% unruptured). Peri-aneurysmal dissection and appropriate brain relaxation are, of course, more challenging if subarachnoid blood is present and thus this condition favours post-surgical residuals.

Several authors report of scissor-like deformation of surgical clips that consists in twisting of the clip blades and it is associated with incomplete clipping [17]. A highly calcified neck might prevent the correct closure of the clip blades hence leading to continued slow filling of the aneurysm [17, 18]. A subsequent endovascular coil embolization of the aneurysm though the narrow calcified neck can help definitively thrombose the aneurysm.

Limitations

This study presents several limitations. First, the majority of the included papers were case series including a small number of patients (only four papers report on a number of patients > 10). In addition, the reported evidence is observational and non-comparative. Therefore, the proportions reported in this review only reflect the published cases and may be influenced by some form of publication bias. In particular about the bleeding rate of residuals, it should be acknowledged a selection bias as failed clipping is discovered primarily because of bleeding; hence, their real bleeding rate cannot be accurately determined.

Moreover, we limited our research to the cases published since the 1990s, before the endovascular coiling was not available earlier. Finally, clinical outcome at follow-up was available only in about two third of patients; therefore, this study includes a not totally reliable evaluation of long-term prognosis.

Conclusions

The study confirms that the risk of bleeding from aneurysm remnants is not negligible, and it can also occur after several years from primary surgery. Remnants are more often observed when difficult anatomical locations (paraclinoid/BA) or SAH make aneurysm dissection more challenging, and proximal control is not securable. Incomplete/partial clipping is not an expected result in the majority of cases, and the secondary coiling is considered a rescue strategy to secure the aneurysm remnant by the most of authors. Only in a minority of cases is this considered a staged treatment aimed to 'remodel' the aneurysm neck.

Since the field of vascular neurosurgery has continued to evolve, combined therapies can represent successful treatment strategies in cases of complex aneurysms or offer a feasible and safe option for the treatment of incompletely clipped aneurysms.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval Not required (literature review and retrospective case series).

Informed consent Yes, signed at the moment of procedure, stating that the patients authorises the use of medical information and imaging for scientific purposes in anonymous way.

Disclosure statement The authors declare no interest to disclose; they have any personal or institutional financial interest in drugs, materials or devices described in this submission and that they did not receive any specific funding. The paper and any of its contents has never been presented previously.

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