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INSTITUTO DE CIÊNCIAS BIOMÉDICAS ABEL SALAZAR
UNIVERSIDADE DO PORTO

centro hospitalar do Porto

Artigo de revisão bibliográfica

Mestrado Integrado em Medicina

Endovascular treatment of intracranial aneurysms: review of prognostic factors

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Junho 2017

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Abstract

Background and Purpose: Endovascular treatment of intracranial aneurysms has substantially developed in the past two decades. The aim of the present review is to evaluate some of the most impactful determinants of clinical outcome with the objective of projecting a more concise standpoint on endovascular treatment.

Methods: A comprehensive review of literature from 1968 to 2016 was performed, reporting on relevant contributing factors to prognosis related to endovascular approach of intracranial aneurysms.

Results: The PHACES score and the Unruptured Intracranial Aneurysm Treatment Score both have limitations and need further evaluation. A recommendation has been made for the use of PAASH to the detriment of the most frequently used WFNS scale. The treatment of patients admitted more than 72 hours after haemorrhage can be delayed, if the estimated risk of rebleeding is low. The preferred protocol should focus on early resuscitation and stabilization followed by safe transfer rather than a hyperacute transfer paradigm. Thromboembolic complications and intraoperative rupture rates associated with coiling alone were 7.3% and 2.0% for unruptured aneurysms, and 13.3% and 3.7% for ruptured aneurysms. Balloon-Assisted Coil Embolization allows for optimal coil packing, particularly in the aneurysm neck and fundus. Pipeline Embolization Device was associated with a high aneurysm occlusion rate and a rate of adverse events comparable to those of more conventional techniques. Long-term durability and safety still remain to be proved by larger series and after prolonged follow-up with both the Surpass Flow Diverter and Flow-Redirection Endoluminal Device. Initial results associated Woven Endobridge device with complete and adequate occlusion rates of 27% and 59% respectively, that increased significantly at a mean follow up time of 7 months.

Conclusions: Given the development of new technologies for the treatment of intracranial aneurysms, the field of neurovascular intervention is only likely to expand further. Supplementary randomized controlled trials are essential for proper outcome assessment.

Key words: endovascular; intracranial; subarachnoid; hemorrhage; treatment; aneurysms; embolization; flow; disrupter; diverter;

Abbreviations and Acronyms

AES = Aneurysm Embolization System; **ATENA** = Analysis of Treatment by Endovascular approach of Non ruptured Aneurysms; **AOR** = Aneurysm Occlusion Rate; **BACE** = Balloon-Assisted Coil Embolization; **CARAT** = Cerebral Aneurysm Rerupture After Treatment; **CLARITY** = Clinical and Anatomical Results in the Treatment of Ruptured Intracranial Aneurysms; **DSA** = Digital Subtraction Angiography; **EVT** = endovascular treatment; **FDDs** = Flow Diverter Devices; **FRED** = Flow-Redirection Endoluminal Device; **GCS** = Glasgow Coma Score; **GDC** = Guglielmi Detachable Coil; **IA** = intracranial aneurysm; **IPH** = Intraparenchymal Hemorrhage; **ISAT** = International Subarachnoid Aneurysm Trial; **MR** = Magnetic Resonance; **PAASH** = Prognosis on Admission of Aneurysmal Subarachnoid Haemorrhage; **PAO** = Parent Artery Occlusion; **PED** = Pipeline Embolization Device; **SACE** = Stent-Assisted Coil Embolization; **SAH** = subarachnoid hemorrhage; **SFD** = Silk Flow-Diverter; **TIA** = Transient Ischemic Attack; **UIAs** = unruptured intracranial aneurysms; **UIATS** = Unruptured Intracranial Aneurysm Treatment Score; **WEB** = Woven Endobridge; **WFNS** = World Federation of Neurological Surgeons Scale;

Resumo

Contexto e finalidade: O tratamento endovascular de aneurismas intracranianos desenvolveu-se substancialmente nas últimas duas décadas. A finalidade desta revisão é avaliar alguns dos determinantes com maior impacto no resultado clínico com o objectivo de dar projeção a um ponto da situação conciso no tratamento endovascular.

Métodos: Efetuou-se uma revisão ampla da literatura desde 1968 a 2016, registando os fatores relevantes que contribuíram para o prognóstico relativamente à abordagem endovascular dos aneurismas intracranianos.

Resultados: Tanto a gradação do PHACES como a gradação do Tratamento do Aneurisma Intracraniano sem ruptura têm limitações e precisam de mais avaliação. Tem sido recomendado o uso do PAASH em detrimento da escala WFNS, que é a mais frequentemente usada. O Tratamento de doentes admitidos mais do que 72 horas depois da hemorragia pode ser adiado se for baixo o risco de novo sangramento. O protocolo preferido deverá ter o enfoque numa ressuscitação e estabilização prévias seguidas de uma transferência segura em vez do paradigma de uma transferência hiperaguda. Complicações tromboembólicas e taxas de ruptura intraoperatória associadas ao coiling foram 7.3 % e 2.0 % em aneurismas não-rotos e 13.3% e 3.7% em aneurismas rotos. Coiling assistido por balão permite uma densidade de empactamento do coil optima,

particularmente no colo e fundo dos aneurismas. O Pipeline Embolization Device está associado a uma taxa de oclusão alta e a uma taxa de eventos adversos comparáveis a técnicas mais convencionais. A durabilidade e a segurança do Surpass Flow Diverter e do Flow-Redirection Endoluminal Device necessitam de comprovação por estudos amplos e de seguimento prolongado. Resultados iniciais do Woven Endobridge mostram taxas de oclusão completa e adequada de 27% e 59% respectivamente, que aumentam significativamente no seguimento a 7 meses.

Conclusões: Dado o desenvolvimento das novas tecnologias no tratamento dos aneurismas intracranianos, o campo da intervenção neurovascular está em clara expansão. São essenciais ensaios suplementares, randomizados e controlados, para uma avaliação adequada dos resultados.

Introduction

We have bare witness, in the past couple of decades, to the astonishing evolution of the endovascular treatment (EVT) of intracranial aneurysms (IAs), from a promising new technology to a front-line therapy based on advanced disease and anatomy-specific devices enabling a minimally invasive approach. These devices have themselves undergone profound changes transitioning from embolization coils to other implantable devices, adjunctive intracranial stents and ultimately to “stand-alone” stent-like devices (David Fiorella, 2008). Alongside these changes, new techniques (such as 3D angiography) and improvements in navigation and occlusion materials have enabled endovascular therapists to treat increasingly difficult, complex-shaped and wide based aneurysms, improving safety, efficacy and feasibility of EVT (Mitsos et al., 2013). The paradigm of treatment has shifted through time from techniques targeting merely the occlusion of the aneurysm sac to those designed also to achieve a durable physiological reconstruction of the parent vessel. Conversely, due to this relative infancy of EVT, a great deal of important questions remain to be answered, particularly regarding long term clinical outcome (Currie et al., 2011). This review intends to elaborate on some of the most important and influential issues relevant to the EVT clinical outcome, sanctioning a clearer decision making and a more concise understanding of the capability and limitations of this treatment modality.

Methods

A comprehensive review of the literature from 1968 to 2016 was performed, reporting on relevant contributing factors related to endovascular approach of IAs. A total of 114 articles, all in the English language, were included base on relevance using PubMed, MEDLINE, Embase and b-on (Online Knowledge Library) search engines. For the search strategy, the keywords " endovascular", "treatment", "Intracranial", "aneurysms", "embolization", "LUNA", "BACE", "unruptured", "ruptured", "timing", " coil", "stent", "FRED", "surpass", "PED", "Woven Endobridge", "silk", "disrupter", "diverter" with combinations and synonyms were used. "Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals (ICMJE 2015)" were taken into consideration.

Management

Management of IAs relies heavily on the correct assessment of the lesion since different types may require drastically different treatment methodologies. IAs can thus be broadly subdivided into two main approach categories: ruptured (associated with subarachnoid hemorrhage [SAH], intraparenchymal hematoma and an intraventricular hemorrhage) and those that remain unruptured (David Fiorella, 2008).

Unruptured Intracranial aneurysms

Through autopsy exams and catheter angiography, unruptured intracranial aneurysms (UIAs) have been known to exist for quite some time, but their true prevalence has only begun to emerge more recently with the widespread use of non-invasive angiograms (Rabinstein, 2013). A recent systematic review and meta-analysis reported on 83 population studies including 1450 UIAs in 94 912 patients from 21 countries. The overall prevalence in a population without comorbidity, with a mean age of 50 years, and consisting of 50% men was estimated to be 3.2% (Vlak et al., 2011). Despite generally being asymptomatic until rupture, UIAs can manifest as they grow and cause compression of adjacent brain structures. Middle cerebral artery aneurysms are known to cause hemiparesis, visual field defect, or seizures; posterior communicating artery or basilar artery aneurysms may lead to third cranial nerve palsy;

cavernous sinus aneurysms can trigger a cavernous sinus syndrome, and basilar aneurysms at times compress the brainstem. Rarely can embolus from the aneurysmal sac cause transient ischemic attack or cerebral infarction due to distal embolization (Ajiboye et al., 2015). The rational to treat an UIA is to prevent the rupture and its consequences as well as to address the symptoms; however, the indications to treat an UIA are complicated by limitations in our current knowledge of their natural history. Age and life expectancy of the patient, estimated risk of rupture, risk of complications attributed to the preventive treatment, and the level of anxiety caused by the awareness of having an aneurysm are critical aspects when considering UIA treatment (Etminan et al., 2016).

The PHACES score is a model developed to aid the prediction of the risk of rupture of incidental intracranial aneurysms (Greving et al., 2014). Based on prospectively collected data from 6 cohort studies on risk of UIA rupture, it entails absolute risk of rupture for the first five years after initial aneurysms detection using both patient related predictors (age, hypertension, history of subarachnoid haemorrhage from another aneurysm and geographical region) and aneurysm related predictors (aneurysm size and location). Individual patient data from 8382 participants was systematically reviewed and submitted to pooled analysis with subarachnoid haemorrhage as outcome (230 had a subarachnoid haemorrhage during follow-up). Predictors were assessed with Cox proportional-hazard regression analysis, and cumulative rupture rates were analyzed with Kaplan-Meier curves/survival analysis. The mean observed one-year risk of aneurysm rupture was 1.4% and the five-year risk was 3.4%. Sex, smoking status at time of aneurysm detection, and presence of multiple aneurysms had limited predictive value on risk of rupture. The estimated five year absolute risk of aneurysm rupture, when studying populations from North America and Europe (Finland excluded), ranged from 0.25% in younger patients (<70 years old) with small-sized (<7mm) internal carotid artery aneurysm and no vascular risk factors associated, to over 15% in older patients (≥70 years of age) with hypertension, giant-sized aneurysms (20mm) of the posterior circulation with a history of subarachnoid haemorrhage. Finnish people had a 3.6-times increased risk of aneurysm rupture by comparison with populations from other European countries and North America, while Japanese people had a 2.8-times increased risk (Greving et al., 2014). This prediction score had, however, significant limitations. Some subgroups may have been underrepresented, such as familial aneurysms patients or young smokers. Limited long-term follow up makes it so that the applicability of the score cannot go beyond the initial 5 years after UIA detection. Moreover, some known or suggested to be risk factors (e.g.: cigarette smoking; drug or alcohol use; clinical or radiologic signs of mass effect (Nima Etminan et al., 2015; Matsumoto et al., 1999)) for UIA rupture in case-control studies could not be included in the PHACES score, not because they were not important risk factors for aneurysm rupture in isolation, but because these factors had no added value to the prediction of aneurysm rupture beyond the six predictors already used in the risk score. Finally, a clinician recommendation for treatment should also take into consideration the inherent risk of the intervention itself, which is not accounted for in the PHACES score (N. Etminan et al., 2015; Greving et al., 2014).

These predictive restrictions in the PHACES score and the high level of variation among clinicians about the individual management of UIA patients laid grounds for alternative and newer treatment scores, such as the UIATS (Unruptured Intracranial Aneurysm Treatment Score) (N. Etminan et al., 2015). The aim was to objectively quantify consensus data on factors which, taken into consideration by specialists, are relevant for proper UIA management and to achieve agreement on UIATS based recommendations amongst specialists. Key factors for clinical decision making regarding UIA management were developed based on relevance rating data using the Delphi method and are sub grouped and risk scaled in correlation to the aneurysm, to the patient and to the treatment modality. To calculate a management recommendation for an UIA, the number of points corresponding to each patient, aneurysms or treatment related feature on both management columns of the scoring form (labeled “in favor of UIA repair” and “in favor of UIA conservative management”) is added up. A numeric difference between these two columns of three points or greater should indicate an individual management recommendation (either aneurysm repair or conservative approach); Cases that have similar aneurysm treatment and conservative management scores (two or less points in difference) have a “not definite recommendation” and both approaches could be supported by additional factors not included in the development of UIATS. This model merits to include many different important decision making factors disregarded in previous observational studies, such as young age or life expectancy, coexistent modifiable or nonmodifiable risk factors, coexistent morbidities, morphologic UIA features or relevance of clinical symptoms related to UIAs (N. Etminan et al., 2015). This treatment score also has its limitations. First, it requires more baseline characteristics than the PHASES score and therefore its applicability is marginally more time consuming. Second, the consensus derived data used in this UIATS, which includes some subjective contributions from experts experience, does not replace evidence and should rather be seen as a way to complement it. Third, the "population" of specialists used to elaborate this score could hardly ever be claimed to be representative of the general "community of UIA experts". Finally, pooled data from meta-analysis was incorporated to define treatment risk percentages into this model which may uncover deviation results due to surgeons or neuroradiologists experience or even treatment modality. UIATS model remains to be prospectively tested with empirical data regarding its applicability and clinical accuracy (N. Etminan et al., 2015).

Ruptured Intracranial Aneurysms

The rupture of an IA is a diagnostic and therapeutic emergency almost always treated, provided that the patient is neurologically and physiologically well enough to undergo the procedure. Management entails a multidisciplinary team of neuroradiologists, neurosurgeons and neurology intensive care physicians (Anxionnat et al., 2015). Spontaneous subarachnoid hemorrhage (SAH) is a devastating event triggered by rupture of an intracranial aneurysm in 80%–90% of cases; it entails significant morbidity and mortality and causes serious systemic and neurologic complications. Rebleeding is the most severe complication in terms of mortality and morbidity and also the most prevalent with up to 80% incidence rate (Kirkpatrick, 2002; Rivero Rodríguez et al., 2014). The mortality for untreated aneurysmal SAH is as high as 50%-60% in the first months, primarily because of rerupture (Westerlaan et al., 2011). Within 6 months, from those patients who recover from the first bleeding episode, roughly one third left with an untreated aneurysm will die from recurrent bleeding (Steiner et al., 2013).

Patient Assessment

Neurological condition of the patient on admission, age, and the amount of extravasated blood seen on CT scans are the three main variables contributing the most to aneurysmal SAH clinical outcome. The level of consciousness evaluated within the neurologic condition is the most influential determinant for SAH clinical outcome, and since neurologic condition is likely to evolve during clinical course after a SAH, a reliable and valid grading system enabling unequivocal and understandable documentation is of the outmost importance (Steiner et al., 2013). Developing scales to clinically grade patients with SAH and measure the severity of initial neurological injury, providing prognostic information regarding outcome, guiding treatment decisions, and standardizing patient assessment across medical centers, has been an imperative and demanding task (Rosen et al., 2005). Most grading scales translate an attempt to convert a qualitative impression of SAH severity into a quantitative measurement with the purpose of early prognosis estimation. With this background, several grading systems have been proposed, such as the Fisher Scale, the Hunt and Hess Scale, the Glasgow Coma Score (GCS), and the World Federation of Neurological Surgeons (WFNS) Scale (Fisher et al., 1980; Hunt et al., 1968; "Report of World Federation of Neurological Surgeons Committee on a Universal Subarachnoid Hemorrhage Grading Scale," 1988; G. Teasdale et al., 1974). The Fisher Scale is based on the relationship between the amount and distribution of subarachnoid blood detected by computerized tomography and the later development of cerebral vasospasm (Fisher et al., 1980) (Annex table 1). Clinical assessment and grading of SAH severity is most commonly determined using either Hunt and Hess classification or the (WFNS) scale (D'Souza, 2015) (Annex table 2 and 4). Delaying intervention and proceeding with conservative therapy until the patient's condition spontaneously improves to a more favorable grade has been advocated for high grade Hunt and Hess patients because of their poor prognosis (Bracard et al., 2002; G. M. Teasdale et al., 1988). However, Hunt and Hess scales reliability and validity have shown issues related to the unclear definition of neurological status. A committee of the WFNS, recognizing the advantage of a reasonable inter-observer agreement provided by the GCS, proposed a grading scale of five levels, essentially based on the GCS, with focal deficits making up one extra level for patients with a GCS of 14 or 13 (Steiner et al., 2013) (Annex table 3). The initial clinical presentation of patients with SAH is presumed to be the most significant predictor of the final outcome. Within this new system, WFNS high grades remained strongly predictive for extremely poor outcome. Acute interventional therapy of patients with high grade WFNS, by reason of a poor predetermined prognosis, is frequently delayed until any spontaneous improvement, with or without an external ventricular drainage (Wostrack et al., 2013). Another grading scale, the Prognosis on Admission of Aneurysmal Subarachnoid Haemorrhage (PAASH), based solely on the GDS, showed good prognostic value for patient outcome and an even better gradual increase in the proportionate distribution of patients with poor outcome per each increasing PAASH grade than the WFNS scale (van Heuven et al., 2008) (Annex table 5). This led the European Stroke Organization Guidelines for the Management of Intracranial Aneurysms and Subarachnoid Haemorrhage to make a recommendation for the use of PAASH in detriment to the most frequently used WFNS scale (Steiner et al., 2013).

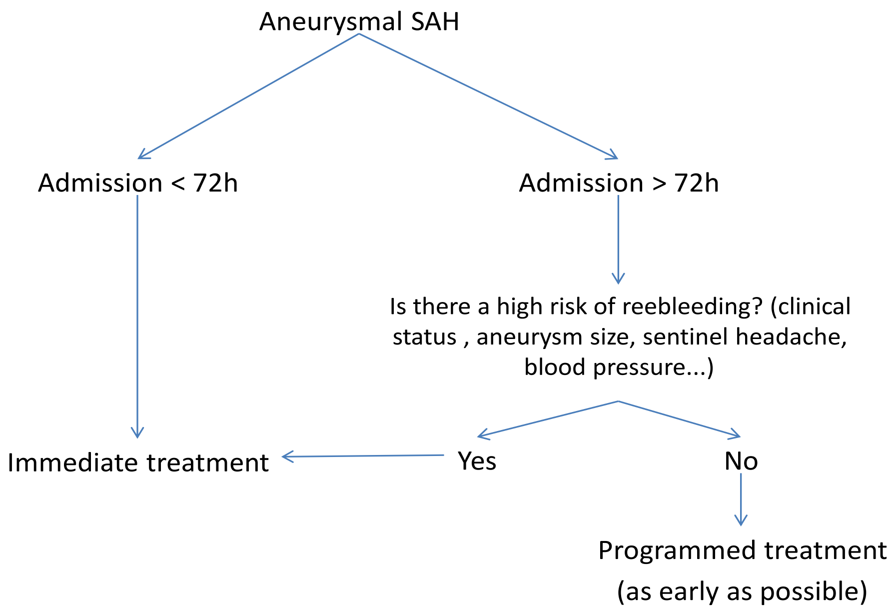
Table 1 - Summary of Relevant Prognostic Factors in ruptured aneurysms

Factor	Purpose	Correlation according to grading	Class of Evidence Or Suggested Power	Overall inter-rater reliability – (κ)	Evaluated signs (assumed as signs of SAH)	Reference
Hunt and Hess Scale	- Aid neurosurgeons in deciding on the appropriate time after SAH at which the patient should be operated on - Assess the severity of SAH	The higher the grade, the poorer the prognosis	N/A	0.42	- intensity of meningeal inflammatory reaction - severity of neurological deficit - level of arousal	Rosen et al., 2005
Fisher Scale	- Predict cerebral vasospasm after SAH	The higher the grade, the poorer the prognosis	4	0.90	- blood visualized on initial computed tomography (CT) scanning	Rosen et al., 2005
Glasgow Coma Score (GCS)	- grading level of consciousness	The lower the grade, the poorer the prognosis		0.69	- eye opening - verbal response - motor response	Rosen et al., 2005
World Federation of Neurological Surgeons Scale (WFNS)	- Include five grades - Be based on the GCS - Acknowledge the presence of a focal neurological deficit	The higher the grade, the poorer the prognosis		0.60	- eye opening - verbal response - motor response - presence of a focal neurological deficit	Rosen et al., 2005
PAASH	- Group GCS grades in order to better assess SAH prognosis	The higher the grade, the poorer the prognosis	N/A	0.64	- eye opening - verbal response - motor response	Steiner et al., 2013

* κ = 1 corresponds to complete agreement between raters, and a κ = 0 corresponds to no agreement between raters (κ values are often reported to measure the inter-rater reliability of grading systems or of various diagnostic tests.

Treatment timing

After patient assessment, it is imperative to occlude the aneurysm promptly given the recurrence risk. Despite the promising results obtained with the endovascular treatment of ruptured intracranial aneurysms, reliable data is still scarce on the effects of the timing of this approach on clinical outcome (Consoli et al., 2013). Although recurrent hemorrhage can occur at any time after the initial SAH in patients with both good and poor clinical grades, the incidence of a recurrent hemorrhage is highest within 24 hours of SAH and increases with the severity of the clinical grade (Park et al., 2015). Nonetheless, in a series consisting of 510 patients (167 M, 343 F; mean age 56.45 years) with 557 ruptured intracranial aneurysms, hyper-early timing (<12 hours) of the neuro-interventional procedure was not significantly related to a good clinical outcome. In fact, it seemed to show an inverse correlation with a good clinical outcome (Consoli et al., 2013). Another study aiming to elucidate the effect of treatment timing on procedural clinical outcomes, compared two groups of patients treated before (early approach) and after 48h, concluded that EVT should be performed as quickly as possible, without considering the latency between the onset of symptoms and the time of arrival at the hospital, given the fact that it did not increase the peri-procedural morbidity and reduced the risk of pre-treatment rebleeding (Baltsavias et al., 2000). In another study published in 2011, two groups of patients treated before (ultra-early treatment) and after (early treatment) 24 hours, presented results showing better outcome at six months in the ultra-early approach group (within 24 hours) (Phillips et al., 2011). Because the advantages of ultra-early treatment are still controversial and currently we have not reached a consensus on this issue, guidelines propose aneurysms should be occluded promptly, within 72 hours and if possible 48 hours (Anxionnat et al., 2015; Matias-Guiu et al., 2013; Oudshoorn et al., 2014). The treatment of patients admitted more than 72 hours after haemorrhage can be delayed, if the estimated risk of rebleeding is low, but it should be done always as early as possible and never more than 10 days (Dorhout Mees et al., 2012; Matias-Guiu et al., 2013).



(Matias-Guiu et al., 2013)

Treatment Centers

Admission and treatment in low versus high-volume hospitals has been considered to be an important aspect in optimizing care for SAH patients. Higher volume tertiary/quaternary specialized centers allow rapid access to specialized treatment improving clinical outcome and reducing mortality (Nuno et al., 2012; Wilson et al., 2015). Even though recommendations have been made so that low-volume hospitals consider transferring patients with SAH to higher volume centers with specialized services, there is currently a wide variance in transfer practices between institutions owing to the uncertainty related to optimal time frame for transfer and to the absence of specific recommendations to guide the process. Complications derived from delayed transfer include a higher risk of secondary brain injury from hemodynamic and respiratory compromise outside of an intensive care unit, rebleeding and delayed implementation of appropriate neurosurgical treatment. A retrospective cohort study was performed to determine how transfer time and subarachnoid grade would affect the occurrence of symptomatic vasospasm, functional outcome, and mortality of transferred patients versus directly admitted patients. Transfer time was concluded not to be associated with the occurrence of symptomatic vasospasm, 12-month outcome, rebleeding, or 12-month mortality, which seems to agree with studies suggesting that ultra-early treatment does not appear to be beneficial (Oudshoorn et al., 2014; Wilson et al., 2015). Thus, factors related to the acute to subacute management of SAH may play a more important role than the hyperacute management in terms of overall prognosis of high-grade patients. Early resuscitation and stabilization followed by safe transfer rather than a hyperacute transfer paradigm should be the preferred protocol; nevertheless, transfer time ought to be minimized as much as possible with a goal of less than 8 hours, so that time to definitive treatment is not delayed (Wilson et al., 2015).

Therapeutic modalities

Coiling

Guglielmi and his co-workers started, in 1991, a new era in the EVT of ruptured IAs with the introduction of an electrically detachable coil system (GDC – Guglielmi Detachable Coil) which was pushed into the aneurysm sac through a microcatheter, repositioned, retrieved, or replaced by different sized coil until an acceptable result was achieved (Guglielmi et al., 1991). Initially, endovascular techniques were used for aneurysms considered inoperable or in patients whose previous surgical treatment had failed (Guglielmi et al., 1992). Since the first GDCs and platinum detachable coils, the standard coil embolization techniques have been developed much further resulting in greater number of patients being managed with endovascular coiling (Shin et al., 2015). Initial large series showed acceptable mortality (≈2%) and morbidity (between 4% and 9%) (Cognard et al., 1998; Vinuela et al., 1997). Subsequent larger series came to confirm feasibility of aneurysm coiling (96.9% in ruptured aneurysms and 94.0% in unruptured aneurysms) along with acceptable procedural mortality (1.4% in ruptured aneurysms and 1.7% in unruptured aneurysms) and morbidity rates (8.6% in ruptured and 7.7% in unruptured aneurysms) (Gallas et al., 2008; Gallas et al., 2005).

The publication of the International Subarachnoid Aneurysm Trial (ISAT) demonstrated improved one-year clinical outcomes for patients with ruptured intracranial aneurysms treated with endovascular coiling compared to surgical clipping (A. Molyneux et al., 2002). The trial showed that for 2,143 SAH patients eligible for both surgery and endovascular coiling, recruited between 1994 and 2002, randomized allocation to coiling was associated with better one-year clinical outcomes defined as survival without dependency, demonstrating that coiling should be adopted as the first-line treatment for ruptured aneurysms, at least for patients with the types of lesions included in the ISAT (Darsaut et al., 2013). The management of unruptured intracranial aneurysms (UIA), however, remains challenging. In untreated patients, the risk of aneurysm rupture is multifactorially mediated and has to be weighed against the risk associated with preventive aneurysm obliteration consisting of either microsurgical clipping (MS) or endovascular aneurysm occlusion (Brundl et al., 2016). Although for unruptured aneurysms (UIA) a direct comparison between EVT and surgery is not yet available, EVT has also been widely used in this subgroup (L. Pierot et al., 2013).

Two large, prospective, multicenter series were conducted in order to analyze thromboembolic complications and intraoperative rupture (the two most frequent aneurysm coiling complications), in ruptured aneurysms (Cognard et al., 2011) and unruptured aneurysms (Laurent Pierot et al., 2008). Laurent Pierot presented the unruptured aneurysms series showing thromboembolic complications and intraoperative rupture rates associated with coiling alone of 7.3% and 2.0% respectively. For both specific complications, no clinical worsening was observed in approximately half the cases, but the mortality rate was higher after intraoperative rupture (16.7%) than after thromboembolic complications (4.1%) (L. Pierot et al., 2013). In ruptured aneurysms, the rates of thromboembolic complications and intraoperative rupture were as high as 13.3% and 3.7%, respectively (Cognard et al., 2011). Intravenous heparin for anticoagulation and aspirin as an antiplatelet agent have been adopted for unruptured aneurysms and, in some cases, also for ruptured aneurysms because thromboemboli are the most frequent complication associated with aneurysm coiling (L. Pierot et al., 2013).

As experience developed, evidence came to light demonstrating crucial challenges presented to coiling EVT. First and foremost the unfavorable shape of the aneurysm made them very difficult to treat, particularly large neck aneurysms, fusiform aneurysms, large and giant aneurysms and aneurysms with unfavorable size relationship between aneurysms dome, neck and parent artery. Soon new technologies and techniques developed in order to better address this issue, including balloon-assisted coiling (known as the remodeling technique), aneurysm coiling supported by stenting and more recently the introduction of flow diversion or disruption. Recanalization also became a great challenge to aneurysm coil embolization reducing its durability. Since aneurysms are due to plastic deformation of vessel wall and its underlying factors are not just operational at the sac but also around the neck region, recurrences following EVT are not unlikely. In 2009, a systematic review of forty-six studies including 8161 coiled aneurysms was published reporting a recanalization rate of 20.8% and a performed retreatment rate of 10.3% (Ferns et al., 2009). Although recanalization and regrowth are often used interchangeably, recanalization means the opening of the previously embolized aneurysms. In recanalized cases, the aneurysm sac has the same size, but the coils have been displaced from the neck. Even in densely packed aneurysms, coils can only occupy about 30% of the sac volume, leaving the rest of the volume to be filled by cloth. Hemodynamic stress can then press the coil mass towards the dome leaving the neck region exposed and vulnerable to the blood flow once again. Regrowth, on the other hand, implies that the aneurysm size has become larger and the coil mass is no longer sufficient to occlude it (Islak, 2013). ISAT trial results showed that only about 66% of coiled aneurysms achieve complete occlusion at the end of the treatment and those incompletely embolized convey a greater concern for retreatment (A. Molyneux et al., 2002; A. J. Molyneux et al., 2005). For over 10 years, packing coils as tightly as possible has been reported to be crucial in order to avoid recanalization. However, residual volume after coil embolization, which is a composite variable of packing density and aneurysm volume, has been demonstrated to be the most influential risk factor for recanalization (Sadato et al., 2016). The goal of embolization should not be established as a fixed value for packing density because the larger the aneurysm volume, the greater the packing density needs to be in order to minimize the residual volume and the risk of recanalization (Sadato et al., 2016). Surface modified coils have also been developed as an effort to reduce the recanalization rate, including polyglycolic-lactic acid coils and Hydrocoils (Microvention, Tustin, CA) but large multicenter series have shown that they were not more efficacious than bare platinum coils (L. Pierot et al., 2008; White et al., 2011; White et al., 2008). The clinical significance of aneurysm recanalization is still not entirely understood. Early rerupture of treated aneurysms occurs more frequently than delayed rerupture and has major clinical consequences. The Cerebral Aneurysm Rerupture After Treatment (CARAT) study established the degree of aneurysm occlusion after the initial treatment as a strong predictor of the risk of subsequent rupture in patients presenting with subarachnoid hemorrhage (SAH), therefore justifying attempts to completely occlude aneurysms (Johnston et al., 2008). Anatomical follow-up with digital subtraction angiography (DSA) and magnetic resonance (MR) imaging became mandatory as surveillance for the risk of aneurysm recanalization (L. Pierot et al., 2006; L. Pierot, Portefaix, et al., 2012).

Balloon-Assisted Coil Embolization (BACE)

Wide necked aneurysms or unfavorable anatomic conditions (e.g., access or parent vessel tortuosity or vessel angulation) can be technically challenging for conventional EVT of IA. Coils deployed without supporting devices may herniate from the aneurysmal sac into the parent artery, causing thromboembolic complications or vessel occlusion. The effort to overcome these difficulties has brought alternative strategies such as stent-assisted coil embolization (SACE) and balloon-assisted coil embolization (BACE; also known as remodeling technique). BACE, as it has been initially described by Moret, allows for optimal coil packing particularly in the aneurysm neck and fundus (Moret et al., 1997). A nondetachable balloon is temporarily inflated in front of the neck of the aneurysm during each coil placement (L. Pierot, Cognard, et al., 2012). In sidewall aneurysms, the balloon is simply placed in the parent vessel in front of the aneurysm neck. As for bifurcation aneurysms, a more complex approach is required and multiple options are available: using 2 balloons, a hyper-compliant balloon, a round shaped balloon, or even using a double lumen balloon. When the procedure is over, the balloon is deflated and removed, and no extra-aneurysmal device is left in place unless a stenting is subsequently performed (L. Pierot et al., 2013). Some retrospective, single center studies have reported an increase in mortality associated with BACE or a trend towards a higher thromboembolism complication rate (Sluzewski et al., 2006; van Rooij et al., 2006). The rates of thromboembolic events and intraoperative rupture were higher in the BACE group (9.8% and 4.0%, respectively) as compared with the coiling alone subgroup (2.2% and 0.8%, respectively). However, these concerns could not be reproduced by several larger, more recent studies and literature reviews. In fact, two large multicenter prospective series using BACE in both ruptured (Clinical and Anatomical Results in the Treatment of Ruptured Intracranial Aneurysms [CLARITY]) and unruptured (Analysis of Treatment by Endovascular approach of Non ruptured Aneurysms [ATENA]) aneurysms, re-evaluated the complication rates comparing BACE to coiling alone (Laurent Pierot et al., 2011; L. Pierot et al., 2009). In ruptured aneurysms the rate of thromboembolic events was similar in both groups (12.7% in the coiling group and 11.3% in the BACE group) and a similar result was reported for the rate of intraoperative rupture (4.4% in both groups). The treatment morbidity was 3.9% in the coiling group and 2.5% in the BACE group, and treatment mortality 1.2% in the coiling group and 1.3% in the BACE group (Laurent Pierot et al., 2011). As for the unruptured aneurysms, ATENA showed that the rate of thromboembolic events was not higher in the BACE group as compared with coiling alone (5.4% versus 6.2%) with similar clinical outcome in both groups. The rate of intraoperative rupture was 3.2% in the BACE group and 2.2% in the coiling alone group, with clinical worsening (permanent deficit or death) in 0.6% in the coiling group and 1.4% in the BACE group. The treatment morbidity was 2.2% in the coiling group and 2.3% in the BACE group, whereas treatment mortality was 0.9% in the coiling group and 1.4% in the BACE group (L. Pierot et al., 2009).

Table 2 - Ruptured Intracranial Aneurysms (CLARITY)

Complications	**Coiling (%)**	**BACE (%)**
Rate of Thromboembolic Events	12,7	11,3
Rate of Intraoperative Rupture	4,4	4,4
Morbidity	3,9	2,5
Mortality	1,2	1,3

Table 3 - Unruptured Intracranial Aneurysms (ATENA)

Complications	**Coiling (%)**	**BACE (%)**
Rate of Thromboembolic Events	6,2	5,4
Rate of Intraoperative Rupture	2,2	3,2
Morbidity	2,2	2,3
Mortality	0,9	1,4

In a literature review, anatomic results were better with BACE (Shapiro et al., 2008). Postoperatively, a total occlusion was observed in 73% of patients in the BACE group and in 49% of patients treated with coiling alone. At follow-up, similar results were observed. A total occlusion was observed in 72% of patients using BACE and in 54% of patients treated with coiling alone. The Cerebral Aneurysm Rerupture after Treatment trial suggested that the rate of early repeat bleeding is directly related to the degree of postoperative aneurysm occlusion (Elijovich et al., 2008; Laurent Pierot et al., 2011). Pierot published results showing a significantly higher adequate occlusion rate in the remodeling group compared to the conventional coil embolization group (94.9% versus 88.7%) despite the less favorable anatomic characteristics of aneurysms treated with BACE (Laurent Pierot et al., 2011). In the ATENA series (unruptured aneurysms only), postoperative anatomic results were not better in patients treated with BACE (L. Pierot et al., 2009).

BACE, initially developed to better address the treatment of wide-necked aneurysms, has shown in recent series that in the setting of intraoperative rupture, balloon assistance was associated with a higher probability of unchanged or improved clinical outcome as compared with standard coiling (Santillan et al., 2012). In this retrospective analysis it is suggested that balloon assistance should not only be used as an enabler to coiling but could also be helpful in obtaining rapid hemostasis if intraprocedural aneurysmal rupture occurs resulting in better short-term outcomes. The balloon stays deflated across the neck of the aneurysm and is inflated only in case of intraoperative rupture. Perhaps because of this sentinel property, a steady increased over time use of the remodeling technique has been reported in the period between 2008 and 2010. BACE was used in a similar percentage of cases independent of aneurysm characteristics (aneurysm status, location, size, and neck size), except dome-to-neck ratio (L. Pierot, Rajpal, et al., 2012).

<u>Stent-Assisted Coil Embolization</u>

Stent-assisted coil embolization (SACE) was introduced over ten years ago to overcome some limitations of standard coiling alone particularly concerning the treatment of some complex aneurysms, including those with low dome-to-neck ratios and those with wide necks (Beller et al., 2016). Preventing coil prolapse and allowing higher packing density are benefits attributed to SACEs mechanical effects, but flow diversion may also contribute to potential hemodynamic effect. Stent struts can directly reduce flow velocity and also have a relevant role straightening the vessels-aneurysm complex (Kono et al., 2014). Initially conceived for the treatment of sidewall aneurysms, with gained experience and further technical refinement, bifurcation complex-shaped wide-neck aneurysms have successfully been treated with SACE (Piotin et al., 2014). The development of low-profile stents is a further interesting evolution that allows for the association of both BACE and SACE (Kadziolka et al., 2013). Different stent-placement methods have allowed treatment of a subset of wide necked aneurysms not amenable to reconstruction with a single stent due to anatomical conformation. Y-stent reconstruction is an example of one of these methods, indicating that a second stent is advanced through the first stent interstices and into the contralateral branch vessel, enabling a variety of complex aneurysms to be treated with SACE safely and with satisfactory mid-term results (Spiotta et al., 2011).

Risk of implant thrombosis is higher in SACE than with coiling alone since stents are implanted in the parent artery, bridging the aneurysm neck. Acute SAH is a hypercoagulable state in which the tendency for thrombosis is high and the insertion of an endovascular stent induces an even higher risk of parent vessel occlusion, thus making antiplatelet therapy during and after the procedure mandatory (L. Pierot et al., 2013). Presently, in the setting of SAH, most operators are reluctant to use antiplatelet therapy because of the potential need for a ventriculostomy, the potential for infarction secondary to vasospasm, and the high likelihood of future invasive interventions (in which antiplatelet therapy may be anticipated as harmful). This is the main reason why stent placement is generally avoided in acutely ruptured aneurysms in favor of clip ligation or other endovascular techniques that do not mandate dual antiplatelet therapy (Bechan et al., 2015). Though this initially limited SACE to unruptured aneurysms, gaining experience during the past years has extended its use towards ruptured aneurysms (L. Pierot et al., 2013; Tahtinen et al., 2009). Intracranial stents are considered to be thrombogenic until they are covered by endothelium with reacquired normal intrinsic fibrinolytic activity. Stent deployment in unruptured intracranial aneurysms usually requires pre- and post-procedural treatment with clopidogrel and acetylsalicylic acid; however, these drugs are contraindicated in cases of acute SAH and nonsecured aneurysm. Perioperative infusion of acetylsalicylic acid has been shown effective at reducing thromboembolic events rate without increasing the intraoperative bleeding rate, thus being advocated in the EVT of aneurysms, including during acute SAH (Tahtinen et al., 2009).

The safety and efficacy of SACE as compared with standard coiling has been evaluated in few and mostly retrospective single-center series. Prospective, multicenter series performed and published are scarce and presently no prospective randomized clinical trials have been published comparing standard coiling with SACE.

A recent observational study with prospectively collected data found that the symptomatic complication rate with early adverse events of SACE in patients with ruptured aneurysms was very high and 10 times higher (22% versus 2.2%) than that in stent-assisted coiling of unruptured aneurysms (Bechan et al., 2015). Mortality was attributable mostly to early rebleed and in addition, ruptured aneurysms patients treated with SACE also underwent fatal hemorrhagic complications from extraventricular drain placement or even spontaneous remote intracranial hemorrhages. In ruptured aneurysms SACE was associated with increased morbidity-mortality rate (13%) prompting recommendation to consider this option only when less risky ones had been excluded (Bechan et al., 2015).

A systematic review and meta-analysis has been conducted precisely to compare SACE with coiling-only for intracranial aneurysms in terms of immediate occlusion, progressive thrombosis, recurrence, and complication profile (Phan et al., 2016). There were 14 observational studies involving 2698 SACE patients and 29388 coiling-only patients harboring ruptured and unruptured aneurysms. 12 studies reported immediate occlusion rates with no significant statistical difference in pooled immediate occlusion rates for the SACE group (57.7%) and for the coiling-only group (48.7%). For progressive thrombosis (increases in packing density on follow up) six studies reported a higher pooled progressive thrombosis rate in the SACE group (29.9%) in comparison with the coiling-only (17.5%). 10 studies reported recurrence rates showing a significantly lower likelihood of aneurysm recurrence in the SACE group (12.7%) than in the coiling-only group (27.9%). Stents divert flow away from the aneurysm sac, thus favoring stasis and thrombosis within the aneurysm and they can also provide a scaffold for endothelialization and growth of fibroelastic tissue at the aneurysm neck level.

Stented-coiling cases were frequently biased towards aneurysms with particularly wide necks (>4 mm) and low dome-to-neck ratios, which are known predictors of aneurysm recurrence, reinforcing SACEs aneurysm recurrence rates results. The pooled rate of all complications was similar in both groups (12.2% versus 12.0%) showing no significant difference. Pooled rate of permanent complications also had no significant statistical difference between groups, although it was higher in the SACE group (4.1% versus 3.5%). Thrombotic complications rate was analogous in both SACE and coiling-only groups (4.5% versus 4.1% respectively). Pooled mortality rates were significantly higher in SACE group (1.4%) compared to the coiling-only group (0.2%). Procedure-induced mortality occurred in 4.6% (10 of 216) of stent-assisted coiling versus 1.2% (13 of 1109) of coiling without stents. However, almost all studies had no significant increase in mortality for stented patients compared to coiling-only. This pooled increased risk of death might be explained not only by the significantly larger aneurysm sizes in the stented patients compared to the non-stented patients, but also by the type of stents used (balloon-expandable stents were used early in the study while self-expandable stents were not yet available). Despite stented aneurysms often having more difficult morphologies, this technique was associated with lower rates of aneurysm recurrence, higher rates of progressive thrombosis and similar complication outcomes compared to coiling-only. However, SACE was associated with a higher mortality rate (Phan et al., 2016).

Another systematic review and meta-analysis sought out to review the literature concerning SACE in comparison with coiling without stents in terms of safety and effectiveness profiles (Feng et al., 2016). 16 studies clearly reporting patient outcomes were included with a total of 4294 aneurysms. 1466 aneurysms were treated with SACE and 2828 aneurysms were addressed with conventional coiling. The mean proportion of patients with ruptured aneurysms included in the stent-assisted group was 13.14%, significantly less than in the nonstent group, which was 33.71%. Immediate occlusion rates showed no statistical significant differences between the two groups. (53.18% vs 55.59%). However, 2917 patients were subsequently analysed for follow up angiographic occlusion rate revealing a higher angiographic occlusion rate in the SACE group relative to the nonstent group (60.58% vs 36.05% respectively). Better results were also reported in the SACE group than in the nonstent group for progressive thrombosis rate (44.09% vs 22.68% respectively) and lower recurrence rate was reported (13.31% vs 29.13%). Overall complication rates showed no statistically significant difference between the two groups (11.85% versus 8.00%). 12 retrospective studies also conveyed no significant statistical difference concerning hemorrhage stroke rate in the perioperative period (2.46% versus 2.72%) but instead revealed a higher incidence of ischemic stroke in the SACE group than the nonstent group (4.68% versus 1.99%) (Feng et al., 2016).

The question remains of whether stent-assisted techniques should be systematically used for all aneurysms regardless of their morphology. Randomized controlled trials are required to answer this question (Phan et al., 2016).

Flow-Diversion

Flow Diverter Devices (FDDs) represent a recent and important effort emerging from endovascular treatment technology aimed at obtaining higher occlusion rates, decreasing recurrence and recanalization of difficult-to-treat intracranial aneurysms (IA) - wide-necked, fusiform, giant aneurysms or those with complex morphology - comparatively to more conventional endovascular techniques (F. Briganti et al., 2016; Francesco Briganti et al., 2014).

Endoluminal approach with FDDs allows reconstructive treatment and vascular remodeling for these challenging aneurysms. These new devices consist of highly dense mesh stents, placed in the parent artery at the level of the neck, reducing hemodynamic exchange with the aneurysm and thus promoting thrombosis within the aneurysm sac (Giacomini et al., 2015). The device also provides scaffolding for strong neointimal overgrowth, remodeling the parent artery and curing the neck (Giacomini et al., 2015) while preserving patency of adjacent small vessels (Francesco Briganti et al., 2014). The result seems to be a more anatomically definitive and durable treatment of the aneurysm (Becske et al., 2013). Determining the type of endovascular procedure with FDDs and its indications remains a challenging task. A great deal of variables need to be taken into account as influencing factors for occlusion, such as aneurysm size, location and morphology, parent vessel geometry, blood coagulation parameters, previously regular stent use as well as resulting flow changes (Giacomini et al., 2015).

Flow diversion can be combined with coil embolization, further expanding the treatment options (Amuluru et al., 2016). Despite the high occlusion rate obtained by FDDs techniques, the associated morbidity and mortality should not be neglected and in fact, as the popularity of such techniques grows higher, various complications inevitably appear, such as spontaneous rupture, intraparenchymal hemorrhage (IPH), ischemic stroke, parent artery aneurysm stenosis, and neurological complications (Ye et al., 2016). To date, the safety issues and efficiency of FDDs have not been fully evaluated (Zhou et al., 2016).

Flow-Diversion Devices:

Silk

In 2007, the Silk flow-diverting stent (SFD; Balt Extrusion, Montmorency, France) became the first FDD ever to enter clinical use for intracranial circulation (Amuluru et al., 2016). Silk FDD consists of 48 braided Nitinol strands offering a high-coverage mesh once expanded and is available in different diameters (2–5 mm) and lengths (15–40 mm) for the treatment of aneurysms of different sizes and in different locations (Maimon et al., 2012).

A systematic review of the published literature concerning SFD in the treatment of intracranial aneurysms, including results from eight studies, was presented by S.B. Murthy (Santosh B. Murthy et al., 2014). This review examined a total of 285 patients with 317 intracranial aneurysms, of which 87% (n=275, 95% CI: 83-90.5%) were present in the anterior circulation and the remaining 13% (n=42, 95% CI: 9.5-16.9%) were found in the posterior circulation. In terms of size, 17.7% (n=52, 95% CI: 13.3-22.1%) of aneurysms were classified as giant, 44.4% (n=130, 95% CI: 38.7-50.1%) of aneurysms were classified as large (10-24 mm) and 37.9% (n=11, 95% CI: 32.4-43.5%) were classified as small. The cumulative aneurysm occlusion rate (AOR) was 81.8% (95% CI: 77.1-86.5%) with complete occlusion in 216 aneurysms from a total of 264 aneurysms with available angiographic follow-up information at 12 months. Periprocedural complications rate was 12.5% (n=36, 95% CI: 8.7-16.3%), while the delayed complication rate was 9.9% (n=28, 95% CI: 6.4-13.4%). Ischemic (including both stroke and transient ischemic attack – TIA) and parent artery occlusion (PAO) were the most common complications, each occurring in a total of 29 (10.2%) patients.

The overall observed mortality rate was 4.9% (n=14, 95% CI: 2.4-7.4%) (Santosh B. Murthy et al., 2014).

The SFD has undergone multiple revisions since its first clinical implementation in 2008. As a result, a second generation of SFD has been developed, the Silk+ stent (Amuluru et al., 2016). According to B. Lubicz, the Silk stent has been significantly improved with the release of the Silk+ stent, which has flared ends, a higher radial force, and a higher radio-opacity (Lubicz et al., 2015). In a series of 58 patients (32 treated with Silk stent and 26 treated with the Silk+ stent) the second generation device provided better stent tolerance at the acute phase of endovascular treatment and no clinical complication was experienced both during periprocedural phase and follow-up (Lubicz et al., 2015).

Pipeline Embolization Device (PED)

In 2008, the Pipeline Embolization Device (PED; ev3/Covidien, Irvine, CA) was launched. PED is an endoluminal, self-expanding, bimetallic braided device, comprised of platinum (25%) and cobalt-nickel alloy (75%) (S. B. Murthy et al., 2016).

Three major studies have been published establishing safety profile and aneurysm occlusion rate (AOR) of PED: (1) Pipeline for Uncoilable or Failed Aneurysms: Results from a Multicenter Clinical Trial (PUFS) (Becske et al., 2013); (2) Pipeline Embolization Device for the Treatment of Aneurysms (PITA) (Nelson et al., 2011); (3) International Retrospective Study of Pipeline Embolization Device (IntrePED) (Kallmes et al., 2015). These important trials concluded that Pipeline Embolization Devices (PEDs) were associated with high aneurysm occlusion rates (AOR) and rates of adverse events comparable to those of more conventional techniques.

The IntrePED study (Kallmes et al., 2015) retrospectively evaluated 793 consecutive patients with 906 intracranial aneurysms (91% unruptured) treated with the Pipeline Embolization Device in 17 centers worldwide. Most (838 aneurysms) were located in the anterior circulation (92.5%), while 59 aneurysms were in the posterior circulation (6.5%) – no combined information on location/size was available for 9 aneurysms. 66 aneurysms (7.3%) were classified as giant, 357 aneurysms (39.8%) were large and 473 aneurysms (52.8%) were small. Median follow-up was 19.3 months with 706 (89%) of patients having follow-up of >12 months. Intraparenchymal hemorrhage

(2.4%) and ischemic stroke (4.7%) were the most common complications. The overall mortality rate was 3.8% with high heterogeneity among the groups. Patients with posterior circulation aneurysms had higher rates of neurologic mortality (10.9%) as well as patient with giant aneurysms (9.6%) or patients who presented with ruptured aneurysms (10.5%) (Kallmes et al., 2015). A recent prospective study from the same author, included 191 patients with 207 aneurysms treated with PED, established a complete occlusion rate of 75% at 8 months angiographic follow-up (Kallmes et al., 2016).

New flow diverts have been developed in order to optimize the effect on flow reduction within the aneurysmal sac while keeping the side branches (perforators) patent and thus reducing the need for additional device implementation.

Surpass

The surpass flow diverter (Stryker Neurovascular, Fremont, California) currently available in Europe, is composed of cobalt-chromium with a low porosity (metal surface area coverage of 30%); a high mesh density (20-32 pores/mm) and a self-expanding single-layer braided, tubular structure (Wakhloo et al., 2015). It comes in various diameters and lengths but its design allows the porosity to remain 70% across all Surpass sizes (Fargen et al., 2015). A prospective multicenter study, with 165 patients treated with Surpass for 190 intracranial aneurysms of the anterior and posterior circulation, concluded a clinical safety profile for these diverters comparable with that of stent-assisted coil embolization as well as a high rate of intracranial aneurysm occlusion (75%) (Wakhloo et al., 2015).

FRED (Flow-Redirection Endoluminal Device)

FRED (Microvention, Inc., Tustin CA, USA) consists of a braided self-expandable closed-cell dual-layer stent (known as “stent within a stent”) with a low-porosity inner mesh of higher pore attenuation (48 nitinol wires) and an outer stent with high porosity (16 nitinol wires (Yoshimura, 2016).

A single-center observational study has been reported to assess the clinical safety and efficacy of FRED (Mohlenbruch et al., 2015). This study included 29 patients with 34 aneurysms elected to be treated by endovascular intervention fulfilling the following registration criteria after informed consent: aneurysm fondus-to-neck ratio <2 or neck diameter >4 mm, fusiform, dissecting, or giant aneurysms. The efficacy end point was O'Kelly Marotta grading scale D (complete angiographic occlusion) immediately after procedure and at follow-up after 3 and 6 months. Primary clinical safety end point was established as the absence of death, absence of major or minor stroke, and absence of transient ischemic attack. The device was successfully placed in all patients and the primary end point of safety was reached in 26/29 (89%) of patients; in the remaining 3 patients, 1 disabling ischemic stroke and 2 minor strokes with complete recovery at follow-up were observed. Angiographic (DSA and MRA) and clinical follow-up at 3 months were available for all patients (100%) while the 6 months follow-up (MRA) was performed in 25/29 patients (86%), reaching complete occlusion in 19/34 (56%) and 22/30 (73%), respectively. Deployment of the FRED flow-diverter stent was concluded to be safe and effective for the management of difficult-to-treat or otherwise untreatable intracranial aneurysms.

Flow-Disruption Devices

Woven Endobridge (WEB)

Flow-Disruption Devices are intra-saccular braided-wire embolization devices designed to disrupt blood flow at the level of aneurysm neck–parent artery interface. Two models are available in the market: the Woven Endobridge (WEB II) device (Sequent Medical, Inc., Aliso Viejo, CA, USA) and LUNA Aneurysm Embolization System (AES) (NFocus Neuromedical, Palo Alto, California) (Klisch et al., 2011).

A recent systematic review of literature has been conducted by Ivo S. Muskens aiming at evaluating clinical outcomes of intracranial aneurysms (especially bifurcation and wide-neck aneurysms) treated with a WEB device (Muskens et al., 2016). This review included 19 papers (prospective/retrospective studies; multicenter/case-series) reporting on clinical outcome with WEB devices in 687 patients with 718 aneurysms (both ruptured and unruptured). The two most significant prospective multicenter studies in this review (WEBCAST and the French Observatory Trial) presented rates of complete aneurysm occlusion with the WEB device of 56%-52% respectively. Adequate occlusion is, however, often regarded as complete occlusion or a small neck remnant, which would increase the rate to 85%-79% respectively with this standard. No significant difference was found between ruptured and unruptured aneurysms rates in this review, but the authors state that no adequate comparison can be made due to great variability in patient characteristics and few studies reporting the use of WEB device for ruptured aneurysms (Muskens et al., 2016). Both the WEBCAST and the French Observatory Trial had limited follow-up (6 and 12 months respectively) as well as incomplete follow-up (85% and 94% respectively) (Muskens et al., 2016). Procedural aneurysm rupture was reported associated with WEB device placement in 10 patients, while thromboembolic events were reported more frequently with 71 patients (10.3% of all cases) and infarction in 8 cases (1.2% of all cases). Rebleeds were reported in just 5 patients in two studies with mean follow-up of 3.3 and 14.4 months (Muskens et al., 2016). The WEB device is potentially associated with a considerable learning curve making a practice model a necessity (Muskens et al., 2016).

S. Asnafi published the most recent systematic review and meta-analysis of existing literature on the Woven Endobridge device in the treatment of intracranial aneurysms (Asnafi et al., 2016). Fifteen uncontrolled series with 565 patients harboring 588 aneurysms (of which 127 ruptured) were included. Initial results presented a complete and adequate (complete occlusion or a small neck remnant) occlusion rates of 27% and 59% respectively that increased to 39% and 85% rates at a mean follow up time of 7 months. Again, no significant differences were found in midterm (>3 months) adequate occlusion rates between ruptured and unruptured aneurysms (85% and 84% respectively), as well as, no relevant differences in perioperative morbidity and mortality rates (4% and 1% respectively) (Asnafi et al., 2016).

Literature on the Woven Endobridge device seems to present promising results regarding safety profile and adequate occlusion rates, especially if taken into account the complexity of aneurysms treated (Asnafi et al., 2016). Further studies are needed to better assess complication rate and long term efficacy of the Woven Endobridge device in treating wide-neck and wide-neck bifurcation aneurysms (Caroff et al., 2014).

Table 4 - Summary of Relevant Technical Prognostic Factors in EVT of ICA

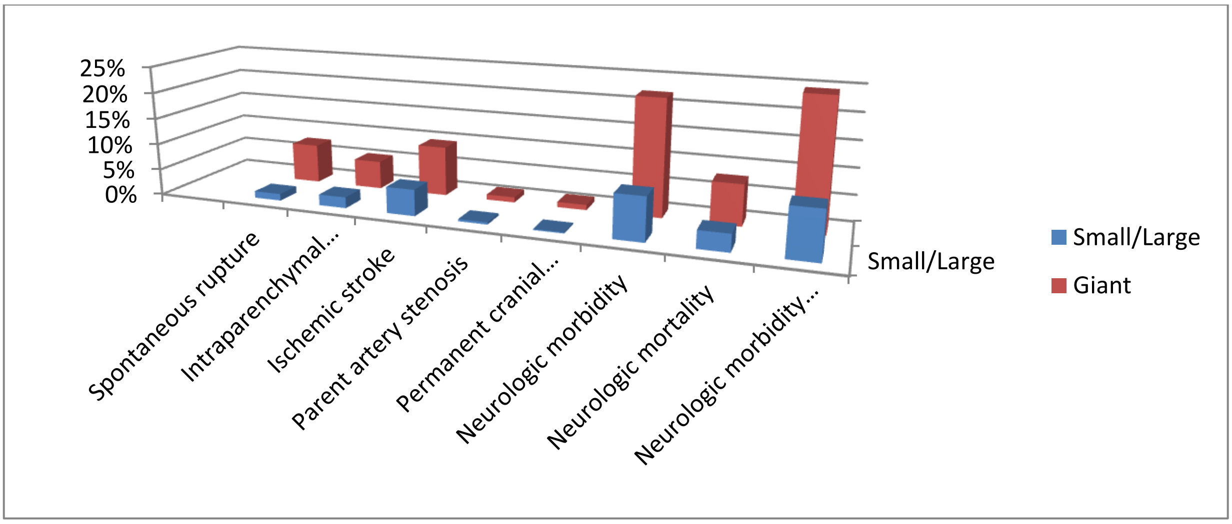
Factor	Analysed complication / Outcome measurement	Favourable / Unfavourable / Controversial / Neutral	Class of evidence Or Suggested Power	Recommendation	Commentary	Reference
Hyper-early treatment (<12h after SAH)	N/A	Unfavourable	2b	Avoid?	Single center study	(Consoli et al., 2013)
Treatment within 24h after SAH	- Degree of disability or dependence in daily activities (modified Rankin Scale)	Favourable	2b	Implement	Single center prospective study	(Phillips et al., 2011)
Early Treatment (12 to 72h after SAH)	N/A	Favourable	2b	Implement	Single center study	(Anxionnat et al., 2015) Consoli et al., 2013)
High vs Low Volume Centers	- Symptomatic vasospasm - 12-month follow up	Unfavourable	2b	- Early resuscitation and stabilization followed by safe transfer rather than a hyperacute transfer paradigm	Retrospective cohort study	Nuno et al., 2012; Wilson et al., 2015
Coiling	- Thromboembolic complications -Intraoperative rupture	- Neutral	2b		Large multicenter prospective series	Cognard et al.
Coiling (Hydrogel-coated coils)	- Thromboembolic events - (angiographic and clinical outcomes at 18 month follow-up)	- Neutral	2b		Large multicenter prospective series	White et al., 2011
Coiling (Matrix coils)	Anatomic results	Unfavourable	2b		Large multicenter prospective series	Laurent Pierot et al., 2008
BACE	- Thromboembolic events –Intraoperative rupture	Unfavourable	2b	Avoid?	Single center studies	Sluzewski et al., 2006; van Rooij et al., 2006
BACE	- Thromboembolic events - Intraoperative rupture	Neutral	2b		Large multicenter prospective series	CLARITY
BACE	- Thromboembolic events and intraoperative rupture	Neutral	2b		Large multicenter prospective series	ATENA
BACE	- Anatomic results	Favourable		Consider using		Shapiro et al., 2008
BACE	- Hemostasis if intraprocedural aneurysmal rupture	Favourable	2b	Consider using (as a safety measure)		Santillan et al., 2012
Degree of postoperative aneurysm occlusion	- Early repeat bleeding	Favourable		To increase the degree of aneurysm occlusion		Elijovich et al., 2008; Laurent Pierot et al., 2011
SACE	- Thromboembolic events - Intraoperative rupture	Favourable	2b	Consider for ruptured wide-necked intracranial aneurysms that are difficult to treat with balloon-assisted embolization	Multicenter retrospective series	Tahtinen et al., 2009
SACE	- Thromboembolic events and early reebleeds	Controversial (complication rate of SACE with early adverse events in ruptured ICA was 10 times higher than that in unruptured ICA)	2b	Ruptured ICA: avoid in favor of other surgical or endovascular treatments without the need for antiplatelet medication	Large multicenter prospective series	Bechan et al., 2015
SACE	- Thromboembolic events - Recurrence rate	Favourable	2a	Further randomized controlled trials are required	Meta-analysis	Phan et al., 2016
SACE	- Thromboembolic events and - Recurrence rate	Favourable	2a	Multicenter, randomized controlled studies are necessary to confirm	Systematic Review and Meta-analysis	Feng et al., 2016

				these findings		
Silk (Flow Diversion Device)	- Thromboembolic events - Parent artery occlusion - Intraoperative rupture	Higher incidence of complications relatively to PED	2a	Further randomized controlled trials are required	Systematic Review	Santosh B. Murthy et al., 2014
Silk (Flow Diversion Device)	- Thromboembolic events - Intraoperative rupture	Favourable (for complex ICA – Silk + Stent appears safer than first generation stents	1b		Single center retrospective series	Lubicz et al., 2015
Pipeline Embolization Device (Flow Diversion Device)	- Thromboembolic events and intraoperative rupture - Follow up at 180 days	Favourable (technically feasible and can be achieved with an acceptable level of periprocedural risk)	2b		Prospective multicenter trial (The optimal application of these devices will continue to be defined as clinical experience evolves)	Nelson et al., 2011 (PITA)
Pipeline Embolization Device (Flow Diversion Device)	- Thromboembolic events - Intraoperative rupture - Follow up at 30 and 180 days after PED placement	Favourable (PED is safe and effective for the target population of large and giant wide-necked anterior cerebral circulation aneurysms)	2b	Continued study of PED to refine therapy and further understand certain complications that occur infrequently is warranted	Multicenter prospective interventional single arm trial	Becske et al., 2013 (PUFS)
Pipeline Embolization Device (Flow Diversion Device)	- Thromboembolic events - Intraoperative rupture	Favourable (The complication rates with PED are comparable with those of other endovascular treatment options such as SACE)	2b	- PED is associated with the lowest complication rates when used to treat small aneurysms of the anterior circulation - Patients with posterior circulation aneurysms and giant aneurysms are at higher risk of thromboembolic complications	Multicenter retrospective study	Kallmes et al., 2015 (IntrePED)
Surpass (Flow Diversion Device)	- Thromboembolic events - Intraoperative rupture	Favorable (acceptable safety profile compared with other FD technology and stent-assisted coil embolization)	2b	- The observed progressive occlusion requires long-term follow-up studies	- Prospective multicenter nonrandomized, single arm study	Wakhloo et al., 2015
Flow-Redirection Endoluminal Device (Flow Diversion Device)	- transient or permanent neurologic deficit or death - Thromboembolic events - Intraoperative rupture	Favourable	2b	- Long-term durability and safety still remain to be proved by larger series and after prolonged followup - Reasonable, safe, and effective to use	Single-center prospective observational study	Mohlenbruch et al., 2015
Woven Endobridge (Flow-Disruption Devices)	- Thromboembolic events - Intraoperative rupture	- Controversial (great heterogeneity in the studies)	2a	- WEB device has been investigated mainly in unruptured aneurysms with a wide neck, which make results difficult to extrapolate to other aneurysms - Long-term results remain unknown	Systematic review	Muskens et al., 2016

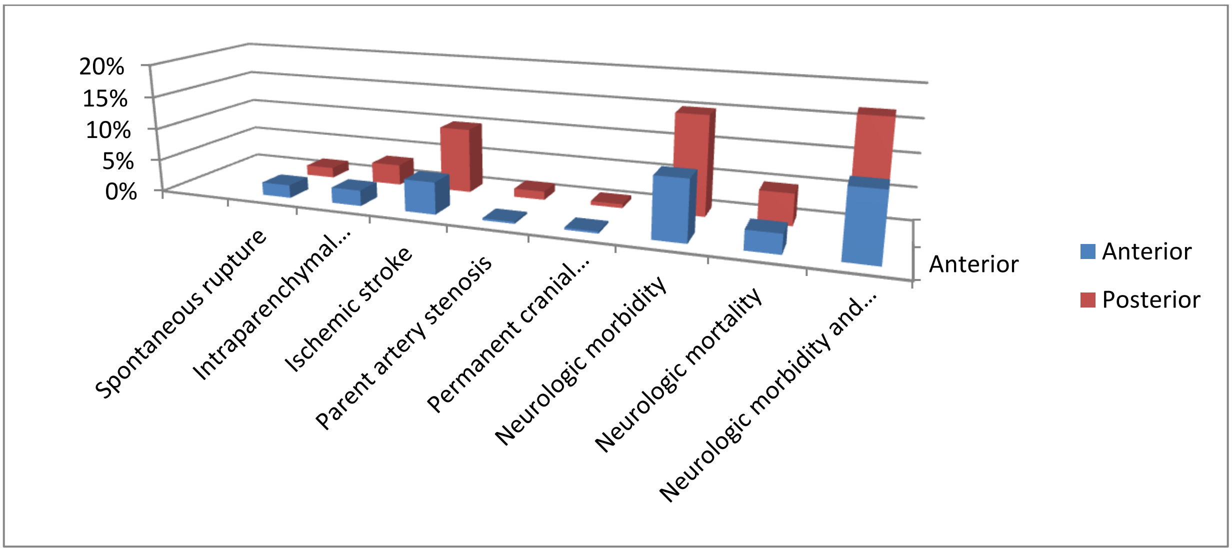
Meta-analysis

A recent meta-analysis included a total of 48 randomized, double-blind, and sham-controlled trials reporting 2508 patients with 2826 ruptured and unruptured aneurysms treated by FDD, documenting aneurysm occlusion, morbidity and mortality rates (Ye et al., 2016). At a mean follow-up interval of 6.3 months, this meta-analysis found an aneurysm occlusion rate of 77.9 % as well as a neurological morbidity and mortality rates of 9.8 % and 3.8 % respectively (Ye et al., 2016). The spontaneous rupture rate after FDD therapy was found to be significantly higher in giant aneurysms than in small/large aneurysms (7.5 % vs 1.3 %) and also higher in ruptured aneurysms than in unruptured ones (3.5 % vs 1.7 %) (Ye et al., 2016). Intraparenchymal hemorrhage (IPH) is another potentially fatal complication after FDD treatment, often resulting in permanent neurological deficits, which appears to have a higher rate in giant aneurysms (Ye et al., 2016). Ischemic stroke is the most common postoperative complication after FDD and it rates higher in aneurysms of the posterior circulation (10 % vs 4.9 %) and in giant aneurysms in comparison to small or large ones (9.5 % vs 5 %) (Ye et al., 2016).

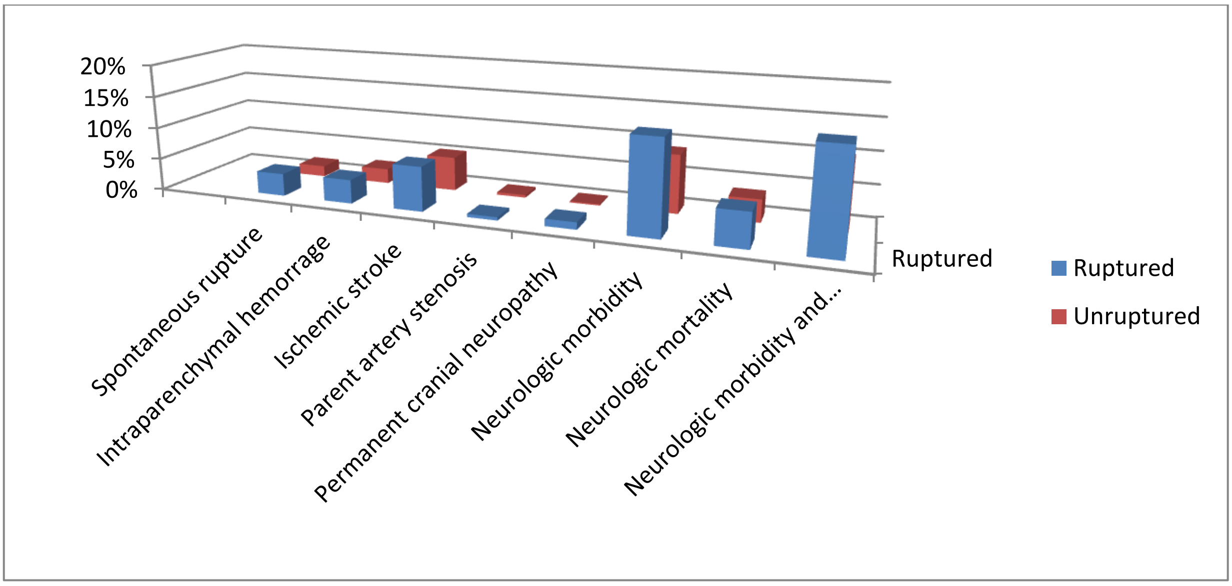
FDD: Complication stratified by aneurysm size (Ye et al., 2016)



FDD: Complications stratified by aneurysm location (Ye et al., 2016)



FDD: Complications stratified by aneurysm condition (Ye et al., 2016)



Discussion and Conclusion

IAs management varies substantially and treatment decisions should primarily be based on aneurysm related factors, clinical status of the patient, and technical endovascular considerations.

For asymptomatic UIAs the best management is still uncertain. A precise assessment of multiple significant elements such as age and life expectancy of the patient, estimated risk of aneurysm rupture, risk of complications attributed to the preventive treatment, and the level of anxiety caused by the awareness of having an aneurysm are critical when defining therapeutic management. Several models have been developed to help predict the risk of rupture of incidental intracranial aneurysms. Despite considering both patient related predictors and aneurysm related predictors, the PHASES score has some limitations such as subgroup underrepresentation, limited long-term follow up and not considering the inherent risk of the intervention itself. Alternative models like UIATS (Unruptured Intracranial Aneurysm Treatment Score) encompass variables like young age or life expectancy, coexistent modifiable or nonmodifiable risk factors, coexistent morbidities, morphologic UIA features and relevance of clinical symptoms related to UIAs. However, its applicability is not as simple and the "population" of specialists used to elaborate this score is arguably representative of the general "community of UIA experts".

Management of ruptured IA requires a multidisciplinary team of neuroradiologists, neurosurgeons and neurology intensive care physicians. Aneurysmal SAH clinical outcome is predicted primarily by neurological condition of the patient on admission, age, and the amount of extravasated blood seen on CT scans. Scales (including Fisher Scale, the Hunt and Hess Scale, the Glasgow Coma Score (GCS), and the World Federation of Neurological Surgeons (WFNS) Scale) have been projected to provide prognostic information regarding outcome. The Prognosis on Admission of Aneurysmal Subarachnoid Haemorrhage (PAASH) scale, grounded solely on the GDS, showed good prognostic value for patient outcome and an even better gradual increase in the proportionate distribution of patients with poor outcome per each increasing PAASH grade than the WFNS scale (van Heuven et al., 2008).

Recurrent hemorrhage can follow at any time after the initial SAH in patients with both good and poor clinical grades, but the incidence of a recurrent hemorrhage is highest within 24 hours of subarachnoid hemorrhage (SAH) (Park et al., 2015). So it might seem reasonable to suggest that an even earlier treatment of the aneurysm would result in a better prognosis. But this would imply other complications, such as a greater risk of periprocedural unfavorable events, an increased need for retreatment and an increase in the number of patients transferred to different hospitals. Few data are available with reference to the effects of the EVT timing on clinical outcome. Hyper-early timing (<12 hours) for the neuro-interventional procedure doesn’t seem to be related with good clinical outcome, quite the opposite it appeared to show an inverse correlation with a good clinical outcome (Consoli et al., 2013). In another study published in 2011, two groups of patients treated before (ultra-early treatment) and after (early treatment) 24 hours, presented results showing better outcome at six months in the ultra-early approach group (within 24 hours) (Phillips et al., 2011). Lack of consensus on this issue is still a major concern. Guidelines propose aneurysm occlusion should be done promptly, within 72 hours and if possible 48 hours. Treatment should always be done as early as possible. However, if the patient is admitted more than 72 hours after hemorrhagic event and is considered to have a low risk for rebleed, treatment can be withheld if not for more than 10 days (Anxionnat et al., 2015; Matias-Guiu et al., 2013; Oudshoorn et al., 2014).

Low-volume hospitals should consider transferring patients with SAH to higher volume centers with specialized services, but there is currently a wide variance in transfer practices between institutions owing to the uncertainty related to optimal time frame for transfer and to the absence of specific recommendations to guide the process. Complications derived from delayed transfer have to be weighed against a hasty transfer process. Early resuscitation and stabilization followed by safe transfer rather than a hyperacute transfer paradigm should be the preferred protocol; however, transfer time should be minimized as much as possible with a goal of less than 8 hours, so that time to definitive treatment is not delayed (Wilson et al., 2015).

The International Subarachnoid Aneurysm Trial (ISAT) demonstrated improved one-year clinical outcomes for patients with ruptured intracranial aneurysms treated with endovascular coiling compared to surgical clipping (A. Molyneux et al., 2002). Two large, prospective, multicenter series reviewed the two most frequent aneurysm coiling complications (thromboembolic complications and intraoperative rupture), and a good safety profile was found for both ruptured and unruptured aneurysms (Cognard et al., 2011; Laurent Pierot et al., 2008). Avoiding recanalization and approaching aneurysms with unfavorable characteristics were still presented as great challenges for coiling EVT and soon new technologies and techniques developed in order to address these limitations.

BACE allows for optimal coil packing, particularly in the aneurysm neck and fundus (Moret et al., 1997). Despite initial concerns about safety profile, two large multicenter prospective series (CLARITY and ATENA) evaluated the complication rates comparing BACE to coiling alone (Laurent Pierot et al., 2011; L. Pierot et al., 2009). In ruptured aneurysms the rate of thromboembolic events was similar for both groups and an analogous conclusion was found for the rate of intraoperative rupture. Treatment related morbidity was lower in the BACE group and mortality was similar for both groups (Laurent Pierot et al., 2011). As for unruptured aneurysms, thromboembolic events had a lower prevalence in the BACE group as compared with coiling alone and intraoperative rupture rate was slightly higher in the BACE group as compared to the coiling alone group. Safety of both techniques seems to be similar despite the fact that aneurysm characteristics treated with standard coiling are quite different from those treated with remodeling technique. Also, a higher anatomic efficacy is achieved with remodeling technique leading the authors to propose a wide use of remodeling technique (L. Pierot, Cognard, et al., 2012).

Stent-assisted coil embolization (SACE) was introduced over ten years ago to overcome some limitations of standard coiling alone when applied to the treatment of complex aneurysms (Beller et al., 2016). Risk of implant thrombosis is higher in SACE than with coiling alone since stents are implanted in the parent artery, bridging the aneurysm neck. Antiplatelet therapy during and after the procedure is mandatory (L. Pierot et al., 2013). This is why stent placement may generally be avoided in acutely ruptured aneurysms in favor of other endovascular techniques that do not mandate dual antiplatelet therapy (Bechan et al., 2015). Safety and efficacy SACE profile as compared with standard coiling has been evaluated in few and mostly retrospective single-center series. In ruptured aneurysms SACE was linked with an increased morbidity-mortality rate and recommendations were made to consider this option only when less risky ones had been excluded (Bechan et al., 2015). A systematic review and meta-analysis compare SACE with coiling-only. Pooled immediate occlusion rates showed no significant statistical difference between both techniques while increases in packing density on follow up (pooled progressive thrombosis rate) were substantially higher with SACE. A significantly lower likelihood of aneurysm recurrence was associated with the SACE technique despite a bias towards cases with wide necked (>4 mm) and low dome-to-neck ratio aneurysms. The question remains of whether stent-assisted techniques should be systematically used for all aneurysms regardless of their morphology. Randomized controlled trials are required to answer this question (Phan et al., 2016).

Even though safety and efficacy of intrasaccular detachable coil embolization are fairly well documented**,** the rate of aneurysmal total occlusion remains suboptimal and coil compaction achieved frequently result in post treatment recanalization and recurrence.

Flow Diverter Devices (FDDs), highly dense mesh stents, are designed to further expand EVTs range and efficacy. The objective of getting a higher occlusion rates while decreasing recurrence and recanalization of difficult-to-treat intracranial aneurysms is attempted by reconstructive treatment and vascular remodeling (IA) (F. Briganti et al., 2016; Francesco Briganti et al., 2014). Knowing which type of FDD to use and its precise indications remains, however, a controversial issue (Giacomini et al., 2015).

A systematic review of the published literature on SFDs applied primarily to giant or large aneurysms (63.1%) predominantly from the anterior circulation found a high cumulative aneurysm occlusion rate (AOR). The most common complications registered with this technique were ischemic events and parent artery occlusion (Santosh B. Murthy et al., 2014). More recently, an improved second generation of SFD has been developed, the Silk+ stent, with promising results. However, further evaluation of this device is needed at multiple centers with adequately trained operators (Binning et al., 2011; Lubicz et al., 2015).

A greater amount of published data is available with regard to Pipeline Embolization Device (PED; ev3/Covidien, Irvine, CA). Major trials conducted have concluded that PED was associated with a high aneurysm occlusion rate (AOR) and a rate of adverse events comparable to those of more conventional techniques (Kallmes et al., 2015). Moreover PED treatment elicited a very high rate (93%) of complete angiographic occlusion at 6 months in a population of the most challenging anatomic subtypes of cerebral aneurysms (Nelson et al., 2011).

A prospective multicenter study on the Surpass Flow Diverter (Stryker Neurovascular, Fremont, California) concluded a clinical safety profile comparable to stent-assisted coil embolization as well as a high rate of intracranial aneurysm occlusion. Additionally, long-term follow-up studies are required due to the observed progressive occlusion (Wakhloo et al., 2015).

FRED (Microvention, Inc., Tustin CA, USA), a 2-layer structure, consisting of high-porosity outer and low-porosity inner layers, is easy to guide or insert in or into a catheter, and wall apposition is favorable, facilitating recapture during insertion. Although showing promising results, most prospective studies on FREDs safety profile and efficacy include a very limited number of patients, short follow-up periods and lack randomized comparisons with other potentially efficacious therapies. Long-term durability and safety still remain to be proved by larger series and after prolonged follow-up (Matsumaru et al., 2016; Mohlenbruch et al., 2015).

Despite showing excellent occlusion rates, even in large and giant aneurysms, flow diverters have had limited clinical utility in rupture aneurysms (due to the requirement for concomitant dual antiplatelet therapy and because immediate aneurysm occlusion usually does not occur) and in bifurcation aneurysms owing to the inherent design limitations (Kwon et al., 2011). In this context, intra-saccular braided-wire embolization devices were designed to disrupt blood flow at the level of aneurysm neck–parent artery interface (WEB and LUNA)(Kwon et al., 2011).

A recent systematic review of literature has been conducted to assess clinical outcomes of intracranial aneurysms treated with a WEB device. Initial results presented a complete and adequate (complete occlusion or a small neck remnant) occlusion rates of 27% and 59% respectively, that increased significantly at a mean follow up time of 7 months. No significant differences were found in midterm (>3 months) adequate occlusion rates between ruptured and unruptured aneurysms, as well as no relevant differences in perioperative morbidity and mortality rates (Asnafi et al., 2016). Again, further studies are needed to better assess complication rate and long term efficacy of the Woven Endobridge device in treating wide-neck and wide-neck bifurcation aneurysms (Caroff et al., 2014).

The LUNA Aneurysm Embolization System (AES) is a self-expanding ovoid device that serves as an intra saccular flow diverter as well as a scaffold for endothelization across the neck. Preliminary results determine a good safety profile and the first short-term angiographic follow-up are promising. However, more and longer follow-up study results are impending (Kwon et al., 2011).

Conflict of Interest declaration

The author declared no conflicts of interest.

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Annex

Table 1 : Modified Fisher and Fisher Grading Scale for Subarachnoid Hemorrhage

Grade	Modified Fisher	% of Vasospam	Fisher	% of Vasospam
0	No SAH or IVH			
1	Thin SAH, no IVH	24	No SAH or IVH	21
2	Thin SAH with IVH	33	Diffuse or thin layer of blood < 1 mm thick	25
3	Thick SAH, no IVH	33	Localized clots and/or layers of blood > 1 mm thick in the vertical plane	37
4	Thick SAH with IVH	40	Localized clots and/or layers of blood > 1 mm thick in the vertical plane	31

Table 2: Hunt and Hess Grading Scale

Grade	Criteria	Index of Perioperative Mortality (%)
0	Aneurysm is not ruptured	0 - 5
I	Asymptomatic or with minimal headache and slight nuchal rigidity	0 - 5
II	Moderate to severe headache, nuchal rigidity, but no neurologic deficit other than cranial nerve palsy	2 - 10
III	Somnolence, confusion, medium focal deficits	10 - 15
IV	Stupor, hemiparesis medium or severe, possible early decerebrate rigidity, vegetative disturbances	60 - 70
V	Deep coma, decerebrate rigidity, moribund appearance	70 - 100

Table 3: Glasgow Coma Scale

Eye Opening	Points
Eyes open spontaneously	4
Eyes open to verbal command	3
Eyes open only with painful stimuli	2
No eye opening	1
Verbal Response	**Points**
Oriented and converses	5
Disoriented and converses	4
Inappropriate words	3
Incomprehensible sounds	2
No verbal response	1
Motor Response	**Points**
Obeys verbal commands	6
Response to painful stimuli (UE)	
Localizes pain	5
Withdraws from pain	4
Flexor posturing	3
Extensor posturing	2
No motor response	1

Total Score = eye opening + verbal + motor

GCS < 5: 80 % die or remain vegetative

GCS > 11 : 90 % completely recover

From Teasdale G, Jennett B: Acta Neurochirurg 34:45, 1976

Table 4: WFNS Grading Scale

WFNS Grades	GCS Score	Motor deficit
I	15	Absent
II	14 - 13	Absent
III	14 - 13	Present
IV	12 - 7	Present or absent
V	6 – 3	Present or absent

Table 5: WFNS and PAASH - SAH grading scales with criteria per grade and relation with outcome

Scale	Grade	Criteria	Proportion of patients with poor outcome	OR for poor outcome
WFNS	I	GCS 15	14-8 %	ref
	II	GCS 13-14 no focal deficits	29.4 %	2.3
	III	GCS 13-14 focal deficits	52.6 %	6.1
	IV	GCS 7-12	58.3 %	7.7
	V	GCS 3-6	92.7 %	69
PAASH	I	GCS 15	14.8 %	ref
	II	GCS 11-14	41.3 %	3.9
	III	GCS 8-10	74.4 %	16
	IV	GCS 4-7	84.7 %	30
	V	GCS 3	93.9 %	84

Poor outcome defined as Glasgow outcome scale 1–3 or modified Rankin score 4–6. WFNS = World Federation of Neurological Surgeons Grading Scale for Subarachnoid Haemorrhage . PAASH = Prognosis on Admission of Aneurysmal Subarachnoid Haemorrhage grading scale. GCS = Glasgow Coma Score. Data in this table are adapted from Steiner et al., 2013

Table 6: SACE - Advantages and disadvantages

Stent–assisted coiling of intracranial aneurysms	
Advantages	Disadvantages
• **Aneurysms with complex morphologies, wide necks or unfavorable dome–to–neck ratio** • **More stable access during coil placement (''jailing'')** • **Mechanical scaffold for microcoils** • **Allows increased packing density** • **Improved neck coverage** • **Prevention of coil protrusion into parent artery** • **Flow diverting properties** • **Facilitate aneurysm thrombosis and durability of coil embolization** • **Scaffold for endothelialization and growth of fibroelastic tissue at the aneurysm neck**	• Potential for infarction secondary to vasospasm due to stent • Requires antiplatelet therapy • External ventricular drain: intraparenchyma hematoma risks • High likelihood of future invasive procedures