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Paraclinoid aneurysms: Outcome analysis and technical remarks of a microsurgical series

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ABSTRACT

Introduction: A critical appraisal of the surgical results of paraclinoid aneurysms is essential in the flow diverters era.

This study overviews the data of a three-decade surgical series of paraclinoid aneurysms while focusing on their technical remarks.

Methods: Overall data of a surgical consecutive series of paraclinoid aneurysms treated between 1993 and 2021 were retrospectively reviewed. Aneurysms were classified according to size and projection. Indications for surgery were different based on the availability of endovascular techniques, especially flow diverter, at the time of treatment. A statistical comparison between ruptured and unruptured aneurysms was accomplished.

Results: 58 patients were operated upon. Ophthalmic aneurysms were 68%, giant aneurysms 20%, and ruptured aneurysms 45%. Clipping and bypass were executed in 91% and 9% of cases, respectively. An mRS of 0–2 was achieved in 77% of patients, independently by the clinical onset. The mortality rate was 5%. Visual field was improved or unchanged in 71% of elective patients, whereas the incidence of de novo third and sixth cranial nerves deficit was 8% and 5%, respectively. On an average follow-up of 53.3 ± 38 months, a complete and durable aneurysm exclusion was achieved in 91.3% of patients with a single surgery.

Conclusions: Microneurosurgery is still a valuable treatment option for selected ruptured and unruptured paraclinoid aneurysms. In our experience, it has proven to be definitive and durable, with acceptable morbidity and mortality. Clipping is the treatment of choice in most surgical cases, achieving a good visual outcome in symptomatic patients.

1. Introduction

Paraclinoid aneurysms comprehend the clinoidal and ophthalmic segment of the internal carotid artery (ICA) [1]. Accounting for 5% to 15% of all intracranial aneurysms [2,3], they represent a spectacular topic in neurosurgery because of the complex three-dimensional anatomy of the anterior clinoid process and neurovascular structures around it, proximity to the optic nerve, possible variations in the origin of the ophthalmic artery (OA) and superior hypophyseal arteries, difficulty in achieving proximal control of the ICA, and safe aneurysm exposure. Over the years, a wide heterogeneity has characterized the nomenclature of the ICA segments [1,4–7], classifications of paraclinoid aneurysms [2,8–27], as well as their surgical treatment strategies [9–12,14,15,20,23,25,28]. These aspects contributed to delineate a broad discrepancy about the overall surgical results related to the paraclinoid aneurysms. Conflicting data has been reported also about the

Abbreviations: BTO, Balloon Test Occlusion; CT, Computed Tomography; DSA, Digital Subtraction Angiography; ICA, Internal Carotid Artery; ICG, Indocyanine Green; mRS, Modified Rankin Scale; OA, Ophthalmic Artery; OR, Odds Ratio; PED, Pipeline Embolization Device; PITA, Pipeline Embolization Device for The Intracranial Treatment of Aneurysms; PUFS, Pipeline for Uncoilable Or Failed Aneurysms.

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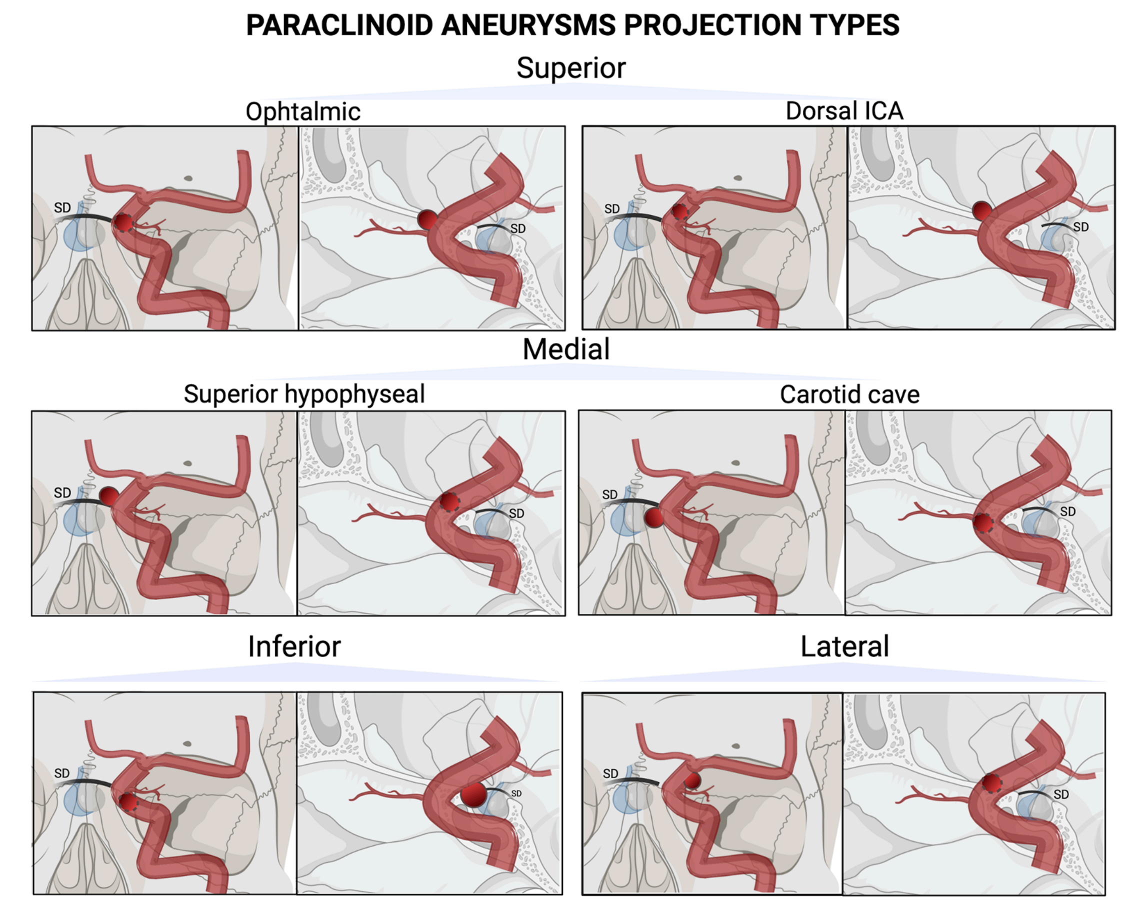

Fig. 1. Classification scheme based on the projection of paraclinoid aneurysms.

risk of rupture of those incidentals [29–32], although the presence of visual impairments at diagnosis is recognized to be as an indication for treatment. In the last decade, the paraclinoid ones represent the type of aneurysms mostly affected by the progressive refinement of the endovascular techniques and implementation of the pipeline embolization device (PED [Covidien, Irvine, California, USA]), the progenitor of all the flow diverters. Just think that for years, the only on-label indication for PED has been giant unruptured aneurysms of the ICA, from the petrous to the paraclinoid segment [33–36]. In this scenario, flow diverters have been the major contributors of a gradual but progressive decrease of the surgical case volume of paraclinoid aneurysms, especially those broad-based and giant [37–39]. A further aspect regards the similar critical reduction of the surgical neurovascular training. Despite this trend, microneurosurgery has proved to hold a primary role in younger patients (<40 years of age), ruptured aneurysms, cases of severely tortuous or stenosed cervical and/or intracranial ICA, and also conditions requiring immediate aneurysms occlusion, as the warning syndromes [3,8–10,12,13,40–54]. In comparison with PED and specifically to the paraclinoid aneurysms, microneurosurgery has also shown a higher and more durable occlusion rate, with an acceptable morbidity [8–17,55]. All these aspects confirm how effective microsurgical clipping and bypass can be for paraclinoid aneurysms in carefully selected patients. Equally important are the practical observations coming from the larger surgical series, along with the need for a critical appraisal of their outcomes.

This study aims at an overview of the overall results of a surgical case series of paraclinoid aneurysms operated on during the last three decades.

Some technical remarks aimed to optimize the patients' outcome and decrease the complications are also reported.

2. Materials and methods

The records of the present study were collected across three tertiary Italian hospitals after formal approval by the local Institutional Review Board. The results are stated according to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement [56]. The reference period of the present case series extended from January 1993 to January 2021. Overall demographic, clinical, imaging and surgical data of a cohort of patients consecutively managed because harbored an ICA aneurysm were retrospectively reviewed. Only those patients with a paraclinoid aneurysm, intended as one affecting the clinoidal and ophthalmic segment of the ICA, and who underwent surgery were eligible. Aneurysms previously treated by endovascular therapy were excluded. Blood blister-like, dissecting, transitional, mycotic and traumatic aneurysms were also excluded because of their peculiar characteristics. Patients operated on for more than the single paraclinoid aneurysm during the same surgery were also excluded to reduce the risk of bias. Admission computed tomography (CT) angiography was performed in all cases and digital subtraction angiography (DSA) in the vast majority. In elective cases, DSA also involved the superficial temporal arteries in case of a planned bypass, whereas a balloon test occlusion (BTO) of the ICA was always preoperatively accomplished. Magnetic resonance imaging was performed in all elective giant aneurysms to reveal eventual intraluminal thrombosis.

Aneurysms' size was calculated from the maximal diameters of the dome on DSA or, in case of thrombosed aneurysms, on CT angiography. The classic size categorization of the ISUIA study into small (<7 mm), medium (7–12 mm), large (13–24 mm), and giant (≥25 mm) was used [57]. The projection types classification, proposed by Krisht, was also adopted [58–61] (Fig. 1).

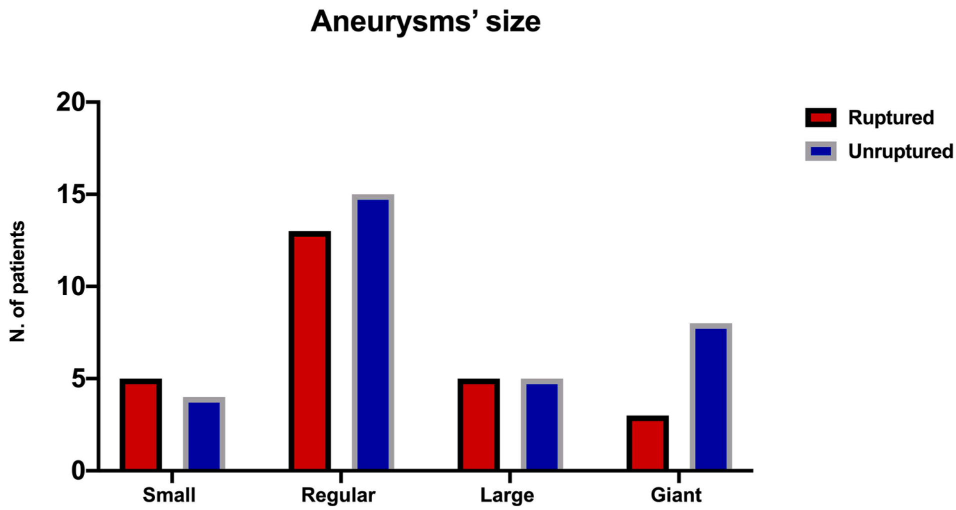

Fig. 2. Bar graph showing the aneurysms' sizes according to the ISUIA study types.

2.1. Treatment strategy

In all three hospitals, the treatment strategy was discussed within a multidisciplinary neurovascular team composed of experienced neurosurgeons and interventional neuroradiologists. The indications for surgery were different as it related to before and after the availability of PED in Italy since early 2011. As a rule, the clinical onset, neurological status, patient's age, comorbidities, aneurysm's size and angioarchitecture, the navigability of the ICA, BTO findings, patient's availability to antiplatelet anticoagulation, and the patient's preference were the main factors.

Before PED, surgery was considered the most robust option in comparison with coiling, or stent (Neuroform/Enterprise)/coiling, for ruptured aneurysms in young patients (≤55 years) with a Hunt-Hess grade ≤ 3, especially if no on anticoagulant therapy. About the elective cases, microsurgical clipping continued to be considered more suitable especially for broad-based, large to giant ophthalmic aneurysms (dome-to-neck ratio ≤ 1.5) in young and visually symptomatic patients, despite the reported low risk of bleeding in ISUIA study [57]. Clipping was also indicated in case of impossible or too risky navigability of the cervical or intracranial ICA because of atheromatic occlusion or prohibitive tortuosity. Planned or unplanned bypass with aneurysm trapping was generally necessary for elective fusiform and giant aneurysms, these last especially when having severe atherosclerotic changes of the neck or an intraluminal thrombosis >50%. Patients who were a candidate for bypass underwent to a preventive preparation marking the site of the graft harvesting according to what already reported by our group. Antiplatelet prophylaxis was started one week before surgery.

Since the implementation of PED, broad-based aneurysms became an indication for flow-diverter, regardless of the involvement of the OA, except for those patients unavailable to chronic antiplatelet therapy. Surgery was still preferred in young patients harboring ophthalmic aneurysms with evidence of visual impairment at diagnosis, and it was always the first option also in case of sentinel headaches. Conversely, endovascular treatment was preferred in patients with large or giant aneurysms who failed BTO.

Neurological outcome was reported as modified Rankin Scale (mRS) at the 6-month follow-up. All the times it was possible, the patients underwent postoperative DSA and, in cases of no remnant, to a 6-month DSA followed by yearly CT angiography up to two years after surgery. The subsequent imaging follow-up involved a CT angiography every two years. Otherwise, imaging follow-up was decided in the setting of the multidisciplinary team on a case-by-case basis. In a limited number of patients with severe allergic diathesis or renal failure, a time-of-flight MRI angiography-based imaging follow-up was executed. In the case of incomplete aneurysm exclusion, the need and type of treatment were weighted based on the specific patient's clinical features, comorbidities, angioarchitecture, and endovascular options available at the time of the treatment. Permanent cranial nerve deficits and overall visual outcome was based on the neurological exam and campimetry test, both at 6-months.

2.2. Statistical analysis

A comparison between ruptured and unruptured aneurysms in terms of demographic, angioarchitecture, neurological, angiographic, visual

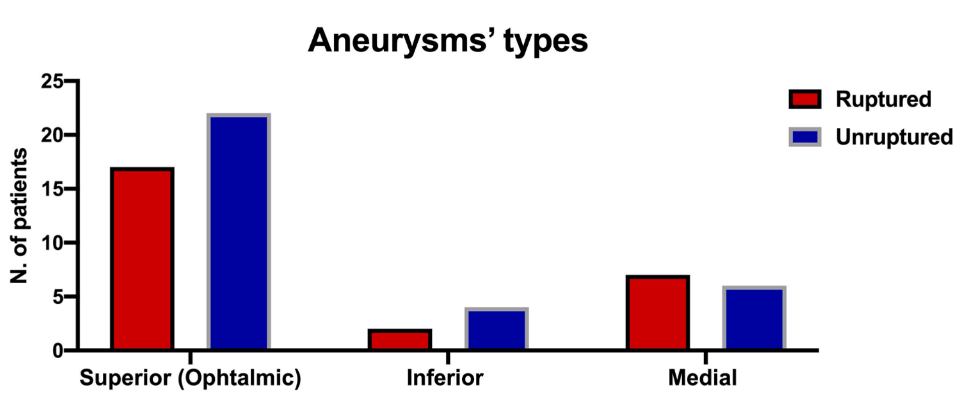

Fig. 3. Bar graph reporting the aneurysms' type according to Krisht classification.

Table 1
Demographic, clinical, and surgical data.

Data	Value
Timeframe	Jan. 1993–Dec. 2020
Pts. no.	58
Average patients' age (years ± SD)	46.8 ± 17
Sex	
Male no. (%)	27 (47)
Female no. (%)	31 (53)
Aneurysms type according to size	
Small (7 mm) no. (%)	9 (15)
Regular (7–12 mm) no. (%)	28 (48)
Large (13–24 mm) no. (%)	10 (17)
Giant (25 mm) no. (%)	11 (20)
Aneurysms type according to Krisht classification [58–61]	
Superior no. (%)	39 (68)
Inferior no. (%)	6 (10)
Medial no. (%)	13 (22)
Onset	
Ruptured no. (%)	26 (45)
Hunt-Hess grade (mean ± SD)	2 ± 1
Fisher grade (mean ± SD)	2.4 ± 0.7
Unruptured no. (%)	32 (55)
Amaurosis no. (%)	2 (3)
Impaired vision no. (%)	9 (15)
Third cranial nerve palsy no. (%)	4 (7)
Transient ischemic attack no. (%)	2 (3)
Warning syndrome no. (%)	4 (7)
Incidental no. (%)	11 (19%)
Surgical approach	
Pterional no. (%)	47 (80)
Cranio-orbito-zygomatic no. (%)	11 (20)
Surgical technique	
Clipping no. (%)	53 (91)
Bypass w/ aneurysm trapping no. (%)	5 (9)
Re-treatment rate no. (%)	5 (8.6)
Patients lost at follow-up no. (%)	14 (24)
Average FU (months ± SD)	53.3 ± 38

FU: Follow-up; Pts: Patients; SD: Standard Deviation.

Table 2
Comparison between ruptured and unruptured paraclinoid aneurysms.

Data	Ruptured	Unruptured	*p*-value
Pts. no. (%)	26 (45)	32 (55)	0.185
Average patients' age (years ± SD)	51.5 ± 17	43 ± 17	0.073
Sex			
Male no. (%)	9 (15)	18 (30)	0.119
Female no. (%)	17 (30)	14 (25)	
Aneurysms' size			
Small no. (%)	5 (9)	4 (7)	0.587
Regular no. (%)	13 (22)	15 (25)	
Large no. (%)	5 (9)	5 (9)	
Giant no. (%)	3 (5)	8 (14)	
Aneurysm type			
Superior no. (%)	17 (30)	22 (38)	0.679
Inferior no. (%)	2 (3)	4 (7)	
Medial no. (%)	7 (12)	6 (10)	
Neurological outcome			
Good (mRS 0–2) no. (%)	18 (30)	27 (47)	0.448
Moderate (mRS 3–4) no. (%)	5 (9)	4 (7)	
Poor (mRS 5) no. (%)	1 (2)	0	
Death (mRS 6) no. (%)	2 (3)	1 (2)	
Angiographic outcome (on 53 patients)			
Complete aneurysms exclusion			
Clipping no. (%)	21 (80.7)	27 (68.7)	0.740
Bypass w/ aneurysm trapping no. (%)	–	5 (31.3)	

mRS: modified Rankin Score.
There were no statistically significant differences in the parameters between ruptured and unruptured paraclinoid aneurysms ($p < 0.05$).

outcome, and complications involved an unpaired *t*-test for numerical data, a Welch test for continuous variables with different variances, and a chi-square test for categorical variables. The following dependent variables were tested in univariate and multivariate logistical regression analysis for the identification of independent predictors of poor (mRS 3–6) surgical outcome: age > 50 years, male sex, subarachnoid hemorrhage, Hunt-Hess grade, Fisher grade, aneurysm size > 25 mm, aneurysm projection, intraoperative aneurysm rupture, and hydrocephalus. Prism 5 (GraphPad Software, Inc., La Jolla, California, USA) software was used for statistical analysis. A *p*-value < 0.05 was considered statistic.

3. Results

3.1. Demographics, angioarchitectural and clinical data

Fifty-eight patients in total were operated on. The average patients' age was 46.8 ± 17 years, and the male/female ratio was 0.9. Regular size aneurysms (7–12 mm) were predominant (48%), while small and giant ones were 15% and 20%, respectively (Fig. 2). About types, ophthalmic aneurysms were widely prevalent (68%), whereas no lateral type aneurysms were treated (Fig. 3). Subarachnoid hemorrhage was the onset in 26 patients (45%) with an average admission Hunt-Hess score and Fisher grade of 2 ± 1 and 2.4 ± 0.7, respectively. Within unruptured aneurysms, visual impairments, III cranial nerve palsy, and sentinel headaches were present in 15%, 7%, and 7% of patients, respectively. A transient ischemic attack was the clinical manifestation in two patients with giant thrombosed aneurysms. The remaining 47% of the aneurysms were incidental. (Tables 1 and 2)

3.2. Microsurgical technique

3.2.1. Clipping

Clipping was performed in 91% of patients. Cervical ICA exposure was performed in all cases except selected cases of small superior aneurysms of the dorsal ICA lying distally to the OA. For clipping, an ipsilateral pterional route with anterior clinoidectomy was performed in all but eleven complex or giant aneurysms, for which a cranio-orbito-zygomatic approach has been necessary. An intradural clinoidectomy was performed by default in all large and giant aneurysms, and most of the regular ophthalmic ones. In all the clinoidal (C5) aneurysms, in those ophthalmic ones (C6) where the OA raised from the clinoidal (C5) segment of the ICA, and also in those where the superior hypophyseal artery came from the C5 segment as reported by Kobayashi et al. [20], the cutting of the distal dural ring has been the key to achieve a complete aneurysm exclusion. A wider unroofing of the optic canal, aimed at the cutting of the falciform ligament and mobilization of the optic nerve, has been generally performed for aneurysms that involved the take-off of the OA. Temporary ICA occlusion and bipolar shrinking of the dome were frequently used techniques. Stacking-seating clipping technique, retrograde suction-decompression "Dallas" technique [62], aneurysmorraphy, and aneurysmectomy were employed almost exclusively in giant or heavily thrombosed aneurysms. Micro-Doppler ultrasound, indocyanine green (ICG) video angiography, somatosensory- and motor-evoked potentials neuromonitoring, and fluorescein angiography were used since 2007, 2009, 2012, and 2018, respectively. In three elective cases (2 inferior projecting and 1 ophthalmic) managed between 2009 and 2011, clipping was performed after an initial unsuccessful endovascular coiling where the decrease in packing attenuation occurred at 4 months on average after treatment.

3.2.2. Bypass

In five aneurysms (9%), an extracranial-to-intracranial high flow bypass was performed before the aneurysm trapping. Saphenous vein and radial artery were the conduits in two and three cases, respectively.

3.2.3. Non-visual complications

Aneurysm rupture and ICA thrombosis/occlusion were the most frequent intraoperative complications in both ruptured and unruptured

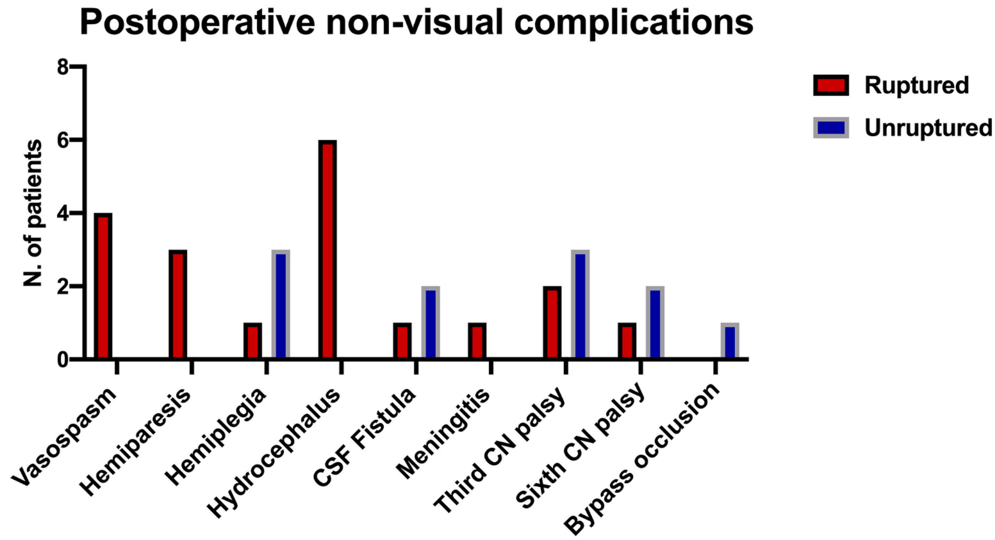

Fig. 4. Bar graph documenting the incidence of postoperative non-visual complications according to the clinical onset.

Table 3
Post-operative non-visual complications.

Data	Ruptured	Unruptured	*p*-value
Intraoperative			
Aneurysm rupture no. (%)	5 (9)	4 (7)	0.735
ICA thrombosis/occlusion no. (%)	2 (3)	1 (2)	
Postoperative			
Vasospasm no. (%)	4 (7)	0	0.044*
Ischemic stroke			
Hemiparesis no. (%)	3 (5)	0	
Hemiplegia no. (%)	1 (2)	3 (5)	
Hydrocephalus no. (%)	6 (10)	0	
CSF Fistula no. (%)	1 (2)	2 (3)	
Meningitis no. (%)	1 (2)	0	
De novo cranial nerves deficits			
Third CN palsy no. (%)	2 (3)	3 (5)	
Sixth CN palsy no. (%)	1 (2)	2 (3)	
Bypass occlusion	–	1 (20)	

CN: Cranial nerve; CSF: Cerebrospinal fluid; ICA: Internal carotid artery.
Post-operative non-visual complications did differ significantly ($p < 0.05$).

aneurysms ($p = 0.735$). Postoperative complications were significantly higher in ruptured aneurysms, and they involved hydrocephalus (10%), clinical vasospasm (7%), and ischemic stroke with hemiparesis/hemiplegia (7%). The incidence of procedure-related cranial nerve deficits was similar in ruptured and unruptured groups and concerned the third and sixth nerves (Fig. 4). A late occlusion of the bypass occurred 22 days after surgery in a young patient harboring a giant aneurysm. He developed a severe motor deficit of the right upper extremity, which was found to be recovered at the third-month post-rehabilitation follow-up. In the four patients with clinical vasospasm, this last occurred on the eighth day on average, involved mainly the middle cerebral artery, and was also confirmed by DSA. The vasospasm-related clinical status was characterized by stupor and hemiparesis in all the patients. Three of them were successfully managed with intravenous or intra-arterial nimodipine, while the other underwent balloon angioplasty after which the patient experienced an abrupt improvement. A patient with a third cranial nerve palsy and another with a sixth nerve deficit had a partial recovery after six months. Overall, the rate of postoperative non-visual complications was higher in the ruptured aneurysms compared with the unruptured ones ($p = 0.044$) (Table 3).

3.2.4. Neurological outcome

A good (mRS of 0–2) and moderate (mRS 3–4) neurological outcome was achieved in 77% and 16% of patients, respectively, and the overall

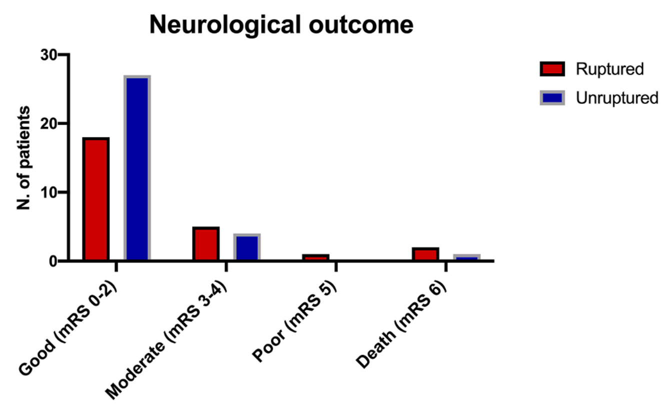

Fig. 5. Bar graph showing the neurological outcome in ruptured versus unruptured aneurysms.

mortality rate was 5%. No differences were found between ruptured and unruptured aneurysms ($p = 0.448$) (Table 2, Fig. 5).

3.2.5. Angiographic outcome and management of remnants

Five patients were lost on long-term imaging follow-up. Complete exclusion of the aneurysms with clipping and with a single procedure was achieved in 80.7% and 68.7% of ruptured and unruptured aneurysms, respectively, without statistical significance ($p = 0.740$) (Table 2). Bypass with aneurysm trapping was successful in all five cases. In five patients, two elective and three hemorrhagic, DSA revealed a remnant which underwent a late successfully endovascular treatment consisting in PED in four cases and stent/coiling in the remaining. The overall re-treatment rate was 8.6%. No aneurysm recanalization was documented on an average follow-up of 53.3 ± 38 months.

Table 4
Visual outcome.

Postoperative vision	Ruptured	Unruptured	TOT	*p*-value
Normal no. (%)	19	15	39 (71)	0.073
Improved no. (%)	0	5		
Worsened no. (%)	3	7	10 (18)	
De novo amaurosis no. (%)	2	4	6 (11)	

There were no statistically significant differences in visual outcome between ruptured and unruptured paraclinoid aneurysms ($p < 0.05$).

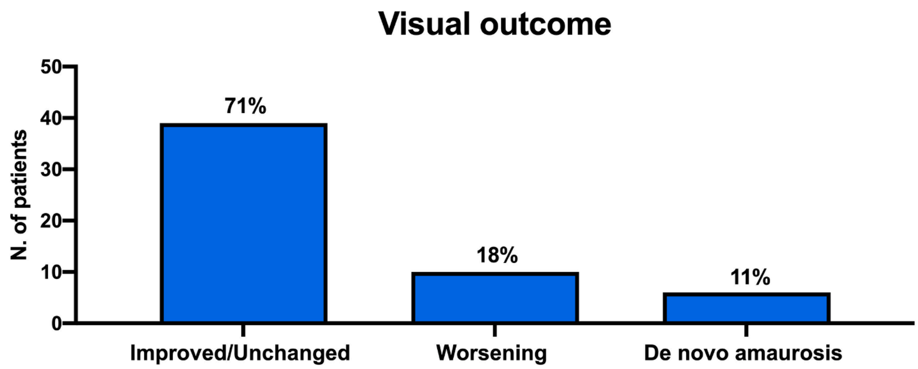

Fig. 6. Bar graph exhibiting the visual outcome.

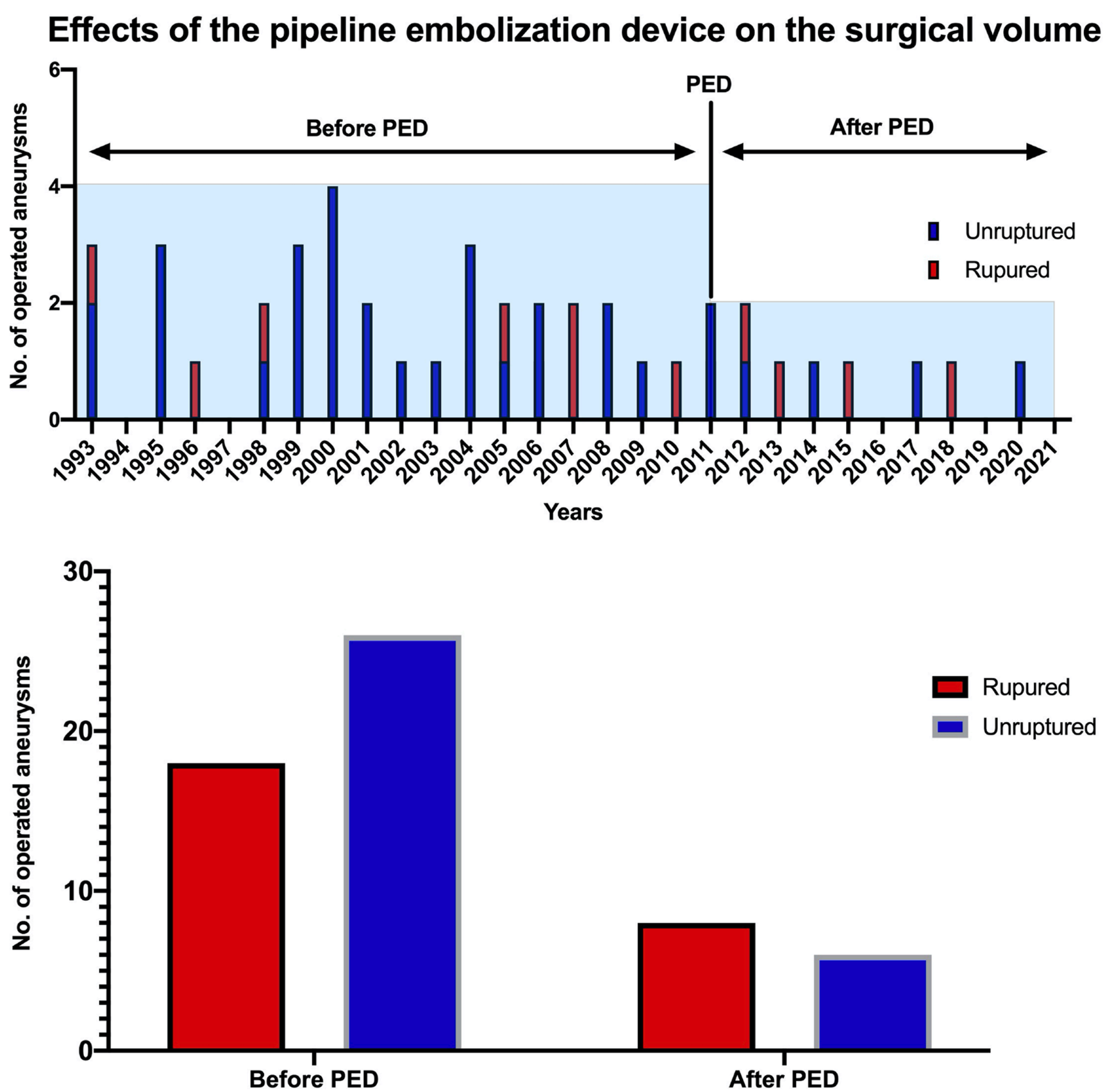

Fig. 7. Graphs showing the effects of the pipeline embolization device on the surgical case volume.

3.2.6. Visual outcome

An improved or unaffected vision at 6-months was observed in 71% of the 55 patients. Visual cut worsened in 18% of cases and six of the patients (11%) experienced de novo amaurosis. No differences were found between hemorrhagic and non-hemorrhagic onset ($p = 0.073$) (Table 4, Fig. 6).

3.2.7. Effects of PED on the surgical case volume

The overall number of operated aneurysms before and after PED was 44 (76%) and 14 (24%), respectively. The number of elective aneurysms surgically treated before and after PED was 26 (81%) and 6 (19%), respectively (Fig. 7).

Table 5
Logistic regression analyses of prognostic factors.

	Odds ratio	95% CI	*p*-value
Univariate analysis			
Age > 50 years	0.31	0.08–1.09	0.069
Male sex	1.45	0.42–5.20	0.549
Subarachnoid hemorrhage	2.40	0.69–9.07	0.169
Hunt-Hess grade	0.55	0.31–0.94	0.031*
Fisher grade	0.34	0.14–0.69	0.002**
Aneurysm size > 25 mm	0.29	0.01–1.77	0.203
Aneurysm projection	0.91	0.38–2.45	0.853
Intraoperative aneurysm rupture	31.50	6.70–198.1	<0.0001****
Hydrocephalus	1.45	0.19–7.83	0.684
Multivariate analysis			
Fisher grade	0.09	0.01–0.40	0.007**
Intraoperative aneurysm rupture	46.27	7.57–538.1	0.0002***

3.2.8. *Logistic regression analyses*

In univariate analysis, Hunt-Hess grade [Odds ratio (OR) 0.55; 95% Confidence interval (CI) 0.31–0.94; *p*-value 0.031), Fisher grade (OR 0.34; 95% CI 0.14–0.69; *p*-value 0.002), and intraoperative aneurysm rupture (OR 31.50; 95% CI 6.70–198.1; *p*-value < 0.0001) were predictors of a poor outcome. Age > 50 years, male sex, subarachnoid hemorrhage, aneurysm size > 25 mm, aneurysm projection, and hydrocephalus were not statistical. In multivariate analysis, intraoperative aneurysm rupture (OR 46.27; 95% CI 7.57–538.1; *p*-value 0.0002) and Fisher grade (OR 0.09; 95% CI 0.01–0.40; *p*-value 0.007) maintained the statistical significance (Table 5**)**.

3.3. *Illustrative cases*

3.3.1. *Case #1: ruptured superior (Ophthalmic) aneurysm*

A 55 years-old female with a subarachnoid hemorrhage (Hunt-Hess grade 4, Fisher score 4), and a left intracerebral front-basal hematoma, was diagnosed with a 1.2 cm left ophthalmic aneurysm having an apical bleb. The patient underwent a pterional approach with an extra-dural anterior clinoidectomy. The aneurysm was successfully exposed and clipped. Severe compression of the left optic nerve was detected intraoperatively. The patient was transferred to ICU and, after two weeks,

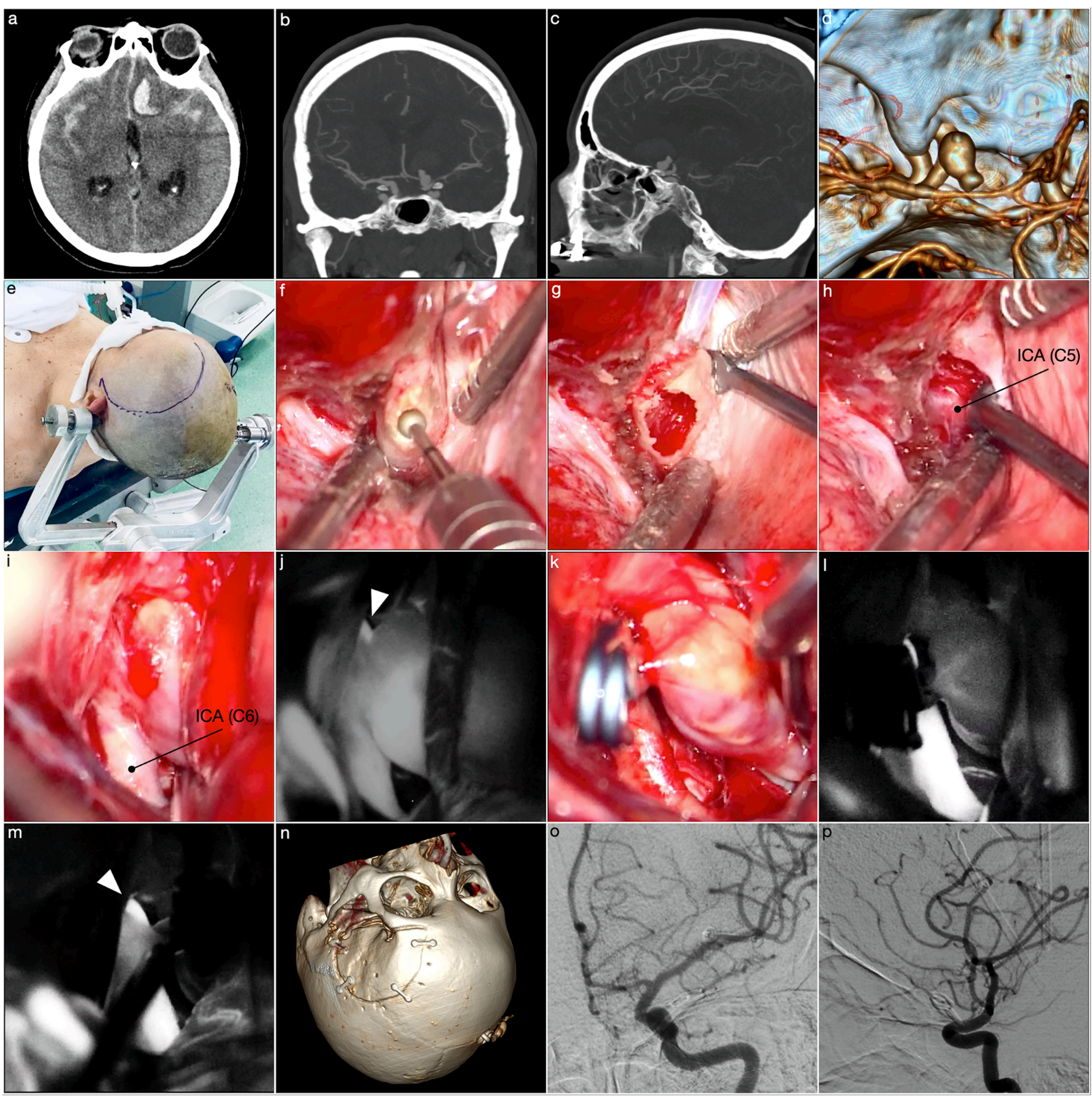

Fig. 8. (a) Preoperative axial computed tomography (CT) scan. **(b-c)** Preoperative coronal and sagittal 2D CT angiography. **(d)** Preoperative 3D CT angiography. **(e)** Surgical position for pterional approach. **(f-g)** Extradural anterior clinoidectomy. **(h)** Exposure of the clinoid segment (C5) of the internal carotid artery (ICA). **(i)** Aneurysm exposure. **(j)** Indocyanine green videoangiography (ICG). Arrowhead shows the take-off of the ophthalmic artery. **(k)** Aneurysm clipping. **(l-m)** Post clipping ICG confirming the exclusion of the aneurysm and the patency of the ophthalmic artery (arrowhead). **(n)** Postoperative 3D CT scan. **(o-p)** Postoperative digital subtraction angiography (DSA) in anterior-posterior and lateral projection. C5: Clinoid segment of the ICA; C6: Ophthalmic segment of the ICA.

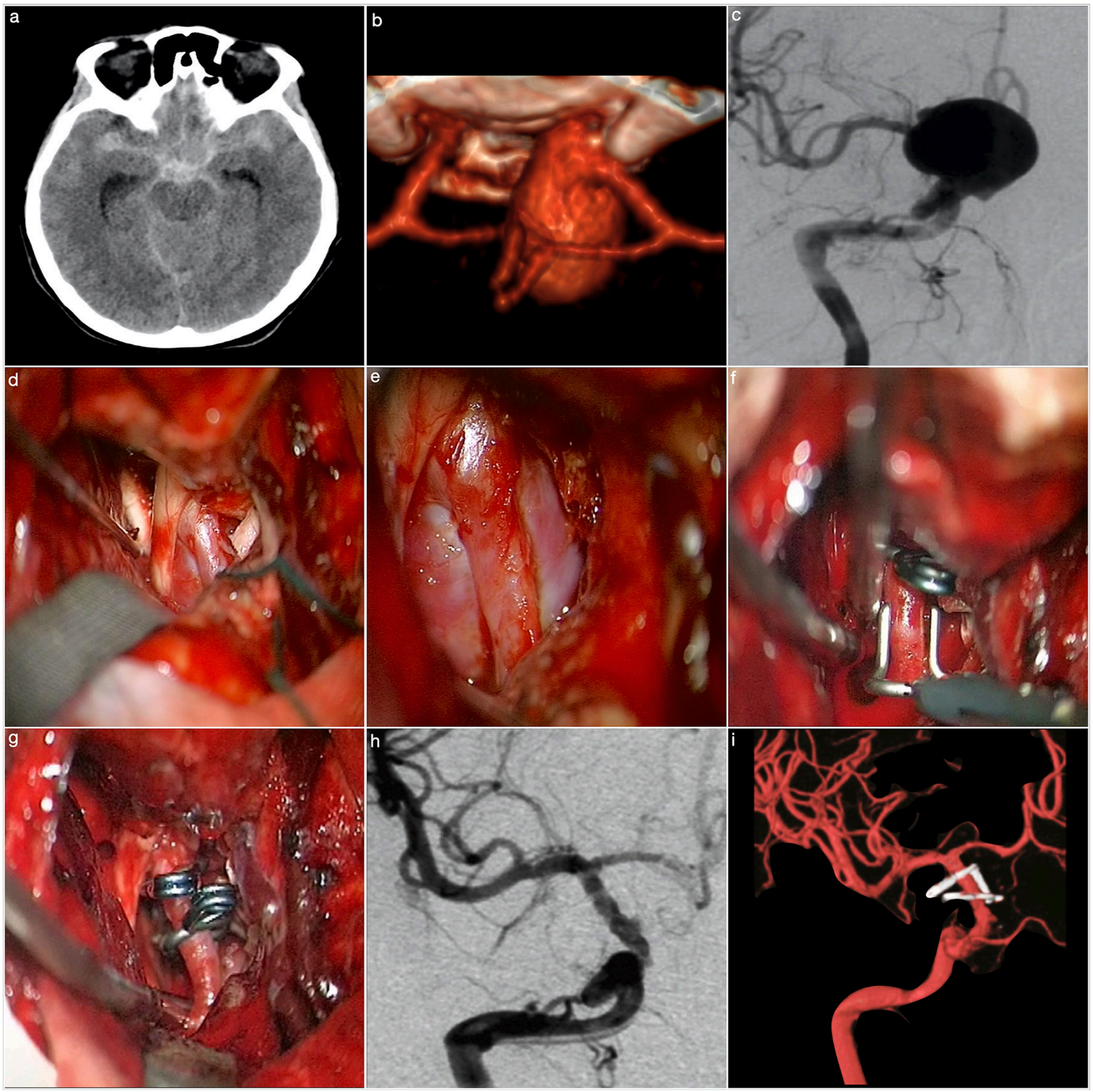

Fig. 9. (**a**) Preoperative axial CT scan. **(b)** Preoperative 3D CT angiography. **(c)** Preoperative DSA of the right ICA in anterior-posterior projection. **(d-e)** Aneurysm exposure after intradural anterior clinoidectomy. **(f-g)** Aneurysm clipping with two fenestrated tandem clips. **(h-i)** 2D and 3D postoperative DSA showing the complete exclusion of the aneurysm.

transferred to rehabilitation where she completely recovered within three months. Postoperative digital subtraction angiography confirmed the complete exclusion of the aneurysm and the full visualization of the OA. Because of the late occurrence of hydrocephalus, she also underwent ventriculoperitoneal shunt (Fig. 8).

3.3.2. Case #2: ruptured large inferior paraclinoid aneurysm

A 37 years-old female was diagnosed with a subarachnoid hemorrhage. She was in Hunt-Hess grade 2. CT angiography and DSA revealed a right large inferior paraclinoid ICA aneurysm. After the exposure of the cervical ICA, the patient underwent a right cranio-orbito-zygomatic approach with an intradural anterior clinoidectomy. Aneurysm was excluded using two fenestrated tandem clips without complications. Post-operative DSA confirmed no remnants and the patient was discharged with an mRS 0 and a normal vision. No refilling of the aneurysms was found after 57 months (Fig. 9).

3.3.3. Case #3: unruptured giant medial paraclinoid aneurysms

A 34 years-old female suffered from a transient third cranial nerve palsy and visual impairment in the right eye. CT angiography and DSA revealed a right giant medial (superior hypophyseal) paraclinoid aneurysm. A right pterional approach with an intradural anterior clinoidectomy was performed and the aneurysm was successfully clipped. The patient was discharged with an mRS 2. DSA revealed a small remnant that underwent follow-up. Three months after surgery, the patient had a significant recovery of the campimetric deficit. After 3 years, the remnant was stable in size (Fig. 10).

4. Discussion

The present study was targeted at a critical appraisal of the overall results of a cumulative surgical series of paraclinoid aneurysms, which were consecutively managed during the last three decades. Our data indicated that clipping is the treatment of choice in most of those cases where surgery is indicated. It allowed a definitive and durable exclusion in many ruptured and unruptured aneurysms, regardless form their projection type or clinical onset, with acceptable morbidity and mortality. Notably, a good to the moderate outcome was achieved in 93% of patients, who also experienced an improved or unaffected vision in 71% of cases. In our experience, the occurrence of an intraoperative aneurysm rupture was found to be a strong predictor of an unfavorable outcome on multivariate logistical regression analysis. Our data is

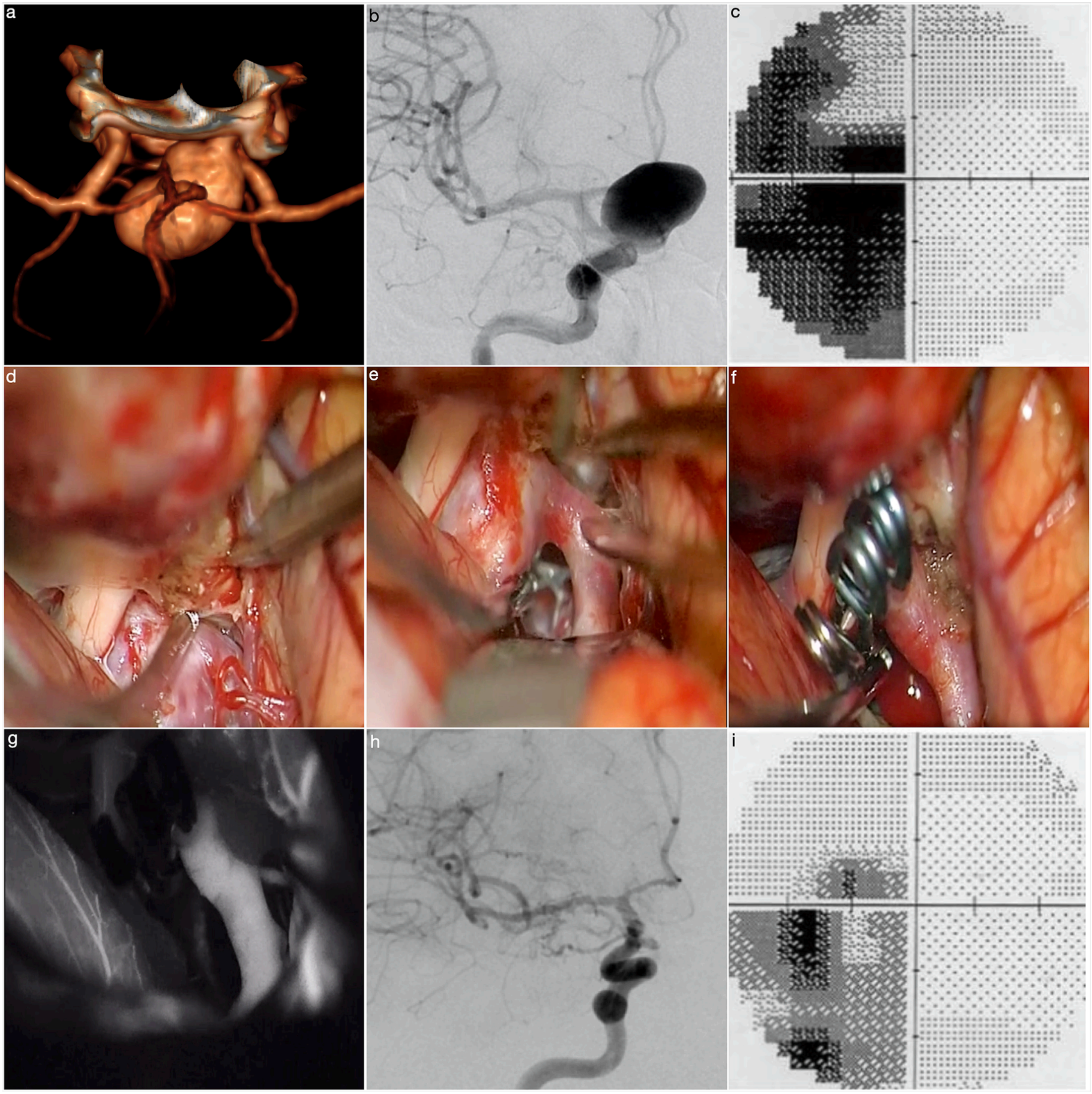

Fig. 10. **(a)** Preoperative 3D CT angiography. **(b)** Preoperative DSA of the right ICA in anterior-posterior projection. **(c)** Preoperative campimetry. **(d)** Intradural anterior clinoidectomy. **(e-f)** Aneurysm exposure and clipping with multiple Yasargil straight clips. **(g)** Indocyanine green videoangiography. **(h)** Postoperative anterior-posterior DSA of the right ICA. **(i)** Postoperative campimetry executed at the 6th-month follow-up.

mostly similar to those of larger surgical series where the reported average rate of clipping, complete aneurysm exclusion, and good neurological outcome is 91%, 93%, and 88%, respectively [3,8,10,13,41,43,53–55,63–74] (Table 6). Morbidity and mortality were also equivalent. Conversely, our retreatment rate was higher than that of other surgical series (8.6% vs. 1%) because other authors considered "retreatment" as only patients who underwent a redo surgery rather than an endovascular treatment after a failed surgery. The high rate of postoperative oculomotor deficits was the main weakness of this surgery in our like in other cohorts and, not surprisingly, it was found to be higher in ruptured aneurysms. About the type, ophthalmic aneurysms have been characterized by the best surgical outcome and, therefore, those types for which surgery is still considered as a valid option in carefully selected patients. Recently, on a series of 40 unruptured paraclinoid aneurysms, Otani and colleagues confirmed this indication for clipping, with regard to superior projecting aneurysms in young patients [75]. Similar conclusions were reported by Matano et al. based on a larger cohort of 127 consecutively operated patients [54]. Today, the remaining types are better candidates for flow diversion, which have widely proven its safety and efficacy in the PITA (Pipeline Embolization Device for the Intracranial Treatment of Aneurysms Trial) [76] and PUFS (Pipeline for Uncoilable or Failed Aneurysms) trial [77], and many more meta-analyses and case-series studies [39,78–87]. The largest series on PED reported a very low (5%) risk of ophthalmic artery occlusion, and an insignificant (0%) average chance of in-stent stenosis and ischemic stroke [39,79–85]. The average rate of good clinical outcome and Raymond-Roy class I occlusion is reported to be 99% and 86%, respectively (Table 7). The rate of post-surgery severe visual complications was 11% in our series and ranged between 0% and 19% in others. Definitive data about the visual outcome of PED versus microsurgery for paraclinoid aneurysms, especially the ophthalmic ones, come from two meta-analyses by Silva et al. and Touzé et al., both confirming the superiority of the former in achieving an improvement of the visual cut [78,88]. Matsukawa and colleagues identified in the carotid cave location and plug-in method during dural closures tow potential sources of visual morbidity in patients who underwent microneurosurgery [89].

In our practice as in those of other series, the implementation of PED caused a significant decrease in the surgical case volume of paraclinoid aneurysms, especially those electives (Fig. 7).

Endovascular coiling, stand-alone, stent-assisted, and balloon-assisted has been related to an occlusion rate significantly lower than both PED and surgery, along with an inferior durability

Table 6
Main surgical series of paraclinoid aneurysms.

Author, Year	No. of Aneurysms	Ruptured aneurysms	Clipping	Bypass*	Occlusion rate	Good Neurological Outcome**	Visual Complications°	Non visual Complications		Morbidity rate†	Mortality rate††	Retreatment rate	Clinical follow-up [range (average months)]
								Intraoperative°°	Postoperative°°°				
Heros, 1983 [63]	34	35%	68%	14.7%	68%	82.3%	8.8%	3%	8.8%	7%	3%	0%	NA
Dolenc, 1985 [64]	14	78.5%	100%	0%	100%	86%	0%	0%	14%	14%	7%	0%	NA
Day, 1990 [13]	80	35%	96.3 %	0%	100%	87%	5.5%	1.2%	13.7%	8.7%	0%	0%	NA
Batjer et al., 1994 [65]	149	44%	95.5 %	0.7%	100%	86.5%	NA	NA	NA	NA	3%	0%	NA
De Jesús et al., 1999 [10]	35	24%	88.6 %	8.6%	88.5%	96.4 %	4%	2.8%	14%	11.4%	0%	0%	6–84 (39)
Hoh et al., 2001 [3]	180	25%	94%	0.5%	94.1 %	89.4 %	3.7%	3%	22%	6%	2.8 %	0%	NA
Barami et al., 2003 [8]	61	NA	95.1 %	NA	NA	93.4 %	8.1%	NA	NA	NA	1.6 %	NA	NA
Iihara et al., 2003 [66]	35	0%	97.1 %)	0%	73.5%	NA	5.7%	0%	2.8%	2.8%	NA	0%	NA
Silveira et al., 2004 [67]	55	76.5%%	100%	0%	100%	82%	6%	0%	6%	6%	0%	0%	NA
Khan et al., 2005 [68]	81	46%	94%	5%	96%	93.1 %	3.7%	2.5%	2.5%	5%	0%	1.2%	NA
Raco et al., 2008 [43]	108	9.2%	81.5 %	14.8%	93.2 %	81.1 %	1%	1.8%	0.9	2.7%	0%	6.8%	30–137 (98)
Fulkerson et al., 2009 [69]	126	27%	91.3 %	0.7%	89.6%	93.2 %	4.7%	3%	8%	11%	1.1 %	0%	5.5%
Eliava et al., 2010 [70]	83	57.9%	92.7%%	0%	90.4 %	83.1 %	17.5%	18.1%	2.5%	20.6%	3.6 %	0%	NA
Sharma et al., 2010 [71]	78	60.2%	94.6 %	0%	100%	82.1 %	0%	0%	21%	21%	3.6 %	1.2%	2–93 (8)
Xu et al, 2010 [72]	59	70%	84%	14%	90.9 %	77.5 %	6%	0%	3.3%	9.3%	4%	0%	6–95 (13.5)
Nanda & Javalkar, 2011 [73]	86	42.4%	100%	1%	92.6 %)	86.3 %	2.6%	9.3%	8.1%	17.4%	5.8%	0%	(27.3)

(*continued on next page*)

Table 6 (*continued*)

Author, Year	No. of Aneurysms	Ruptured aneurysms	Clipping	Bypass*	Occlusion rate	Good Neurological Outcome**	Visual Complications°	Non visual Complications: Intraoperative°°	Non visual Complications: Postoperative°°°	Morbidity rate†	Mortality rate††	Retreatment rate	Clinical follow-up [range (average months)]
Colli et al, 2013 [41]	106	59.5%	98.1 %	1.9%	96.1 %	76.8 %	1.6%	33.7 %	13.7 %	24.2 %	7.4 %	0%	1–192 (51.7)
Lai & Morgan, 2013 [53]	182	0%	88.4%	5%	95.1%	98%	3.2	2.9%	3.2%	6.4%	0.6%	1.7%	1.6–195.9 (24.7)
Kim, 2014 [55]	44	0%	54.4%	45.6%	83%	97.5%	4.5%	0%	24%	11.3%	0%	10%	1–51 (16)
Matano, 2015 [54]	127	0%	85%	15%	93.7%	99.2%	18.8%	0%	8.6%	8%	0%	5.5%	(8.9)
Kamide, 2019 [74]	231	27	100%	0%	91.1%	99.6%	13%	1.3%	20.4%	20%	0%	NA	NA

*Bypass and aneurysms trapping, or bypass and ICA occlusion; ** Glasgow outcome scale score 4–5, modified Rankin score 0–2, WFNS (World Federation of Neurosurgical Societies) grading system 1–3; °: Worsened visual acuity, or de-novo amaurosis; °°: Aneurysm rupture, or internal carotid artery thrombosis/occlusion; °°°: Include vasospasm, ischemic stroke, hydrocephalus, cerebrospinal fluid fistula, meningitis; †: Permanent; ††: Directly related to the surgical procedure; NA: not available.

[3,38,44,55,81,90–99] (Table 8).

The natural history of paraclinoid aneurysms is characterized by a progressive and slow growing to reach large or giant size without rupture. The reason has been linked with their proximity to the skull base and optic pathways, which partially counterbalance the shear stress on the aneurysm dome [51]. The closeness of the paraclinoid aneurysms to all these structures accounts for additional difficulties in achieving an adequate proximal hemodynamic control of the ICA. Furthermore, part of the morbidity of these aneurysms comes from the frequent need to manipulate the optic nerve or even chiasm during surgery. Relationships of the ventral aneurysms with perforating arteries arising from posterior communicating and anterior choroidal artery is a further reason for technical complexity. Several classifications have been reported for paraclinoid aneurysms [8,9,15,18,100], this aspect is sometimes the source of confusion. De Oliveira et al. classified paraclinoid aneurysms in two groups, namely superior and inferior ones, the remaining types being considered medial or lateral extensions of these two [51]. While admitting the advantages coming from the easiness of this classification, we preferred to adopt that reported by Krisht and Hsu, which better addresses the technical difficulties related to the exposure of the aneurysm [58–61]. Apart from the superior (ophthalmic) and the ventral type, this classification also encompasses a medial and a lateral type. Superior type comprises aneurysms involving the take-off of the OA and those of the dorsal ICA, these two types being different from the technical standpoint. The medial type includes superior hypophyseal aneurysms and carotid cave ones. The lateral type grows within the anterior clinoid process which undergoes a cavitation process evident on CT scan.

4.1. Surgical planning

Throughout understanding of the preoperative neuroimaging of the aneurysm's angioarchitecture, and an exhaustive knowledge of the anatomy of the paraclinoid region are both essential to correctly classify these aneurysms, mentally configure the surgical field, prevent premature rupture, and especially decrease the risk of complications. A series of structural and hemodynamic parameters have been described by Duan and colleagues as part of the angioarchitecture of intracranial aneurysms; they are the aspect ratio, size ratio, height-width ratio, and flow angle [101]. The analysis of these features is pivotal for both planning and estimation of the risk of rupture in these side-wall aneurysms similar to what reported in the end-wall ones [101]. Surgical planning is nowadays widely aided by multiplanar and 3D rendered reconstructions of the intracranial vasculature. Although DSA remains the gold standard for diagnosis of paraclinoid aneurysms, CT angiography adds several bony details of great value in the differential diagnosis between intradural and intracavernous aneurysms, but also in the planning of the anterior clinoidectomy. When a long temporary clipping of the ICA is expected, a bypass ought to be performed especially in case of failed BTO, and the patient should be put on aspirin before surgery.

4.2. Technical remarks

From a technical standpoint, the position of the patients' head is of utmost importance. Chaddad-Neto and colleagues recommend avoiding any extension during the pterional approach for paraclinoid aneurysms to facilitate the clinoidectomy [102,103].

A prompt and safe proximal hemodynamic control of the ICA is not always easy to achieve during the early steps of surgery, especially in giant aneurysms. Accordingly, we strongly advise the exposure of the cervical ICA. Anterior clinoidectomy is universally considered a must for paraclinoid aneurysms [9,13,50,104–113]. It represents a condictio sine qua non for superior and lateral aneurysms, as well as an advantageous maneuver also for ventral and medial ones.

Regarding the need for clinoidectomy within the ophthalmic group, a distinction is imperative between the so-called "true" ophthalmic

Table 7
Main series of paraclinoid aneurysms treated with pipeline embolization device*

Author, Year	No. of Aneurysms	Ruptured aneurysms	Good Neurological Outcome**	Complications				Morbidity rate†	Mortality rate††	Raymond class I angiographic outcome	Retreatment rate	Clinical follow-up [range (average months)]
				Total	Opthalmic artery occlusion	In-stent stenosis	Ischemic stroke					
Moon et al., 2014 [83]	38	0%	NA	13.7%	2.7%	13.7%	0%	0%	0%	78.8%	0	NA
Vedantam et al., 2014 [84]	49	0%	98%	8%	4%	2%	0%	0%	0%	NA	NA	NA (12.8)
Chalouhi et al., 2015 [80]	83	6%	100%	2%	0%	0%	2%	3%	0%%	72%	8%	NA (7.3)
Di Maria et al., 2015 [81]	95	6.3%	97.3%	2.6%	1%	0%	2.6	3.9	0%	85.3%	2.1%	NA (18.8)
Burrows et al., 2016 [79]	50	0%	NA	NA	0%	0	NA	2%	2.2%	96%	0%	0–65 (29)
Rangel Castilla et al., 2016 [40]	42	26%	NA	19%	19%	0%	0%	NA	0%	NA	NA	3–34.7 (10)
Bhogal et al., 2017 [85]	80	0%	100%	6.5%	5.3%	1.2%	0%	NA	1.2%	NA	NA	NA (22.3)
Griessenauer et al., 2017 [82]	160	8%	NA	8.3%	7.1%	0%	8.3%	3.1%	0%	89%	0.9%	NA (18)

*Stand alone, or with coiling; ** Glasgow outcome scale score 4–5, modified Rankin score 0–2, WFNS (World Federation of Neurosurgical Societies) grading system 1–3; †: permanent; ††: directly related to the surgical procedure; NA: not available.

aneurysms and those of the dorsal wall of the ICA. Dorsal ICA aneurysms arise distally to the origin of the OA. Accordingly, an optic foraminotomy, followed by the cutting of the falciform ligament and gentle mobilization of the optic nerve, can be sufficient to clip the aneurysms. Anterior clinoidectomy allows to cut circumferentially the distal dural ring of the ICA, allowing its gentle mobilization. This maneuver is the key to avoid the sling effect and the consequent ICA stenosis after clipping. The unroofing of the optic canal, followed by the cutting of the falciform ligament, is of utmost importance in allowing a delicate medialization of the optic nerve. The choice between an extra- rather than intra-dural clinoidectomy is largely influenced by the surgeon's preference since no studies have demonstrated the superiority of a given technique. Nevertheless, many experienced surgeons prefer to perform an intradural clinoidectomy because allowing an early visualization of the dome, along with easier handling of the aneurysm in case of premature rupture. During anterior clinoidectomy, the potential risk of mechanical or thermal damages to the optic nerve is a source of visual morbidity during surgery of paraclinoid aneurysms, especially the medial ones. Constant irrigation during the bone drilling and a meticulous inspection of the OA are both essential to decrease the risk of postoperative blindness. The risk of blindness is also related to the manipulation of the optic nerve and OA. The use of patties soaked with papaverine on the OA is a good trick to avoid mechanical vasospasm. Overpacking of the surgical site with hemostatic material after clinoidectomy ought to be avoided since potentially associated with thrombosis of the OA and postoperative blindness [89].

Despite the elegant results of Kobayashi and colleagues traced back to the PED [20], the medial paraclinoid aneurysms, namely superior hypophyseal and carotid cave ones, are today the ideal candidates for flow diverters because of the reported higher surgical morbidity coming from the risk of superior hypophyseal arteries occlusion.

Kalluri et al. specifically reported the very good natural history of the carotid cave aneurysms putting into serious question even the need for their treatment [114]. Intraoperatively, the position of the superior hypophyseal arteries is a very good landmark in distinguishing the medial from the inferior type, as reported by De Oliveira and Krisht [51,59,61]. Superior hypophyseal arteries lie hidden inferiorly to the aneurysm when it is medially projecting. That is the main reason why they are at higher risk of occlusion during clipping. Conversely, the inferiorly projecting aneurysms tend to push upward the superior hypophyseal arteries in their growth, making them easily visualizable during surgery. In our experience, particularly useful has been the endoscopic assistance during clipping of inferior and medial projecting paraclinoid aneurysms for checking the aneurysm exclusion and post-clipping patency of superior hypophyseal arteries [115].

In 2018, Serrano et. al. reported in a literature review about the contralateral approaches to ICA paraclinoid aneurysms that it can be effective for clipping carefully selected cases of medial aneurysms [116]. We believe that the advantages of better visualization of the OA from the contralateral side should be practically related to the impossibility to perform an anterior clinoidectomy when a contralateral approach is planned. That's the reason why we have opted for an ipsilateral approach in all our cases.

During the last years, the increased availability and the refinements of neuromonitoring and flow visualization techniques represented the most innovative aspects of vascular neurosurgery. Our and other groups have previously demonstrated and reported that these valid technologies, as indocyanine green and fluorescein videoangiography, micro-Doppler ultrasonography, Doppler flowmetry, and intraoperative DSA, are important tools in neurovascular surgery armamentarium, since they contribute to decreasing the overall morbidity of intracranial aneurysms and arteriovenous malformations [117–122]. We strongly recognize in the microsurgical training and cooperation within a neurovascular team the most important aspect to optimize the patient outcome and avoid complications [123,124].

Table 8
Main series of paraclinoid aneurysms treated with coiling*

Author, Year	No. of Aneurysms	Good Neurological Outcome**	Visual complications°	Non-visual complications					Morbidity rate†	Mortality rate††	Raymond class I angiographic outcome	Retreatment rate	Clinical follow-up [range (average months)]
				Total	Ischemic stroke	Hemorrhagic stroke	Cranial nerves palsy	Others°°					
Thornton et al., 2000 [90]	71	NA	1.1%	14%	3.3%	2.2%	0%	8.5%	3.3%	2.2%	54%	11.5%	6–48 (16)
Hoh et al., 2001 [3]	53	74%	3.7	21%	18%	0%	3%	0%	3%	2%	44%	9%	NA
Park et al., 2002 [91]	73	92.1%	0%	13.7%	7.8%	2.7%	0%	2.7%	8.3%	6.3%	87.8%	27.8%	4–54 (13.9)
Iihara et al., 2003 [44]	77	NA	2.6%	18%	18%	0%	0%	0%	6.5%	0%	66.2%	20%	NA
Sun et al., 2011 [92]	30	94.6%	0%	7.1%	7.1%	0%	0%	0%	1.8%	3.6%	86.6%	3.5%	1–43 (14.8)
Yadla et al., 2011 [93]	147	NA	0%	1.4%	NA	NA	NA	NA	1.4%	0%	48.3%	12.2%	NA (19.1)
D'Urso et al., 2012 [94]	126	95%	0.8%	19.4%	4%	0%	0%	15.4%	0.8%	0%	62%	9%	2–132 (37)
Sorimachi et al., 2012 [95]	140	NA	0.7%	5.7%	2%	2%	0%	0%	0.7%	0%	33.6%	3%	8–144 (65.6)
Wang et al., 2013 [38]	142	90.1%	NA	4.3%	4.3%	0%	0%	0%	0%	0%	43.7%	7%	NA (16.6)
Kim et al., 2014 [55]	38	92%	0%	2%	1%	1%	0%	0%	2.5%	0%	90%	10%	2–60 (23)
Kwon et al., 2014 [96]	116	96.5%	NA	5.2%	5.2%	0%	0%	0%	0.8%	0%	70%	3.5%	6–89 (20.4)
Durst et al., 2014 [97]	65	NA	11%	24.5%	4.5%	0%	0%	20%	4%	0%	55%	30%	NA (12)
Heller et al., 2014 [98]	106	NA	2.8%	12%	3%	0%	9%	0%	6.6%	0%	NA	NA	NA (30)
Di Maria et al., 2015 [81]	61	95%	NA	5%	5%	0%	0%	0%	6.6%	0%	58.2%	9%	NA (37.4)
Shimizu et al., 2016 [99]	400	98.7%	0.5%	3.9%	2.9%	1%	0%	0%	1.2%	0.2%	67.4%	7.4%	6–88 (39)

*Stand alone, or stent-assisted, or balloon-assisted; ** Glasgow outcome scale score 4–5, modified Rankin score 0–2, WFNS (World Federation of Neurosurgical Societies) grading system 1–3; °: Worsened visual acuity, or de-novo amaurosis; °°: Include vascular puncture site complications, and internal carotid artery dissection; †: permanent; ††: directly related to the surgical procedure; NA: not available.

4.3. Limitations

The present study has some important limitations which can be summarized in the retrospective nature of the analysis, the relatively limited number of patients, and the heterogeneity of the surgical and endovascular teams. A further weakness lies in the fact that the decision-making process was predetermined and based on several factors as age, comorbidities, clinical onset, neurological status, and aneurysm angioarchitecture.

5. Conclusions

Microneurosurgery remains as a valuable treatment option in selected patients with paraclinoid aneurysms.

In our experience, it was proven to be definitive and durable for ruptured and unruptured aneurysms, especially the ophthalmic ones, with acceptable morbidity and mortality.

When surgery is indicated, clipping is the treatment of choice in the vast majority of these aneurysms, allowing for good visual outcomes in symptomatic patients.

The perfect knowledge of the skull base anatomy, careful planning, mastery of neurovascular techniques, and interdisciplinary with interventional neuroradiologists are essential aspects of the surgical management of paraclinoid aneurysms.

CRediT authorship contribution statement

Sabino Luzzi: Conceptualization, Writing – original draft, Writing – review & editing, Supervision, Validation. **Alice Giotta Lucifero:** Conceptualization, Data curation, Formal analysis, Methodology. **Matias Baldoncini:** Investigation, Methodology. **Mattia Del Maestro:** Software. **Samer K Elbabaa:** Validation, Writing - review & editing. **Renato Galzio:** Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Ethical approval

This study has been approved by the Internal Advisory Board of Ospedale Mazzini, Teramo, Italy, Ospedale San Salvatore L'Aquila, Italy and Policlinico San Matteo, Pavia, Italy.

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