Unruptured Intracranial Aneurysms

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Introduction

Unruptured intracranial aneurysms (UIAs) are increasingly encountered in cerebrovascular practices around the world. This is due to increased utilization of noninvasive cerebral imaging as well as a significant improvement in the quality of these imaging modalities. By definition, UIAs are those aneurysms in which there has been no breach in the aneurysm wall. While these breaches are often clinically obvious through aneurysmal rupture into the subarachnoid or ventricular spaces, clinicians should be aware of more subtle presentation such as headaches suggestive of sentinel bleeds or even MRI findings suggestive of prior rupture and thrombosis. In addition to being incidentally found, UIA can also present with aneurysm-related mass effect such as third nerve palsy secondary to a posterior communicating artery aneurysm.

Management of UIAs can be complex. In general it falls into three categories: observation, endovascular treatment, or open surgical repair. The treatment approach might get more complicated for recurrent aneurysms. Open surgery can be used to treat previously coiled aneurysms and vice versa. Redo surgery or endovascular interventions are also an option. To advise the patient about the optimal approach for their specific aneurysm, it is important for the treating physician to understand the natural history, risk factors for rupture, and risks of treatment.

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Natural History

Our current understanding of the natural history of UIAs comes from a number of retrospective and prospective cohort studies. In the absence of randomization, included aneurysms that get followed longitudinally with no treatment are more likely those that are thought to be "low risk." Further, in the absence of a control arm, the degree of certainty that comes out of these studies remains low. However, despite the inherent limitations of these studies, several factors have emerged and represent our best understanding of the natural history of UIAs. We will discuss these factors below:

Size

Size has been identified as a predictor of rupture risk across several studies. In the International

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Study of Unruptured Intracranial Aneurysms (ISUIA), one of the most cited studies of the natural history of UIAs, 4060 patients were included in the prospective cohort. Of those 1692 patients were not treated. The patients were divided into a group with no previous SAH and a group with previous SAH from another aneurysm. The average follow-up was 4.1 years. The authors found a progressively increasing risk of rupture with increasing aneurysm size. Overall, it appeared that posterior circulation aneurysms ≥5 mm (including posterior communicating artery aneurysms) had a high enough rupture risk to warrant preventative treatment. In the anterior circulation, aneurysms ≥7 mm (excluding the extradural carotid artery where rupture risk was extremely low) were thought to warrant treatment. Aneurysms <7 mm found in the setting of a prior SAH also showed higher rates of rupture justifying treatment [1].

The ISUIA was criticized for showing data that diverged from other clinical studies in which the average diameter of ruptured aneurysms was in the range of 7 mm. Hypotheses to explain these discrepancies included a selection bias, as well as the possibility that ruptured aneurysms shrink in size [2].

In the Unruptured Cerebral Aneurysm Study (UCAS) of Japan, 6697 aneurysms were included. Using the 3–4-mm size as a reference, the hazard ratios for rupture were 3.35, 9.09, and 76.26 for 7–9-mm, 10–24-mm, and >25-mm aneurysms, respectively [3].

Cerebral aneurysms measuring more than 25 mm in diameter are considered giant intracranial aneurysms (GIAs) [4]. These remain some of the hardest aneurysms to treat not only because of their size but also because they frequently (a) are wide necked, (b) incorporate arterial branches into the sac, (c) harbor thrombus in the dome risking thromboembolic events, (d) cause mass effect, and (e) obscure anatomical features important for intervention.

While aneurysm size is clearly an important factor, it cannot be used in isolation to determine whether an UIA should be treated.

Location

The location of an aneurysm is also related to the risk of rupture. The prospective ISUIA cohort identified a relative risk of rupture of 2.3, 2.1, and 0.15 for aneurysms of the basilar apex, posterior communicating artery, and cavernous carotid, respectively, when compared to anterior circulation aneurysms [1]. However, the ISUIA was criticized for classifying posterior communicating artery aneurysms as posterior circulation aneurysms.

The UCAS of Japan identified the anterior communicating artery (ACoA) to be the location with highest rupture risk followed by the posterior communicating artery (PCom) artery, basilar apex/superior cerebellar artery (SCA), middle cerebral artery (MCA), vertebral artery/posterior inferior cerebellar (PICA)/vertebrobasilar junction, and internal carotid artery in descending order. They found that ACoA and PCom aneurysms had a relatively high rate of rupture even when smaller than 7 mm. Posterior circulation aneurysms excluding PCom aneurysms were not more prone to rupture [3].

A meta-analysis by Wermer et al. found the posterior circulation (not including the PCom) had the greatest relative risk of rupture followed by PCom, MCA, and non-PCom ICA aneurysms, with cavernous sinus aneurysms having the lowest relative risk [5].

Morphology

The shape of an aneurysm such as the presence of daughter sacs, the ratio of aneurysm height to neck width (aspect ratio), and the anatomical relationship to the parent vessel may contribute to the risk of rupture. Multiple studies have compared morphological characteristics of ruptured to unruptured aneurysms and found an association between lobulation or daughter sacs and rupture [6, 7]. The UCAS Japan is the only prospective study to identify a daughter sac as a factor that increases the relative risk of rupture.

The presence of a daughter sac was associated with a hazard ratio of 1.63 [3]. There has also been a suggestion that the presence of branching vessels adjacent to the aneurysm, the angle at which the aneurysm arises from the parent vessel, and the aspect ratio may increase the risk of rupture [8, 9]. More recently, the ISUIA investigators, upon investigating 12 morphological metrics in 198 patients, showed that perpendicular height and size ratio, defined as the ratio of the maximum diameter of the aneurysm to that parent vessel diameter, were the only predictors of aneurysm rupture in univariate analysis. In this recent study, aspect ratio, daughter sacs, multiple lobes, aneurysm angle, neck diameter, parent vessel diameter, and the calculated aneurysm volume were not statistically significant predictors of rupture [10].

Presenting Symptoms and Comorbidities

The clinical presentation of patients with UIA is also associated with rupture risk [5, 11]. A history of SAH contributes to the risk of rupture from UIAs. In the retrospective cohort study of ISUIA, there was a tenfold increase in the risk of rupture in the group of patients with a history of SAH and aneurysms less than 10 mm. However, this difference was not noted in larger aneurysms [1, 12]. Patient age, sex (females are more likely to have a ruptured aneurysm), smoking, and hypertension can potentially increase the risk of rupture [11, 13].

Of all the modifiable risk factors, smoking has been found to have the greatest association with multiple aneurysms, growth of UIAs, and to independently increased risk of rupture [14–16]. In the meta-analysis by Wermer et al., both Japanese and Finnish descent increased the risk of rupture [5].

Future Advances

Advances in aneurysm imaging promise to enhance our understanding of which aneurysms are at risk of rupture. Dynamic MRI aneurysm imaging could detect the aneurysm wall permeability to gadolinium which could be a surrogate for an aneurysm risk of hemorrhage [17–19]. Further, biomarkers are being investigated and could help dictate aneurysm management in the future [20]. Such biomarkers include blood and CSF levels of selectins, the elastase-to-alpha-1-antitrypsin ratio, and others.

Noninvasive Management

Although the natural history of an individual aneurysm cannot be predicted with precision, the above factors should be considered when weighing the risk of rupture. The formula for calculating the risk of hemorrhage in a lifetime is $1-(\text{annual chance of not bleeding})\times\text{expected}$ years of life. If a 30-year-old has a 5-mm basilar apex aneurysm (.5%/year based on ISUIA data), their lifetime risk is 22% based on an expected lifespan of 80 years. The aneurysm morphology, including the presence of geometric irregularity, and patient factors such as smoking, hypertension, alcohol use, and previous history of SAH also have to be taken into consideration.

Noninvasive or "conservative" management is often equated with doing nothing. However, patient education, modification of risk factors such as smoking and hypertension, and routine screening can improve the outcomes in patients with UIAs. Patient education, immediate steps to modify lifestyle, and general medical health are imperative to reducing the risk of rupture and new aneurysm formation.

Because of decreased perioperative morbidity for both surgical and endovascular techniques, conservative management is usually only offered to patients with a low lifetime risk of rupture. Typically, these are patients with small aneurysms and a relatively short life expectancy. However, patients might opt for conservative management even when they have high-risk aneurysms.

When patients opt for conservative management, aneurysms need to be monitored on a regular basis. A change in aneurysm morphology or

interval growth may imply a risk of impending rupture. New onset of headaches is more worrisome in the setting of known UIA. Yasui et al. evaluated 25 aneurysms that were initially treated conservatively and went on to rupture. A majority of these aneurysms increased in diameter at the time of rupture [21]. The initial size of the aneurysm has been identified as a risk for growth on noninvasive imaging [22].

Surgical Management

Small and Large Aneurysms

The first ever surgical clipping of an intracranial aneurysm was performed at Johns Hopkins Hospital by Dr. Walter Dandy in 1937. Since then, the surgical strategy and techniques have significantly evolved. The goal of surgery is to exclude the treated aneurysm from the circulation, thus making its risk of rupture virtually zero. The options for surgery include direct clip ligation, aneurysm trapping and bypass, and rarely wrapping of a dysplastic vessel or aneurysm.

Classically, after primary clipping of an aneurysm, the risk of residual aneurysm had been quoted at 4–8% [23–26]. In a series of 715 aneurysms that were clipped, there were 3.8% (28 aneurysms) with residual aneurysm sac of which one aneurysm rebled [24]. In a series by David et al., late angiographic follow-up was performed in 160 aneurysms. They found two recurrent aneurysms (1.5%) out of 135 completely occluded aneurysms. Of the group with residual aneurysm, they found an annual hemorrhage rate of 1.9% in those with a dog-ear residual. In those with broad-based residuals, there was a 75% rate of growth. Grouping all incompletely clipped aneurysms, they found a risk of recurrence of 2.9% per year and 1.5% risk of hemorrhage per year [23]. These numbers have recently improved with the introduction of intraoperative standard angiography or indocyanine green angiography [27, 28].

Based on the ISUIA prospective cohort of 1917 patients who underwent surgical clipping of UIAs, the 1-year mortality was 2.3% and 1-year morbidity 12.1%. Age >50 years was a strong predictor of poor outcome. Other factors that were predictive of poor surgical outcome were diameter greater than 12 mm, location in the posterior circulation, previous ischemic disease, and aneurysm symptoms other than rupture. The Cleveland Clinic looked at their series of 449 UIAs treated by ten neurosurgeons. They compared the baseline modified Rankin Scale scores (mRS) with 6-month mRS and found that 94% of patients showed no functional worsening. They found that surgeons with greater than 5-year experience prior to the onset of the study achieved better outcomes. Increasing patient age and aneurysm size were predictors of worsened functional outcome [29].

The surgical approach to GIAs is significantly more challenging than the approach to smaller aneurysms. Stand-alone clip ligation is often impossible to perform safely due to difficulty in visualizing the aneurysm neck and inflow/outflow vessels due to the large size of the aneurysm sac. Several alternative and adjunctive techniques have been utilized in this setting. Specifically, clip ligation, parent vessel occlusion, aneurysm trapping, and extracranial-intracranial bypasses are some of the techniques that have been described.

Endovascular Management

Endovascular surgery is an increasingly utilized option for the treatment of UIAs. At a large majority of centers, it has overtaken open surgery as the primary treatment modality. To best evaluate endovascular treatment, it is important to critically assess the initial occlusion, recanalization, and re-rupture rates. The standard endovascular therapy for aneurysms with a favorable neck to dome ratio is coil embolization. The advent of balloon remodeling, stent-assisted coiling, and flow diversion has enabled the extension of endovascular techniques to treat less favorable aneurysms such as wide-neck aneurysms or GIAs.

Equipment Review

- *Sheath*: A 6-F sheath is the minimum size required for UIA coiling. A 35-cm or longer sheath is recommended to bypass tortuous iliac and femoral vessels and enhance guide catheter control. At times a guide sheath positioned in the common carotid artery or proximal internal carotid artery may be needed to provide support or a larger inner diameter.
- *Guide catheter*: A 6-F guide catheter is recommended in most instances. Several varieties are currently on the market. The traditional iteration has a fixed angle tip designed to be positioned in the distal cervical carotid artery (e.g., MPC ENVOY; Codman Neurovascular, Raynham, MA). Newer guide catheters have a flexible straight tip that can be positioned in the petrous segment safely (e.g., Neuron MAX; Penumbra Inc., Alameda, CA). While the distal purchase is helpful at times, the trade-off is less stability/support.
- *Microcatheter*: A wide range of microcatheters is available for intracranial use. Optimal design features include trackability, stability within the aneurysm, and the ability to accommodate both 0.010-in. and 0.018-in. coil sizes. Most catheters are available in both preshaped and straight (may be steam shaped if desired) varieties.
- *Microwire*: Most practitioners employ a 0.014-in. 200-cm microwire for intracranial navigation and aneurysm entry. Ideal wire characteristics include 1:1 extracranial/intracranial torquability, a soft distal tip, and a supportive proximal shaft.
- *Coils* (Fig. 10.1):
  - *Framing*: Creates a shell that conforms to the inner surface of the aneurysm and bridges the aneurysm neck. Longer coil lengths may enhance neck coverage and reduce the number of coils needed.
  - *Filling*: Used to occlude the body of an aneurysm, these coils are helical or complex in shape and flexible.
  - *Finishing*: The softest family of coils, designed to occlude the aneurysm neck without pushing the coiling catheter out of position.
  - *Coated*: Several coil types are coated with materials designed to enhance initial filling (e.g., HydroCoil; MicroVention-Terumo, Tustin, CA) or aneurysm healing (PRESIDIO; Codman Neurovascular, Raynham, MA).
  - *Bigger and better?*: The Penumbra Coil 400 (Penumbra Inc., Alameda, CA) is the largest diameter coil on the market at 0.020 in. It has the potential advantage of more rapid aneurysm occlusion and less compaction in the setting of large or giant aneurysm. These claims are still being evaluated in practice.
- *Compliant balloon*
  - *Single lumen*: The HyperGlide and HyperForm balloons (Covidien, Irvine, CA) have the longest track record in balloon-assisted coiling (BAC). The HyperForm is the most compliant and effectively herniates into an aneurysm neck. The HyperGlide is somewhat less deformable but also can be used in BAC. These catheters require the use of 0.010-in. microwires (X-Pedion 10; Covidien, Irvine, CA).
  - *Dual lumen*: Newer BAC catheters are designed with central lumen compatible with a 0.014-in. wire and an outer parallel noncommunicating lumen that allows inflation of a compliant balloon at the distal tip of the microcatheter. The inner lumen is designed to deliver compatible therapeutic agents. The Scepter catheter (MicroVention-Terumo, Tustin, CA) is designed for delivering coils but is somewhat more navigable and is compatible with Onyx liquid embolic (Covidien, Irvine, CA).
- *Coiling scaffold stents*: Several such stents are currently available. Most commonly these are constructed from a nickel-titanium (nitinol), laser-slotted tube. However, there are braided stents on the market as well.
- Neuroform Atlas Stent (Stryker, Fermont, California) is a new-generation stent. Early

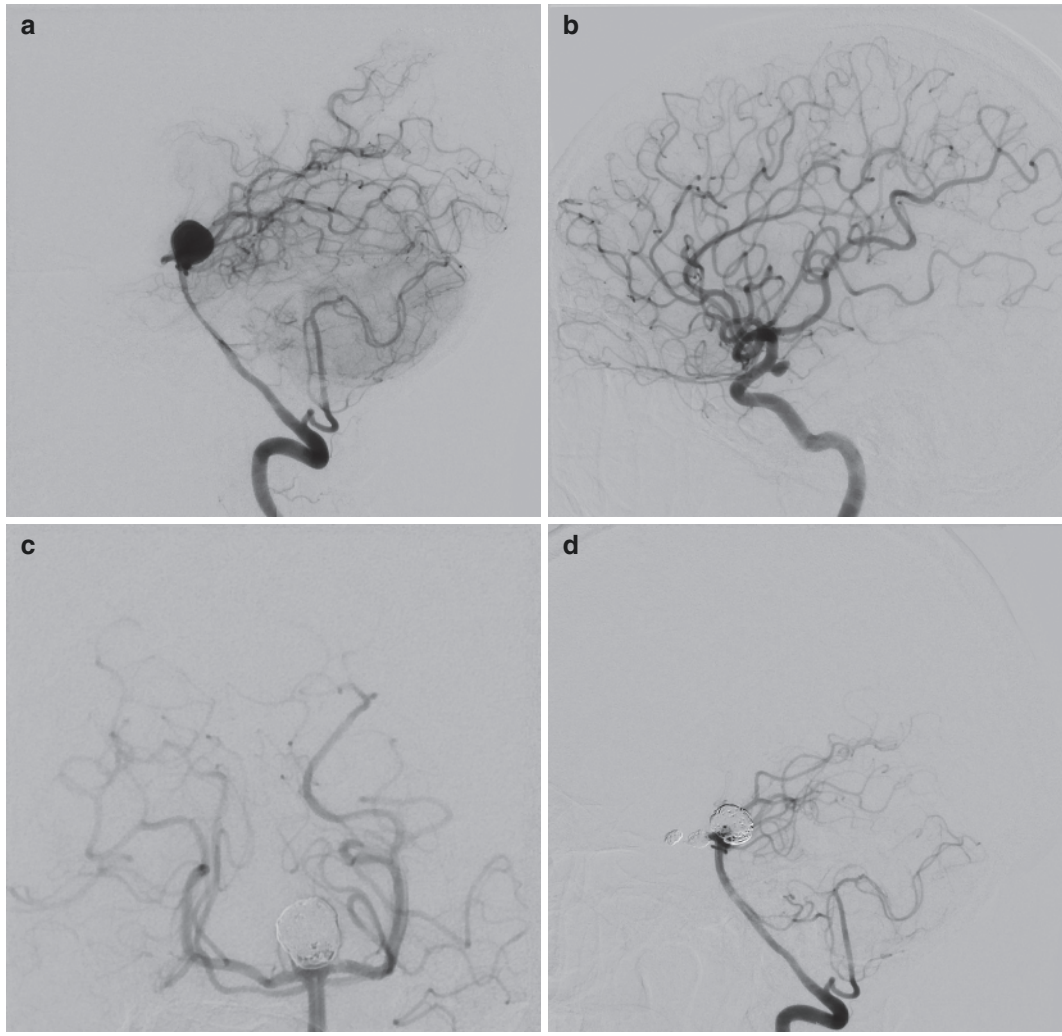

Fig. 10.1 Patient with basilar tip aneurysm and bilateral posterior communicating artery aneurysm. (**a**) Shows a left vertebral artery injection showing the basilar tip aneurysm. (**b**) shows a left carotid injection showing the left P com aneurysm. (**c**, **d**) show post coiling images

data has shown safety, feasibility, and high obliteration rate [30]. It received FDA approval in May 2019. The Neuroform Atlas Stent has an open-cell distal end, a closed-cell distal end, and eight cell structural elements for support, along with 12 cell structural elements for flexibility (Fig. 10.1). It can be delivered through a 0.0165 or 0.017 catheter [31]. The open-cell design augments its conformability and enhances the deployment accuracy; acquiring a higher number of connectors gives it a better scaffolding edge [32]. Several retrospective studies reported immediate obliteration rates ranging from 88% to 52%, with follow-up obliteration rates ranging from 82% to 63% [31–34]. Caragliano et al. in their series have reported 6.2% of intra-procedural complications and less than 3% of mortality related to subarachnoid hemorrhage [31].

- The low-profile visualized intraluminal support junior stent (LVIS Jr. MicroVention-Terumo, Tustin, CA, USA) is also commonly used in current practice. LVIS Jr. stent is a

self-expanding, closed-cell nitinol microstent with a braided construction designed to improve conformability to the vessel's shape. It has three radiopaque and distal markers plus three helical radiopaque threads throughout the stent body, permitting improved visualization. The device is compatible with the 0.017-inch microcatheter [35, 36]. The stent has shown high immediate and long-term total occlusion rates with very acceptable morbidity and mortality rates [37]. Cagnazzo et al., in their systematic review and meta-analysis, have reported a technical success rate of about 96%, with complete or near-complete occlusion in 86% of the cases, morbidity was near 7%, mostly thromboembolic related, and no mortality was reported in their investigational study [38].

- *Flow diverters* (Fig. 10.2):

  Five types of FDDs are currently available for the treatment of intracranial aneurysms. Some are only available in Europe at this time: the Pipeline Flex Embolization Device (PED) (Covidien, Mansfield, MA, USA), the Silk (Balt Extrusion, Montmorency, France), the FRED (Microvention, Tustin, CA, USA), the p64 Flow Modulation Device (Phenox), and the Surpass (Surpass; Stryker Neurovascular, Fremont, CA, USA).

  The Pipeline Embolization Device (PED; Covidien, Irvine, CA) is the first FDD to receive FDA approval. Ultimately, neointimal growth across the aneurysm neck results in arterial wall reconstruction and aneurysm sac occlusion [39]. The flow-diverting properties of the PED come from its design which includes 48 individual cobalt, chromium, and platinum strands providing 30–35% metal surface area coverage when fully deployed [40]. These strands are in stark contrast to the 6–9.5% wall coverage with conventional bare metal stents such as Neuroform EZ (Stryker, Kalamazoo, MI) and Enterprise (Codman Neurovascular, Raynham, MA) [41]. PEDs are available with a nominal diameter from 2.5 to 5 mm in 0.25-mm increments. At the nominal diameter, the pore size is 0.02–0.05 mm^2, and the radial force is approximately 2.0 mN/mm (3.0-mm vessel diameter). The PED is pre-mounted on a stainless steel wire with a radiopaque 15-mm platinum tip extending beyond the end of the PED and is delivered via a 0.027-in. inner-diameter microcatheter [42].

  The Flow Redirection Endoluminal Device (FRED) is a double-layer flow diverter with a stent-like outer layer and a flow diverter inside the stent. That architecture enhances the device's navigation, particularly in tortuous vasculature. The FRED has several radiopaque markers; it is delivered through a 0.027 microcatheter [43, 44]. FRED has shown high feasibility and efficacy in terms of aneurysmal occlusion and technical success. In a European retrospective multicentric study led by Killer-Oberpfalzer et al., the reported aneurysm occlusion was up to 95.3% in the first year, which is similar to the rates of the Italian FRED Registry, a multicentric study in more than 30 Italian centers, which included 196 aneurysms managed; they reported 94% occlusion rate in the first year, which increased to 96% at 12–24 months [44, 45].

  The SAFE study is a multicenter French study. It is the first prospective study to evaluate the safety of the FRED for aneurysmal management, their analysis confirms the high safety of the device with 1-year morbidity of 2.9% and mortality of 1.9%, and they have also reported low retreatment rates at the first year (2.2%) .

  Other flow diverter devices that are less commonly used include the Silk (Balt Extrusion, Montmorency, France), the p64 Flow Modulation Device (Phenox), and the Surpass (Surpass; Stryker Neurovascular, Fremont, CA, USA); several retrospective studies have investigated the morbidity, procedural complications, and mortality of the Surpass and the Silk devices; permanent morbidity in Surpass and Silk was 6% and 9.6%, respectively, and the mortality rates were 2.7% and 3.2%, respectively, in both devices [46, 47].
- Intrasaccular Flow Disrupters

  The Woven EndoBridge (WEB) aneurysm embolization system is a self-expanding mesh

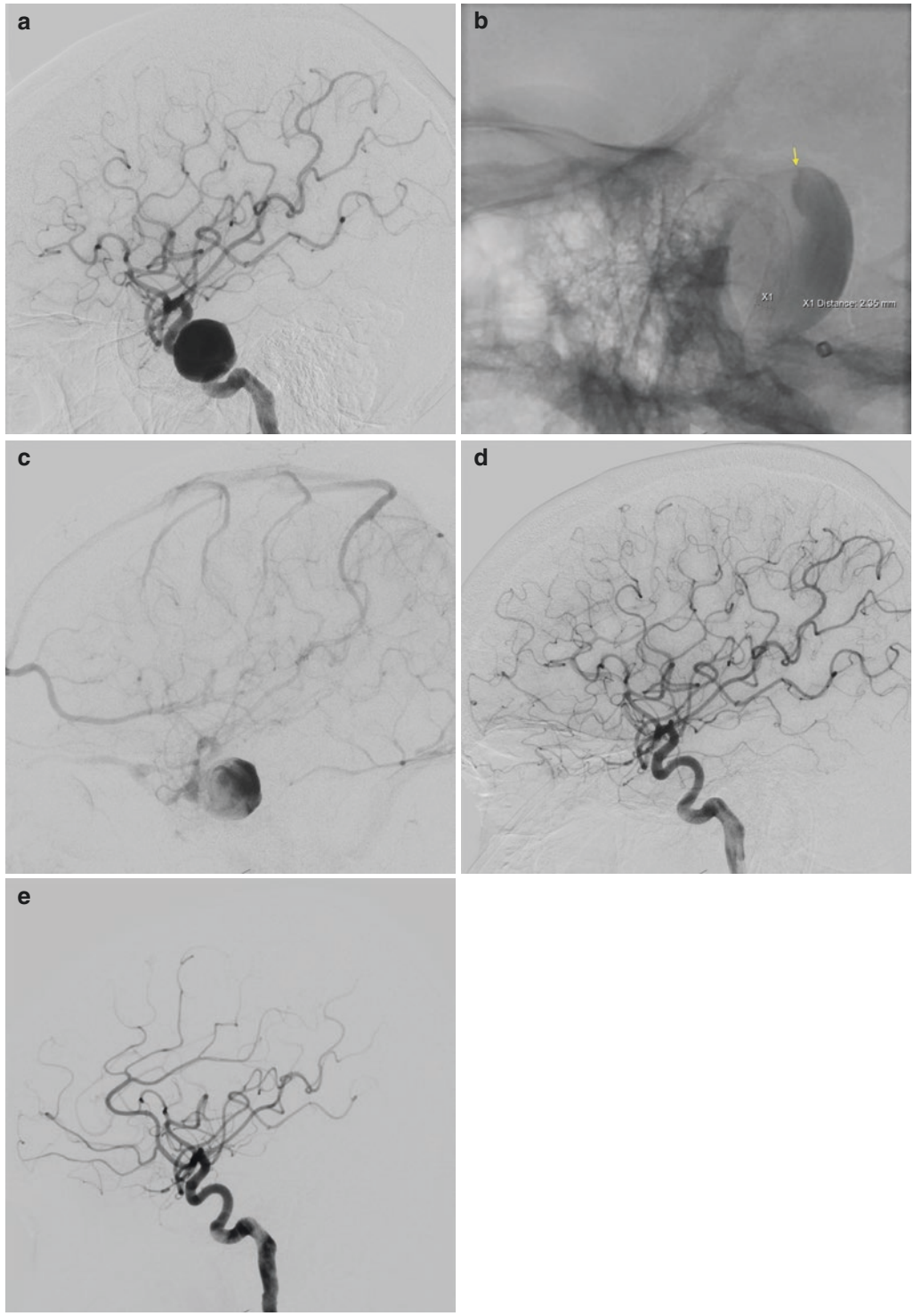

Fig. 10.2 Patient with a 22.5 mm × 18.8 mm fusiform left internal carotid artery cavernous segment aneurysm. (**a**) shows a left carotid injection demonstrating the aneurysm. (**b**) shows deployment of the flow diverter, immediate flow turbulence can be noted in the aneurysm at the yellow arrow. (**c**) Flow turbulence in the aneurysm after deployment of the flow diverter. (**d**) Six months follow up shows almost complete resolution of the aneurysm. (**e**) one year follow up shows complete resolution of the aneurysm

basket implant that was specifically designed for wide-neck intracranial bifurcation aneurysms. However, applications of WEB devices have been extended due to their efficacy [48]. Numerous studies have looked at factors that determine aneurysm occlusion after embolization with WEB devices. Kabbasch et al. found that initial aneurysm thrombosis, recurrent aneurysms, aneurysm size, and simultaneous treatment by WEB and coils were associated with residual aneurysms and aneurysm recurrence [49]. Other studies attempted to evaluate the risk factors of procedural complications related to WEB embolization and found that increased width to height ratio and a lower aspect ratio could predict periprocedural complications [50]. Due to the results of early clinical trials and real-world results, the use of the WEB device is likely to increase in the next few years; however better data is needed to understand their long-term efficacy [51].

Small and Large Aneurysms

- *Coil embolization*: Given the rapid evolution of endovascular techniques and technology, it is important to give greater weight to more recent literature. The ISUIA prospective cohort of 451 patients treated endovascularly found 55% complete obliteration, 24% incomplete obliteration, and no obliteration in 18%. Naggara et al. performed a meta-analysis of 71 studies between January of 2003 and July of 2008 that demonstrated a complete obliteration rate of 86% [52]. This indicates that there has been an increased rate of complete or near-complete aneurysm obliteration over the last 10 years.
  - *Pretreatment*: The practice of pretreating elective coiling patients with antiplatelet agents is gaining popularity because the observed risk of thromboembolic complications outweighs the risk of intraprocedural rupture. Some groups use aspirin alone, while others use a combination of aspirin and clopidogrel [53]. The latter facilitates the safe use of balloon assistance or stent assistance if the need arises during the case.
- *Balloon-assisted coiling*

  Advanced techniques such as balloon remodeling, stent-assisted coiling (SAC), and flow diversion have increased the scope of endovascular treatment in UIAs. These techniques allow endovascular treatment in aneurysms with less favorable morphology such as wide-neck aneurysms. Although a few small series have suggested an increased risk of thromboembolic complications with the use of balloon remodeling, the ATHENA study did not show a statistically significant difference [54]. In addition to a similar safety profile, balloon remodeling has a better immediate and follow-up anatomical result than coiling alone.
- *Stent-assisted coiling*

  Hong et al. performed a meta-analysis of ten retrospective cohort studies comparing standard coiling to SAC and concluded that although there was a slightly lower initial occlusion rate in the SAC group (57.6% vs. 68.7%), there was a significantly lower recurrence rate (16.2 vs. 34.4%) and a higher progressive thrombosis rate (37.5% vs. 19.4%). There was no statistical difference in the complication rate between the two groups.

Giant Aneurysms

In one of the earlier reports on coil embolization of GIAs, 69% of aneurysms were incompletely occluded at 6-month follow-up angiography (range, 1–11 months). These recurrences have been attributed to thrombus dissolution, coil compaction, or coil migration into pre-existing thrombus. In the past GIAs frequently required retreatment, sometimes multiple times. Even the use of BAC and SAC did not adequately addressed these high rates of recanalization [55, 56] (Fig. 10.3).

- *Liquid embolics*

  This technique is largely of historical interest [57].Liquid embolic delivery requires balloon inflation across the aneurysm neck. The

balloon must remain inflated for at least 3 min after injection of the embolic agent, allowing the agent to precipitate inside the aneurysm. These risks, along with concerns about long-term durability, have limited the use of liquid embolic agent use to treat GIAs.

- *Parent vessel occlusion*

  Again, rarely needed in the modern era, parent vessel occlusion (PVO) to treat GIAs of the carotid artery dates back to the eighteenth century when it was first described by Cooper in 1809. PVO can be performed by several techniques including coil embolization and/or Onyx embolization. In most patients with unruptured aneurysms presenting with mass effect on the cranial nerves, symptoms are improved soon after therapy [58]. Complications from endovascular PVO

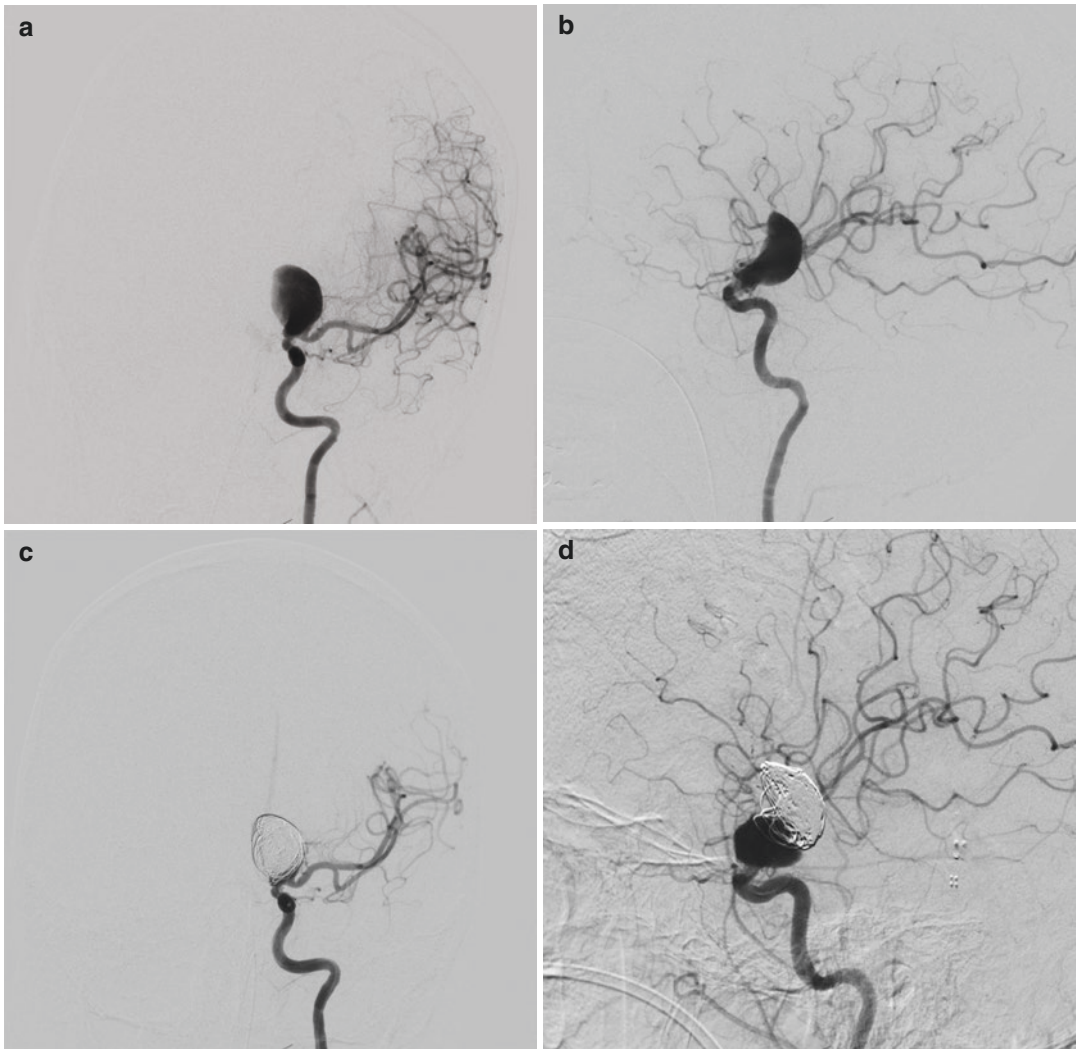

Fig. 10.3 Patient with left ICA terminus aneurysm measuring 20 mm × 10 mm. The patient failed pipeline embolization due to the MCA take-off being in proximity to the aneurysm, patient eventually taken for a craniotomy for extracranial-intracranial bypass with right radial artery graft and obliteration of right internal carotid artery. (**a**, **b**) show a left carotid injection demonstrating the aneurysm. (**c**, **d**) Initial embolization demonstrates a large coil mass. (**e**) Demonstrates recanalization of the aneurysm. (**f**, **g**) demonstrate a patent radial artery graft ensuring good blood flow to the left MCA territory

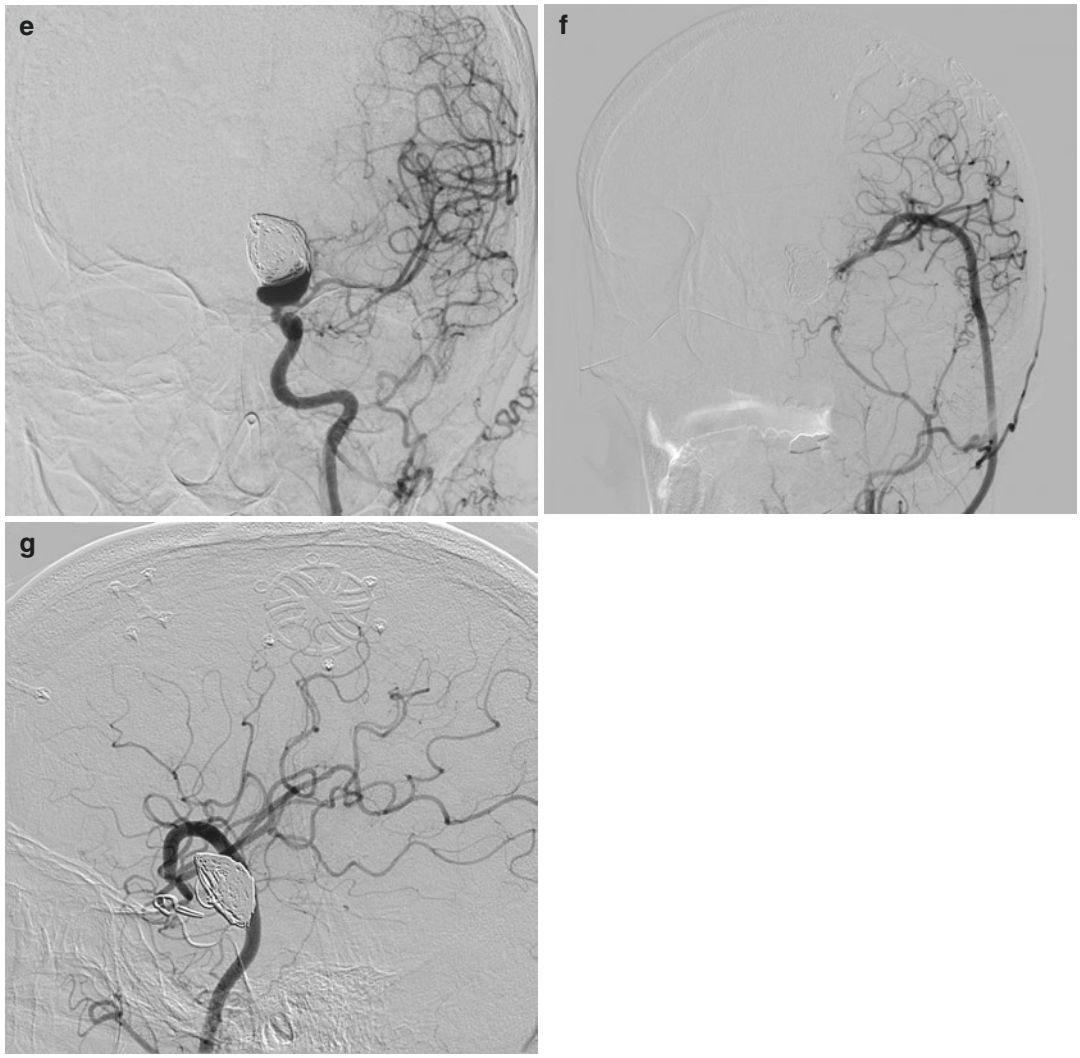

Fig. 10.3 (continued)

therapy for GIAs include (a) increased local mass effect from aneurysm thrombosis or the devices used to achieve aneurysm occlusion, (b) subarachnoid hemorrhage, and (c) stroke from thromboembolic events. In a series of 15 patients undergoing endovascular PVO, one patient developed new sixth cranial nerve palsy, three patients had access site complications, and one died from aneurysm rupture [59].

- *Flow diversion*

  Flow diversion is effective in treating the majority of GIA. The technology was initially developed to treat aneurysms with morphologies not amenable to coil embolization. Flow diversion results in disruption of flow near the aneurysm neck, inducing thrombosis in the aneurysm sac while keeping the physiological blood flow in the parent vessel and adjacent branches intact.

  Reports on the use of the PED include aneurysms of all sizes. A literature review on the outcomes of aneurysmal flow diverters showed immediate angiographic aneurysm occlusion in only 8–21% of patients. However, over time the aneurysm occlusion rates were

higher than conventional treatments with complete occlusion ranging from 69% at 6 months to >90% at 1 year, even with large and giant aneurysms [60, 61]. The PITA trial (Pipeline for the Intracranial Treatment of Aneurysms) included 31 aneurysms, nine were large and two were GIAs. Follow-up complete aneurysm occlusion was observed in 28 of 30 (93.3%) patients, and residual aneurysm filling was noted in two (6.7%). Some users have used a coil-assisted flow-diverter technique, whereby coils are placed into the aneurysm to promote better aneurysm sac occlusion, particularly for large or acutely ruptured aneurysms. This has not been found to be associated with increased aneurysm occlusion rate. Lubicz et al. advocate the use of additional coiling only in aneurysms with high risk of rupture or to restrict the PED coverage to a single device in order to minimize the risk of side branch occlusion [60]. If there is residual aneurysm after placing the PED, some interventionalists will place a second stent across the first one to further increase the metal coverage of the aneurysm neck.

The main limitation of the PED is the potential latency period before aneurysm thrombosis takes place; this is particularly challenging for ruptured aneurysms. Complications of the PED include in-stent thrombosis (6%), in-stent stenosis (1%), intracranial hemorrhage (3.8%), and perforator vessel occlusion [62]. Szikora reported a 1.75% rate of severe hemorrhagic complications (mostly delayed ipsilateral parenchymal or subarachnoid hemorrhage) after using the PED, resulting in a 0.75% permanent morbidity rate and a 1% mortality rate [61, 63]. In PITA, two patients had periprocedural stroke, and no other neurologic deterioration was observed in any of the patients at discharge [64].

Siddiqui et al. [65] reported their experience with flow-diverting stents in the treatment of large or giant intracranial vertebrobasilar aneurysms in seven patients. Pipeline devices were placed in six patients and the Silk device (Balt Extrusion, Montmorency, France) in one patient. Four of seven patients treated with the PED died on follow-up, while the other three had mRS scores of 5 (severe disability), 1, and 0. The deaths resulted from aneurysmal rupture in two patients and poor neurological status related to presenting brainstem infarcts and subsequent withdrawal of care in the other two patients. This report has raised questions about the safety of flow diversion in the posterior circulation.

Conclusion

The treatment of unruptured intracranial aneurysms requires a holistic approach to the patient. A good understanding of the natural history of the disease as well as a careful consideration of all management options is required to ensure good patient outcomes. Novel endovascular options promise to further advance the way we treat aneurysms by providing safer and more efficient treatment options.

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