

Clipping versus Coiling for Intracranial Aneurysms: Recent Trends

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Abstract

Background: Cerebral aneurysms are relevant conditions, and the best therapeutic approach in a patient with Ruptured and Unruptured Intracranial Aneurysm has been debated in the last decades. Coil Embolization therapy has increasingly gained popularity over Surgical Clipping.

Objectives: The aim of this analysis was to review the surgical and endovascular strategies for intracranial aneurysms, and to find out if one intervention is more suitable than other.

Methods: A literature review was carried out identifying studies published from 2002-2017 through Pubmed using the keywords listed below. 75 articles were selected to write this review.

Results: The International Subarachnoid Aneurysm Trial contributed to a change in practice of Intracranial Aneurysms. Endovascular Coiling reduced in 7,4% the proportion of patients who died or became dependent, even if the incidence of late rebleeding was higher at 1 year compared to Neurosurgery (2,9% vs. 0,9%). At 18 years the excess risk of rebleeding has not resulted in a significant worse outcome. Endovascular treatment is usually suitable for anterior and posterior circulating aneurysms. Middle cerebral aneurysms are generally treated through clipping. Asymptomatic Unruptured Intracranial Aneurysms smaller than 7 mm usually benefit from simple observation. Despite its benign natural history the number of Unruptured Intracranial Aneurysms treated has increased overtime. Higher mortality is associated with Neurosurgery compared to Endovascular strategy. Anaesthesia applied in surgical clipping is similar to the one applied in endovascular. The most common approaches are general anaesthesia and conscious sedation.

Conclusions: There is strong evidence to indicate that Endovascular Coil embolization is associated with better outcomes compared to Neurosurgical Clipping in patients amenable to either strategy. Despite the major technical advances in imaging and endovascular treatment of intracranial aneurysms, surgical clipping is still the most efficient treatment for medial cerebral artery aneurysms.

Keywords: Endovascular coiling; Neurosurgical clipping; Unruptured intracranial aneurysms; Ruptured intracranial aneurysm; Subarachnoid haemorrhage; ISAT

Abbreviations: AHA: American Heart Association; ASA: American Stroke Association; BAEPs: Brainstem Auditory Evoked Potentials; CI: Confidence Interval; CT: Computed Tomography; CTA: CT Angiography; DCI: Delayed Cerebral Ischemia; EC: Endovascular Coiling; FDA: US Food and Drug Administration; IA: Intracranial Aneurysm; ISAT: The International Subarachnoid Aneurysm Trial; ISUIA: International Study of Unruptured intracranial Aneurysms Investigators; MRA: Magnetic Resonance Angiography; NC: Neurosurgery Clipping; NIS: Nationwide Inpatient Survey; OR: Odds Ratio; RIAs: Ruptured Intracranial Aneurysms; SAH: Subarachnoid haemorrhage; SSEPs: Cortical Somatosensory Evoked Potentials; TEAM: Trial on Endovascular Management of Unruptured Intracranial Aneurysms; UCAS: Unruptured Cerebral Aneurysms Study; UIAs: Unruptured Intracranial Aneurysms; USA: United States of America

Introduction

Prevalence of Intracranial Aneurysms (IA) varies among populations due to multiple factors. Rupture of IAs is associated with high grades of morbidity and mortality. Therefore it is important to establish an early diagnosis and proceed with an adequate management in order to improve the outcomes of the patients [1].

Prevalence

Unruptured Intracranial Aneurysms (UIAs) are relatively common, found in approximately 3,2% of the general population. Still, the large majority will never rupture [2]. Most aneurysms are asymptomatic, but approximately 300,000 per year in the United States of America suffer a rupture, usually bleeding into the subarachnoid space [3]. Haemorrhagic risk of UIAs is inferior to the risk associated with rerupture of a Ruptured Intracranial Aneurysm (RIA) (1% vs. 30-50% within the first year) [4].

Subarachnoid haemorrhage (SAH) has a grim prognosis and is associated with high morbidity and mortality, and only 1/3 of patients

that suffer from SAH have a good outcome [3]. However, mortality rates from SAH appear to have declined in the past 25 years [5]. Mortality rates vary from 8% to 67% across published epidemiological studies [6].

Risk factors

There is a female preponderance for aneurysms (2:1), and the prevalence increases with age, with a typical age of onset >50 years [7-9]. Known Hereditary Syndromes, such as Ehlers Danlos syndrome and pseudoxanthoma have been associated with the development of IAs. Also, patients suffering from Autosomal Dominant Polycystic Kidney Disease develop IA in 10-15%. Even in the absence of a hereditary disorder, 7-20% of patients with a cerebral aneurysm will report a family history of this diagnosis [3].

Some acquired risk factors include hypertension, smoking, alcohol abuse, estrogen deficiency, hypercholesterolemia and carotid artery stenosis [10].

Congenital weakness, degenerative alterations associated with hemodynamic stress contribute to the loss of integrity of the artery wall and therefore predispose to the aneurysm development [11].

Diagnosis

Since symptomatic UIAs are unusual, they are usually found incidentally or on screening. There is little data on the best diagnosis strategy. Magnetic Resonance Angiography (MRA) and CT Angiography (CTA) are able to detect aneurysms 5mm or larger [12]. Digital Subtraction Angiography (DSA) has shown great sensitivity in detection of aneurysms smaller than 3mm, and constitutes the gold standard for aneurysm diagnosis. Moreover, it is the most sensitive imaging for follow-up in treated aneurysms [2].

Noncontrast Head Computed Tomography (CT) is the gold standard for diagnosis of SAH, and its sensitivity is close to 100% in the first 3 days after the occurrence. Lumbar puncture is needed if there is a strong suspicion of SAH based on clinical presentation despite a normal CT [13,14].

Risk of aneurysm rupture

Predicting the natural history of an UIA is important to determine the appropriate management. [15,16]. Behavioural risk factors such as hypertension, smoking, alcohol abuse, sympaticomymetic drugs have been associated with an increased risk of IA rupture. A history of previous SAH, familial aneurysms and certain genetic syndromes mentioned above favour SAH [1].

Aneurysm rupture is related to its rate of growth. Natural history was found to vary according to the size, location and shape of the aneurysm. Patient's characteristics such as age and country of origin may also influence the risk of rupture.

SAH complications

The rupture of an IA is a neurological emergency. Rebleeding is a common complication within the first 24 hours after the occurrence [17].

After the aneurysm obliteration, cerebral vasospasm and decreased cerebral perfusion may occur, representing important causes of poor outcome. Vasospasm (narrowing) occurs in multiple levels among

cerebral arteries and it is common 7 to 10 days after aneurysm rupture, often resolving spontaneously [1]. Delayed cerebral ischemia (DCI) occurs in about 1/3 to 1/4 of patients. Poor clinical condition at admission and a high amount of blood on the initial CT scan increase the risk of DCI [18].

Acute hydrocephalus occurs in 15-87% of patients with SAH, and is usually managed by external ventricular drainage or lumbar drainage [19]. Seizure-like episodes occur in a high percentage of individuals with SAH. Aneurysm in the middle cerebral artery, presence of a thick SAH clot, intracerebral haematoma, rebleeding, poor neurological grade and history of hypertension predispose to the occurrence of seizures [1].

Treatment

Treatment of IAs may require Neurosurgical Clipping (NC) or Endovascular Coiling (EC). For a long time, NC has been the primary modality of treatment, but in the last 3 decades EC has evolved and became widely used [20]. The International Subarachnoid Aneurysm Trial (ISAT) published in 2002 strongly influenced the change in practice of both RIAs (the focus of the ISAT trial) and UIAs [8].

Endovascular coiling

Coil variations include bare platinum, polymer coated (Matrix) and hydrophilic gel coated (HydroCoil) coils. No clear advantage in preventing recurrence was demonstrated by coating platinum coils [21].

Detachable Guglielmi Coil, a detachable platinum coil device, was first introduced in the USA clinical practice in 1990 and in 1992 in Europe [22,23]. Guglielmi detachable coils were approved by the US Food and Drug Administration (FDA) in 2003 to treat all brain aneurysms [24]. The detachable coil can be considered an "endovascular controllable occlusive soft coil". After detachment, the coil may be repositioned or exchanged so as to obtain better results. The best results are seen in smaller aneurysms with narrow necks [22].

Stent-assisted coiling has been used to treat wide-neck aneurysms. To avoid stent-associated thromboembolic events, antiplatelet therapy during the procedure is required and can complicate SAH. Complete obliteration of the aneurysm is recommended, and to improve the obliteration rate of coiling a high-porosity stent has been suggested [25].

Matrix is a platinum coil modified with polyglycolic acid braid and has been developed to achieve more durable aneurysm occlusion [26]. The hydrogel-coated coil was designed to improve the aneurysm packing, since this embolic treatment targets the aneurysm dead space [27].

In comparison to clipping, coiling has the advantage of requiring a shorter time of procedure, and reduction of surgical complications such as infection. However, there is a frequent necessity of reintervention due to a less permanent effect of treatment [28]. Intraprocedure aneurysm rupture during endovascular treatment presents a major challenge.

Neurosurgical clipping

The first brain aneurysm clipping took place in 1937, and for many decades has been the exclusive treatment for IAs. It is an entirely extravascular procedure, sparing the endovascular space. The

craniotomy, brain retraction, arachnoid dissection and aneurysm manipulation involved in surgery may be rendered as an invasive strategy [29]. Open surgery may be required as a support to the endovascular approach in case of prolapse of a coil through the wall of the aneurysmal sac and intraoperative vasospasm [30].

Methods

A literature review was carried out based on a PubMed research with the following instructions: Title/abstract: (“unruptured intracranial aneurysm” OR “ruptured intracranial aneurysm” OR “intracranial aneurysm” OR “subarachnoid haemorrhage”) AND (“neurosurgery clipping” OR “endovascular coil”) AND “ISAT”. Publications written exclusively in English from 2002 to 2017 were considered. The custom range began in 2002, since it was a decisive year in the intracranial aneurysm treatment story.

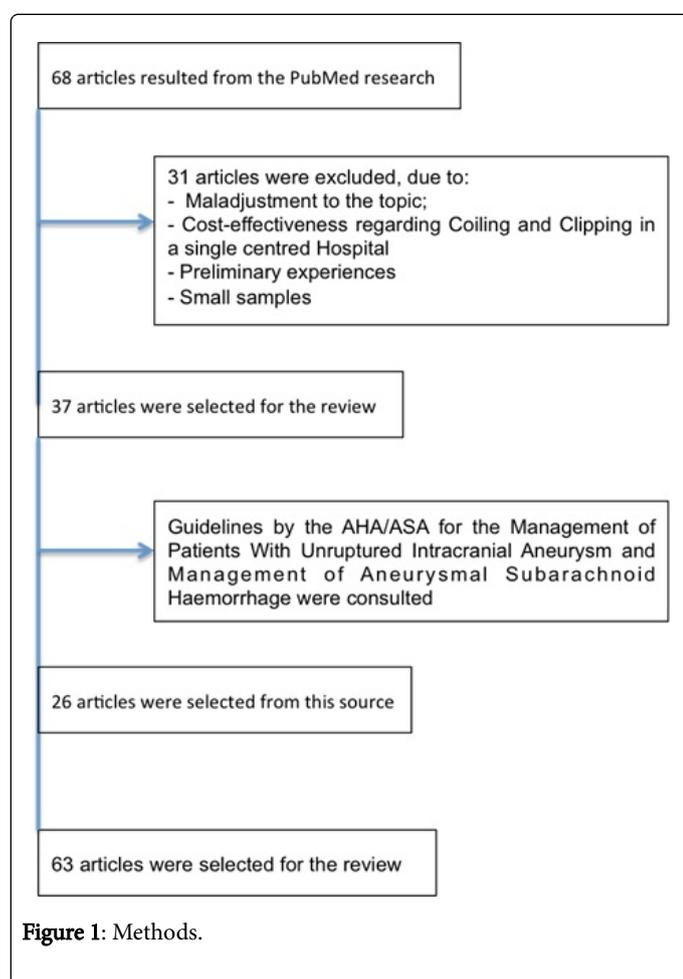


Figure 1: Methods.

From the 68 articles found in the research, 37 were selected for the review taking into consideration the content of the title and abstract. The excluded articles regarded papers that did not adjust to the topics reviewed in this review, publications related to cost-effectiveness of Endovascular Coiling and Neurosurgical Clipping in a single centred Hospital, preliminary experiences of specific techniques and studies regarding small samples.

References from relevant articles and Guidelines presented by the American Heart Association/American Stroke Association (AHA/ASA) for the Management of Patients With Unruptured Intracranial

Aneurysm and Management of Aneurysmal Subarachnoid Haemorrhage were also consulted, in order to better debate the subject. This source added 26 studies to the previous from PubMed, engaging a total of 63 references (Figure 1).

Results

Ruptured intracranial aneurysms

American Heart Association presented in 2012 guidelines for the management of Aneurysmal Subarachnoid Haemorrhage based on literature and recommendations from 2006 to 2010. [1] Medical measures and Surgical or Endovascular treatment are required to achieve the best outcomes in patients who suffered SAH.

Surgical and endovascular methods

ISAT: ISAT was the only multicentre, randomized, and controlled clinical trial that compared outcomes of surgical and endovascular repair across 42 neurosurgical centres, mainly in Europe and in the UK. Patients were randomly assigned to NC (n=1070) or EC (n=1073). To be eligible for the trial aneurysms had to be suitable for surgery and endovascular therapy. Most of the enrolled patients had good clinical grade and the aneurysms were localised in the anterior circulation. Patients older than 70 years old were not randomized [31].

The study concluded that patients who underwent EC had higher survival rates, lower epilepsy and mortality rates at one year than the ones who had NC. A 7,4% risk reduction (95% CI, p=0,0001) in the proportion of patients who died or experienced ongoing dependence due to neurosurgical disability was achieved with coiling. However, incidence of late rebleeding was higher in the endovascular group (2,9% versus 0,9% after surgery), and only 58% of coiled aneurysms were totally obliterated compared to 81% clipped aneurysms [31,32].

ISAT cohort was re-examined 5 years later, and embolization with coil was related to a higher risk of recurrent bleeding than clipping and the proportion of survivors who were independent after 5 years did not differ between the two groups (82% vs. 83%). Still, risk of death was significantly lower in the coiled group (14% vs. 11%) [29,33,34].

One thousand, six hundred and forty-four UK patients included in the ISAT trial were followed up for death and clinical outcomes for 10-18 years, using self-reported Rankin scale (Table 1). At 10 years 83% of patients allocated to EC were alive compared to 79% of patients allocated to surgical clipping (odds ratio [OR] 1.35, 95% CI 1.06-1.73). In both groups, the risk of death and rebleeding from the treated aneurysm up to 18 years was very small. Long-term causes of death result mainly of causes other than from the treated aneurysm. There was a small excess of rebleeding risk in the coiling group, which has not resulted in a significantly worse clinical outcome [23].

0	No symptoms
1	No significant disability, despite symptoms; able to perform all usual duties and activities
2	Slight disability; unable to perform all previous activities but able to look after own affairs without assistance
3	Moderate disability; requires some help, but able to walk without assistance
4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance

5	Severe disability; bedridden, incontinent, and requires constant nursing care and attention
6	Death

Table 1: Modified Rankin Scale [64].

Lin et al. analysed 34899 Hospital discharges with a diagnosis of ruptured or unruptured cerebral aneurysm from 1998 to 2007 identified from the Nationwide Inpatient Survey (NIS), therefore including 5 years before as well as 5 years after publication of the ISAT results. There was an increase in the number of treated aneurysms during this period, being that the trend was towards an increased use of coiling (Figure 2) [8].

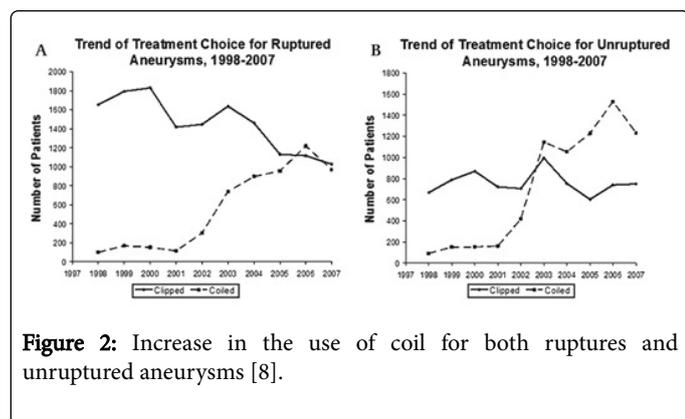


Figure 2: Increase in the use of coil for both ruptures and unruptured aneurysms [8].

A study published in 2011 analysed the national estimates of treatments for RIAs present in the NIS data between 2000-2002 and 2004-2006. There was an increase in utilization of endovascular treatment (3% vs. 17%) for intracranial aneurysms and an increase in the proportion of patients receiving any treatment in the post-ISAT period [24].

BRAT: In response to concerns regarding ISAT, in 2002 investigators at the Barrow Neurological Institute in Phoenix launched BRAT. Every patient admitted to the centre with SAH, regardless if it was amenable to NC and EC, was assigned in an alternating fashion to surgical aneurysm clipping or endovascular coil therapy if agreed to participate. Ultimately, 238 patients were assigned to aneurysm clipping and 233 to coil embolization. A large number of patients first assigned to embolization could not be safely treated with coiling and crossed over to aneurysm clipping. Nevertheless, outcomes at one year were better after coil embolization (33,7% of patients assigned to clipping had poor outcome vs. 23,2% of the coiling group), what is coherent with the ISAT study [35].

Other studies

A prospective multicentre trial was carried out between 1997 and 2014 to compare the treatment results of RIAs following EC and NC across Middle Europe. Six hundred and 61 cases of RIA were recorded. Two hundred and seventy one cases of SAH underwent EC, 390 underwent NC. Seventeen percent of patients treated with EC suffered from symptomatic Ischemic Stroke compared to 6,7% of the NC group (OR 2.86, 95% CI, p<0,0001). The occlusion rate was significantly better in the NC group versus EC group (OR 11.48, 95% CI, p<0.0001), the rebleeding rate was significantly lower in the NC group (OR 14.90, 95% CI, p<0.0001). Direct mortality was not significantly different

across the two arms of the study. No patient who underwent surgery required retreatment compared to 23 patients in the EC group (p<0.0001). Age and co-morbidities played an important role regarding the decision to retreat [36].

Turek et al. analysed 190 RIAs subjected to EC in the period of 2006-2013 to study the early outcomes and perioperative complications of the technique. Localization of the aneurysm within anterior circulation represented a predictor of negative postoperative outcome. In the case of vertebral-basilar aneurysms, complications are less common. Peri-operative complications included aneurysm rupture (main complication), acute vasospasm, thromboembolism, and prolapse of a coil. Hemiparesis/hemiplegia, dysphasia/aphasia, vasospasm and hydrocephalus could appear as post-procedural complications. Coiling was preferred as a first line treatment of poor-grade patients, especially those with large and inaccessible aneurysms when deciding whether to clip or coil [30].

EC of posterior circulating aneurysms has gained popularity throughout the decades, with several studies demonstrating better outcomes in this technique over surgery [1].

Hospital treatment volumes and availability of both endovascular and neurological intensive care services are important determinants for technique's recommendations [1]. Definite repair was significantly higher in urban teaching Hospitals, comparing to nonteaching Hospitals in a study that took place in the US during 2003 [9]. Better outcomes and lower mortality rates especially for clipping techniques were found in teaching Hospitals and larger Hospitals. Therefore, low volume Hospitals should consider early transfer of SAH patients to high-volume units [37].

Hospital costs of both EC and NC are rising within the years. Expenses vary from country to country, and might be different within the same country what makes it difficult to reach a conclusion concerning the cost-effectiveness of the procedures. Nevertheless, the most recent studies revealed that the NC group demonstrated lower Hospital costs compared to the EC group even considering the superior length of Hospitalization associated to clipping [38].

Unruptured intracranial aneurysm

Unlike patients with SAH, patients with UIA generally experience no neurologic deficits. UIAs are usually asymptomatic and often found incidentally on magnetic resonance imaging (MRI) or CT [39].

The interventional options include NC and EC. Simple observation may be beneficial in some situations, and radiographic follow-up is usually recommended, due to possible aneurysm growth. The relatively benign natural history and the increased detection by non-invasive imaging tests make the treatment option controversial [2].

Few observational and small prospective studies addressed the efficacy of each treatment modality in UIA, and therefore the best treatment choice remains doubtful [39]. The decision towards a procedure is based on the aneurysmal location and size, nature of the neck and presence of tortuous arteries, because these factors were shown to influence prognosis. The risk of intervention increases with age, and a conservative approach is usually considered in the elderly [40]. Decisions regarding optimum manage should balance the probability of short-term and long-term rupture and the risks of the intervention.

The Trial on Endovascular Management of Unruptured Intracranial Aneurysms (TEAM) began in 2006 and was designed to study the

long-term efficacy of coiling in prevention of bleeding and clarify if it is beneficial compared to simple observation. However, due to multiple factors this trial was prematurely interrupted and could never reach any conclusions [4].

The International Study of Unruptured intracranial Aneurysms Investigators (ISUIA) and Unruptured Cerebral Aneurysms Study (UCAS) are the most carefully designed large studies on UIA's natural history [2].

ISUIA, first published in 1998, evaluated the natural history of 1937 UIAs influencing contemporary neurosurgical practice. ISUIA analysed two groups: patients with no history of SAH and those with previous SAH who have undergone treatment, because the latter constitutes an independent risk for rupture. Aneurysms of less than 10 mm had a 0,05% risk of rerupture among patients with no history of SAH; the risk became 11 times higher in patients with history of SAH. Aneurysms located in the basilar apex, vertebrobasilar, posterior communicating, and posterior cerebral arteries were more prone to rupture. NC was associated with high morbidity and mortality, and outcome related to EC could not be analysed due to a small number of patients. These data were retrospective and whether the patients were representative was debated [40-42].

A second part of the study was published in 2003, and 4060 patients were analysed prospectively. A smaller cut point for size (<7 mm versus <10 mm) was defined. UIAs <7 mm in diameter had no benefit in treatment, because of the very low rupture risk. Symptomatic UIAs or those with daughter sac constitute exceptions. Risk rates related to EC and NC were higher than in previous studies. Morbidity and mortality rates of NC and EC in patients with no history of SAH from another lesion were 13,7% and 9,3% respectively, whereas in patients with history of SAH the rates were 11% and 7,1% respectively. Location in the posterior fossa and diameter higher than 12 mm were associated with worse outcome after EC. The major drawback in EC was due to incomplete occlusion of lesions [42].

UCAS, a prospective Japanese cohort study published in 2012, analysed 5720 patients who had saccular aneurysms detected on imaging that were ≥ 3 mm. Aneurysms ≥ 7 mm were more prone to rupture, also aneurysms located in the posterior communicating arteries were associated with a higher risk of rupture. Unlike other studies, history of SAH, smoking, presence of multiple aneurysms did not affect the risk of rupture in this study (Table 2) [15].

	Location	Study Type	Number Patients	of	Number aneurysms	of	Follow-up (months)	Predictors of aneurysm rupture
ISUIA	USA and Europe	Retrospective	1449 untreated		1937		99,6	Aneurysm size and location
ISUIA	USA and Europe	Prospective	4060: untreated, NS, 451 EC.	1692 1917	2686		49,2	Aneurysm size and location
Juvela et al	Finland	Retrospective and Prospective	142		181		252	Cigarette smoking, anterior communicating artery location, age
UCAS	Japan	Prospective	5720		2392 surgery, 4305 without early treatment		11660 aneurysm-years	Posterior communicating arteries and age

Table 2: Summary of large cohort studies on Unruptured intracranial aneurysms (UIA) [61].

A meta-analysis from 1990 to 2011 analysed 60 studies harbouring 10845 aneurysms. The majority of studies examining outcomes related to UIA's surgery have been single centre retrospective case series. Clipping of UIAs was associated with 1,7% mortality and 6,7% unfavourable outcomes. Craniotomy with clipping of an UIA provides permanent treatment of the aneurysm, being that recurrence is unusual. Morbidity rates were significantly greater in higher quality studies, and with large or posterior circulation aneurysms [43].

A meta-analysis on the natural history of UIAs published in 2006 integrated 19 studies since 1996. Four thousand seven hundred and five patients were included and several risk factors for aneurysmal rupture were identified. Age >60 years, female sex, Japanese or Finish descent, symptomatic aneurysm, diameter >5 mm and posterior circulation aneurysm were associated with a higher risk of rupture [44].

A retrospective cohort study, published in 2007, using data from 429 USA Hospitals evaluated 2535 treated UIAs. NC was associated with higher morbidity and mortality and longer lengths of stay (7.4 days versus 4.5) [45].

Alshehlee et al. analysed, over a 7-year period, 21104 cases with admission diagnosis of UIA of which 52,5% were admitted electively. Higher mortality and Hospital complication rates were associated with clipping, what was coherent with anterior studies. However, the location and morphologic characteristics of the aneurysms were not taken into consideration (Table 3) [39].

In 2010, Lindner et al. analysed 304 patients with IAs localised in different areas of the brain and assessed diverse risk factors, such as age, gender, smoking, alcohol intake, hypertension and family preponderance, reaching the conclusion that aneurysms at different sites also differ in risk factors. Rupture of aneurysms in the anterior circulation appeared to be more frequent in patients <55 years of age, posterior communicating aneurysms ruptured more frequently in men, and basilar artery aneurysm rupture is associated with lack of use of alcohol [46].

For aneurysms managed conservatively it is generally recommended imaging follow up to assess aneurysm growth. The likelihood of small aneurysm growth is low. Middle cerebral aneurysm location, size greater than 5 mm, presence of multiple aneurysms and family history of SAH were predictors of growth in a follow-up study by Serial 0,5T

MRA, being that 14 among 130 patients suffered aneurysm growth [47].

Complication	Clip n (%)	Coil n (%)	OR (95%)	P Value
Any event*	312 (8.35)	129 (3.69)	2.37 (1.92, 2.93)	<0.0001
Hospital mortality	60 (1.61)	20 (0.57)	2.83 (1.70, 4.71)	<0.0001
Intracerebral haemorrhage	89 (2.38)	48 (1.37)	1.75 (1.23, 4.49)	<0.0001
Postoperative Stroke	251 (6.71)	102 (2.92)	2.39 (1.89,3.03)	<0.0001
Hydrocephalus	33 (0.88)	44 (1.26)	0.69 (0.44,1.10)	<0.0001
Status epilepticus	4	0	...	<0.0001
Pulmonary	79 (2.11)	29 (0.83)	2.58 (1.68, 3.96)	<0.0001
Cardiac	119 (3.18)	74 (2.12)	1.52 (1.13, 2.04)	<0.0001
Systemic Infection	16 (0.43)	3 (0.09)	5.00 (1.45, 17.20)	<0.0001
Acute Renal Failure	37 (0.92)	32 (0.91)	0.92 (0.57, 1.48)	<0.0001

* Any event included a composite outcome of any mortality, intracerebral haemorrhage, or postoperative stroke

Table 3: Hospital Mortality and Complication rates associated with aneurysm clipping and coiling [39].

Anaesthetic management

Usually, anaesthetic principles for NC are similar to the ones applied to EC of IA. The most common approaches are general anaesthesia and conscious sedation, but no studies comparing these two techniques have been done [1,48].

Monitoring intra-arterial blood pressure and intracranial pressure (ICP), oxygen, carbon dioxide, urine and temperature is important. Slow administration of mannitol (0.25-2 g/kg) is recommended to avoid a transient increase in ICP [49].

Increase in blood pressure is worrisome, because it can motivate aneurysm rupture and ought to be controlled with nicardipine, labetalol, and esmolol to keep systolic blood pressure <160 mmHg [49].

Supervision of the patient with special attention for cardiac function, potential hypovolemia and hyponatremia is of great importance before anaesthesia. Hypovolemia and increased ICP heighten the chance of cerebral vasospasm and possible ischemic events. Albumin has neuroprotective properties and minimal effect on coagulation and is reasonable to treat volume imbalances. Hemodynamic control to avoid aneurysm rerupture and strategies to protect the brain against ischemic injury should be enforced. Nimodipine is recommended for vasospasm prophylaxis. Hyponatremia is a common electrolyte abnormality seen in up to 30% of SAH cases and may benefit from intravenous administration of normal saline solution [49].

General anaesthesia

General Anaesthesia is a popular technique among endovascular and surgical strategies, providing a stationary focal point for surgical manipulation and for visualization target area during the endovascular procedure [49].

Induced hypotension has been used in the past to prevent rerupture, but current data associate decrease in mean arterial pressure with poor outcomes [50].

Propofol and rimifentanyl infusion can be used when total IV anaesthesia is considered. Cortical somatosensory (SSEPs) and brainstem auditory evoked potentials (BAEPs) may be used to monitor cerebral function. Volatile anaesthetics interfere with SSEP and BAEP [49].

Conscious sedation

Some centres prefer to use only sedation during the placement of detachable coils in order to monitor the patient's neurologic status during the procedure. However, general anaesthesia is often used [51].

Endovascular coiling

Anticoagulation with heparin is administered during the embolization of aneurysms, unlike surgical clipping. If intraprocedure aneurysm rupture occurs, rapid reversal of anticoagulation with protamine is required [1].

When aneurysm obliteration is delayed, antifibrinolytic drugs (aminocaproic acid or tranexamic acid) have been shown to reduce the chance of rebleeding [49]. More than 33% of rebleeds occur in the first three hours after the symptoms, and approximately 50% within the first six hours [52].

Post-operative medication with paracetamol is recommended to relieve pain [30].

Neurosurgical clipping

Intraoperative Hypothermia for Aneurysm Surgery trial (IHAST) analysed 1001 patients of 30 different centres so as to determine whether intraoperative cooling during craniotomy was associated with improved outcomes, but no benefits in long-term morbidity and mortality were achieved [53].

Intraoperative glucose concentrations >129 mg/dl is associated with increased risk of neurological function decline [54].

Temporary clipping is useful to prevent aneurysm rerupture during the procedure. If temporary clipping is expected to exceed 120 minutes, induced hypertension may be considered, but the value of this measure was not established [1].

Discussion

Endovascular coiling and neurosurgical clipping

Diagnosis strategies, imaging surveillance and aneurysm obliteration techniques have undergone multiple changes throughout the years, and algorithms to determine the proper indications for each treatment are continually in transformation. [39,55]. It has been observed an increasing usage of EC in the treatment of RIAs and UIAs in the last decades, and this strategy has overtaken neurosurgery in

many Hospitals. Both RIAs and UIAs require special and individualised attention in order to decide which strategy will represent a more beneficial measure.

In general, anaesthetic principles are the same for endovascular and surgical managements. The possibility of rebleeding, hypertension, cerebral edema, DCI, electrolyte abnormalities, hydrocephalus, seizures and cardiopulmonary dysfunction should be considered to guide anaesthetic management [49].

Embolization has the advantage of requiring shorter time of and reduction of surgical complications such as infection [28]. Bare platinum, polymer coated and hydrophilic gel coated coils are some available options to proceed with endovascular treatment, being that no clear differences in outcome have been suggested [21].

Aneurysms initially planned for endovascular treatment are eventually clipped, what doesn't happen the other way round. Also, with certain complications that occur after embolization, surgical therapy may be required to resolve the negative sequel. Therefore, even though endovascular technique is becoming more popular it is not expected to completely substitute surgery [28].

It is remarkable how quickly the attitude is changing in favour of coiling of IA, despite the lack of evidence of superiority over the accepted standard treatment. There is evidence suggesting improvement of clinical outcome and effectiveness of coiling since the ISAT period until nowadays. The former technique is evolving overtime; therefore general outcome described in the past cannot be directly compared to today's [23].

Ruptured intracranial aneurysms

ISAT: ISAT together with technologic advances, increased availability of endovascular procedures and contributed to a shift in the USA practice pattern of cerebral aneurysms [31,56]. However, there are still wide variations in the availability and use of EC, among countries and within countries [31].

Even though ISAT has been a strong driver of change in the management of RIAs (and UIAs), the evidence of the superiority of coiling should not be based on this trial alone. After publication of the results of ISAT, there was a lot of discussion among the neurosurgery community, mainly because of its selection bias, ethical dilemma and poorly chosen primary endpoints. It remains unclear whether the trial can be confidently generalized to all patients since it recruited a small portion of the "universe" of patients with RIAs: 88% of the enrolled patients had a favourable clinical grade, 95% were in the anterior circulation, and 90% were smaller than 10 mm. Also, patients older than 70 years old were not randomized. A total of 9559 patients were screened, but only 2143 enrolled. Selection of good clinical grade patients may be required to avoid masking of the outcomes by poor clinical condition of patients. However, this selection criteria has implications in the generalization of the results. The overall in-Hospital mortality associated to ISAT was 6%, comparing to 26% in-Hospital mortality of SAH in the USA [31,56,57]. Other design issues such as lack of requirements for the proficiency of surgical participants and angiographic control need to be taken into consideration [33]. Recommendations following the interpretation of the trial vary among neurosurgeons and neurointerventionalists communities.

In spite of the fact that most of the IAs covered by the ISAT trial are localised in the anterior circulation, they represent a big percentage of the existing aneurysms, 85% of which are placed in the anterior

circulation [58]. This location represents a negative predictor of postoperative outcome [59]. Aneurysms of the anterior cerebral artery are associated to cognitive impairment, deficits of memory and personality changes, because the surgical techniques used to access aneurysms in this location may require resection of frontal lobe structures [31].

Nevertheless, ISAT was a statistically powerful study whose findings can be applied to patients with rupture of small, anterior circulation aneurysms, with a good World Federation of Neurological Societies grade (Table 4). Various studies analysed NIS, the largest all-payer inpatient care in the US, comparing periods before and after the publication of the ISAT study and concluded that there was an increase in usage of EC comparing to NC in both UIAs and RIAs.

WFNS (World Federation of Neurosurgical Societies)	Glasgow Coma Scale score	Motor deficit
I	15	Absent
II	14-13	Absent
III	14-13	Present
IV	12-Jul	Present or absent
V	06-Mar	Present or absent

Table 4: Subarachnoid hemorrhage scale [65].

At one year, EC was associated with higher survival rates, lower epilepsy and mortality rates comparing to clipping. The difference was likely attributable to the greater incidence of technical complications and longer time needed to secure the aneurysm in NC. Incidence of late rebleeding and partial obliteration was higher in the EC group [32].

The poor outcome rate climbs rapidly with advanced age. The absolute difference between the poor outcome rates after coil embolization and clip occlusion is lower in those <50 years old than it is for those >50 years old (3,3% vs. 10,1%). The advantage of coil embolization could not be assumed for patients <40 years old. Rebleeding rates higher 0,1-0,3% per year after coil embolization comparing to surgical clipping, what may overturn the superiority of coiling in young patients over the years [32].

A 10 year follow-up of a group of UK patients included in the ISAT trial concluded that the small risk excess of rebleeding in the coiling group did not result in a significantly worse clinical outcome. [23] The risk of rebleeding after aneurysm haemorrhage persists for 30 years, therefore it is important to continue the follow up of patients enrolled in the ISAT study [60].

Other studies regarding RIAs

Hammer et al. published in 2016 a prospective, non-randomized trial. The data reached back to 1997, and from that time on endovascular treatment technology suffered noteworthy changes, whereby clipping has not undergone significant changes. Considering the location of the treated IAs there has been a misbalance. In the EC group there was a high rate of treated anterior aneurysms, which are known to be associated with worse outcome. Angiographic visualization is performed after EC, which certainly increases detection

of small residuals found post-treatment. On the other hand, occlusion rates for clipping were based on post-operative surgeon reports [36].

In 2012, BRAT was designed to reflect real world practicalities of RIAs in North America, and the conclusions were coherent with the ISAT study.

O'Kelly et al. conducted a nonrandomized and retrospective study using data from the province of Ontario. In order to overcome several limitations associated to the ISAT trial, all patients undergoing repair of RIAs between 1995 and 2004 were analysed. In the adjusted analysis of the entire cohort EC was associated with a significantly increased rate of mortality (hazard ratio 1,25). This study reached to conclusions that disagree with ISAT. Unlike ISAT this study was nonrandomized and retrospective, which limited the ability to measure possible cofounders. The degree of disability could not be directly measured. Similarly to ISAT, the relative expertise of endovascular and neurosurgical practitioners was not assessed [56].

Unruptured intracranial aneurysms

Hospitalizations for clipping and coiling of UIAs in the United States of America from 2001 to 2008 described in the NIS were analysed. In that period it is clear the steady increase in the number of UIAs and the proportion of UIAs treated with EC. The number of UIAs being treated has increased overtime despite its relatively benign natural history. EC was associated with lower morbidity and mortality comparing to NC [61].

Unlike RIAs that have been studied and subjected to a multicentre, randomized, and controlled clinical trial, the study of UIAs is limited to few observational and small prospective studies. There are no randomised clinical trial data regarding management of UIAs, but findings of ISAT may be transposed to UIAs. The number of UIAs treated with EC, overcomes the number of those treated with NC in many Hospitals. Still, the predominant use of the endovascular procedure is not uniform among Hospitals [8,30,39].

EC is likely to be initially less morbid than clipping. The TEAM trial was designed to understand whether EC was associated with lower morbidity than observation. The initial objective was to recruit 2000 patients with UIAs eligible to prophylactic coiling within 3-4 years with a planned follow-up of 10 years. The contrast between the two groups of the trial (intervention versus observation) contributed to the failure of the trial. Also, some neurosurgeons responsible for the decision-making could be reluctant to the endovascular approach what could contribute to an asymmetrical allocation of management. Legal and bureaucratic issues and financial obstacles also contributed to the failure of the trial [4].

ISUIA and UCAS are the most carefully designed large studies regarding UIA's natural history, and guidelines taking into consideration these analyses have been published to better decide the best approach. Imaging control was not required in ISUIA, so it could not address the risk of aneurysms that may change in size overtime. It remains unclear if UCAS can be applied to non-Japanese populations, especially because the incidence rate of SAH is higher in Japan than in Europe or USA.

It has to be balanced if the advantages of the treatment outweigh the potential risks of aneurysm rupture, since UIAs generally have a benign natural history. Decision towards conservative management requires imaging follow-up to control aneurysm growth. Various studies throughout time have concluded that UIAs treated by coiling

have fewer adverse events, lower mortality and shorter Hospital length of stay [8]. Clipping of large aneurysms in a posterior location in older patients is associated with higher rates of morbidity and mortality.

Recent trends

Considering RIAs, several studies have suggested that older patients or patients presenting with low clinical grade carrying anterior circulation aneurysms yield more favourable results with coil embolization rather than clipping [59]. Neurosurgery clipping, even representing a more invasive strategy, has a lower risk of rerupture and better durability, therefore in patients that are able to tolerate this type of surgery (younger patients with good grade aneurysms) this treatment may be preferable [55]. However, data on this matter is still conflicting.

ISAT strongly influenced the change in practice of IAs. However, in real world practice coiling is being offered to types of patients that were not studied in ISAT, and EC of posterior circulating aneurysms has gained popularity over the decades.

Middle cerebral aneurysms are generally treated by clipping not only because of the facilitated access, but also due to specific local angioarchitecture that often requires vascular remodelling of the middle cerebral artery bifurcations, which is better coped with surgery. [59] Van Dijk et al. published in 2011 a study confirming the benefits of surgical clipping in the management of middle cerebral artery aneurysms already mentioned in the literature [62].

Small intracranial aneurysms (≤ 3 mm diameter) represent technical challenges, due to difficulties in obtaining a stable micro catheter position and higher risk rates of perforation related to placing coils in confined spaces. However, with widespread adoption of adjunctive techniques such as balloon and stent successful assisted coiling of small aneurysms has been achieved [63].

Relatively to UIAs, Physicians are able to choose among endovascular, surgical and no treatment of UIA, but the optimum strategy remains unclear. The existent high-quality data is not enough to decide whether intervention is related to better outcome than the natural history without such treatment. In the absence of clinical trial data, decisions regarding treatment or extended follow-up of UIA are based on the natural history. Since the risk of rupture of an UIA is relatively low, the risks associated with the treatment must be even lower.

Guidelines based on ISUIA and UCAS studies have been published recommending observation rather than treatment for aneurysms smaller than 7 mm in patients with no history of SAH, being that those symptomatic or with daughter sac may require treatment. The decision to treat an UIA is not straightforward and aneurysmal factors such as a bigger size and posterior location, whether there is a thrombus within the aneurysm, presence of daughter sac and symptoms; patient factors such as age, sex, comorbidities and family history of SAH ought to be considered. EC is more beneficial than NC for both younger and older patients and for both anterior and posterior circulating aneurysms.

Differences regarding aneurysms' treatment between and within countries mirror the dissimilarities in cost-effectiveness around the world. Hence, it is important to uniform systems of care so as to overcome differences and achieve better results. The risks associated to treatment rely on the surgical and endovascular expertise and caseload of each institution [30].

Regardless of the treatment option, mortality and morbidity associated to treated aneurysms has decreased overtime due to technique evolution, better imaging follow-up and diagnosis. Other factors independent from the aneurysm itself may influence de morbidity and prognosis decay. Therefore, it is crucial to alert the patient for the consequences of smoking, sedentary lifestyle, unhealthy alimentation and salt abuse.

Conclusions

In recent years, multiple publications evaluated the safety of EC and SC. EC is preferred under some circumstances, due to its associated lower morbidity and mortality compared to NC. Nevertheless, the debate about the best choice of treatment is still ongoing and the opinion from the neuroradiology community diverges from the neurosurgery's.

Endovascular treatment has become more popular over the decades in the treatment of anterior and posterior cerebral aneurysms, whereas clipping is usually preferable as the treatment choice of middle cerebral artery aneurysms and very small aneurysms that are often challenging to treat with an endovascular approach.

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