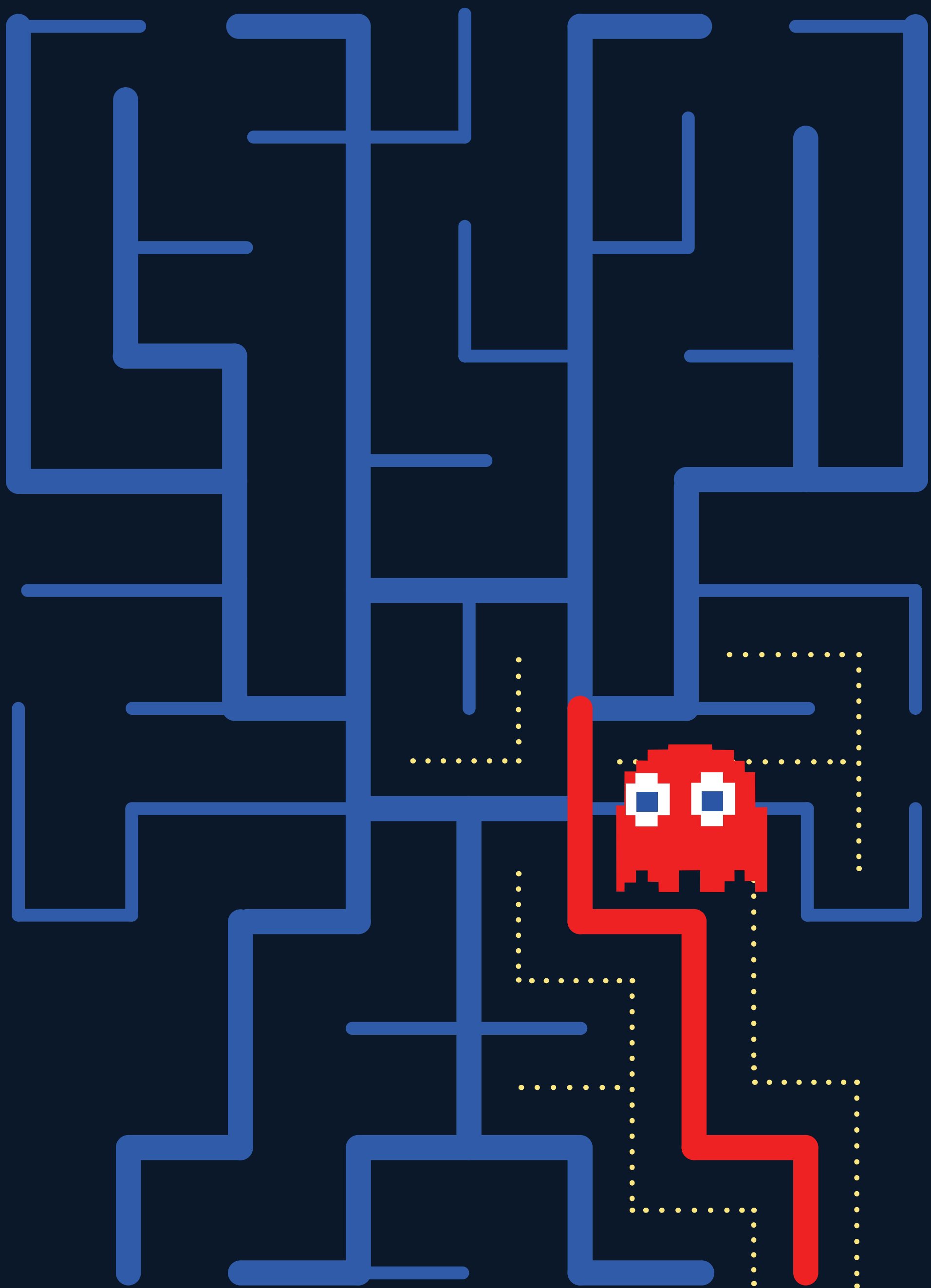
Complex Internal Carotid Artery Aneurysms



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Complex Internal Carotid Artery Aneurysms

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Academic Dissertation

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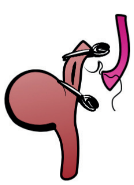

To Helena, Lili and Luka

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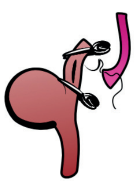

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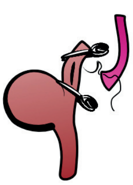


List of original publications

This thesis is based on
the following publications:

I Nurminen V, Lehecka M, Chakrabarty A, Kivisaari R, Lehto H, Niemelä M, Hernesniemi J; *Anatomy and morphology of giant aneurysms – angiographic study of 125 consecutive cases.* Acta Neurochirurgica. 2014;156(1):1–10

II Nurminen V, Kivipelto L, Kivisaari R, Niemelä M, Lehecka M; *Bypass Surgery for Complex Internal Carotid Artery Aneurysms: 39 Consecutive Patients.* World Neurosurgery. 2019;126:e453-e462

III Nurminen V, Raj R, Numminen J, Kivisaari R, Niemelä M, Lehecka M; *Flow Diversion for Internal Carotid Artery Aneurysms: Impact of Complex Aneurysm Features and Overview of Outcome.* Clinical Neurology and Neurosurgery. 2020;193:105782

The publications are referred to
in the text by their Roman numerals.

Abbreviations

3D-TOF-MRA ...... three-dimensional time-of-flight magnetic resonance angiography
A1 .... A1 segment of anterior cerebral artery
ACA .... anterior cerebral artery
AChA ...... anterior choroidal artery
ACP .... anterior clinoid process
Acom ...... anterior communicating artery
ADPKD ... autosomal dominant polycystic kidney disease
ASA .... acetylsalicylic acid
BAC .... balloon-assisted coiling
BBA .... blood blister-like aneurysm
BTO .... balloon test occlusion
C1 .... C1 segment of internal carotid artery
C2 .... C2 segment of internal carotid artery
C3 .... C3 segment of internal carotid artery
C4 .... C4 segment of internal carotid artery
C5 .... C5 segment of internal carotid artery
C6 .... C6 segment of internal carotid artery
C7 .... C7 segment of internal carotid artery
CCA .... common carotid artery
CND .... cranial nerve
CN .... cranial nerve dysfunction
COM .... carotid-oculomotor membrane
CSF .... cerebrospinal fluid
CT .... computed tomography
CTA .... computed tomography angiography
DAPT ...... dual antiplatelet therapy
DSA .... digital subtraction angiography
EEG .... electroencephalography
ECA .... external carotid artery
EC-IC ...... extracranial-to-intracranial
EVD .... external ventricular drain
FD .... flow diverter
FL-VA ...... fluorescein videoangiography
GIA .... giant intracranial aneurysm
HUS .... Helsinki University Hospital
ELANA .... excimer laser–assisted nonocclusive anastomosis
IA .... intracranial aneurysm
IC-IC .... intracranial-to-intracranial

ICA	internal carotid artery
ICG-VA	indocyanine green videoangiography
ICH	intracerebral hemorrhage
IMA	internal maxillary artery
IOM	intraoperative monitoring
LMWH	low-molecular-weight heparin
M1	M1 segment of middle cerebral artery
M2	M2 segment of middle cerebral artery
M4	M4 segment of middle cerebral artery
MCA	middle cerebral artery
MR	magnetic resonance
MRA	magnetic resonance angiography
MRI	magnetic resonance imaging
mRS	modified Rankin Scale
OA	occipital artery
OKM	O'Kelly-Marotta grading scale
OphtA	ophthalmic artery
PAA	posterior auricular artery
PAO	parent artery occlusion
PET	positron emission tomography
PICA	posterior inferior cerebellar artery
Pcom	posterior communicating artery
PED	Pipeline™ Embolization Device
RAG	radial artery graft
RROC	Raymond and Roy Occlusion Classification
SAC	stent-assisted coiling
SAH	subarachnoid hemorrhage
SELANA	seamless excimer laser–assisted nonocclusive anastomosis
SHA	superior hypophyseal artery
SPECT	single-photon emission computed tomography
STA	superficial temporal artery
SVG	saphenous vein graft
TCD	transcranial Doppler
VB-PCA	vertebrobasilar and posterior cerebral artery

Abstract

Objectives

Complex intracranial aneurysms represent vascular lesions with attributes complicating their treatment. Giant intracranial aneurysms (GIA; ≥25 mm) are a rare subgroup of complex aneurysms with a particularly poor natural history. Due to their large size, giant aneurysms often present with cranial nerve dysfunctions. In this retrospective study, we aimed to provide a comprehensive description of the anatomical features of giant aneurysms in the internal carotid artery (ICA). Complex aneurysms are often difficult to approach directly, necessitating indirect treatment strategies. We therefore analysed a case series of bypass surgery and flow diversion in relation to the execution and outcomes in different segments of the ICA.

Methods

All patients were admitted to the Helsinki University Hospital and for the analyses they were retrospectively recalled from the aneurysm database. For the series of giant aneurysms, we identified 125 patients with 129 GIAs (50 aneurysms in the ICA), from 1987 to 2007. For the series of bypass surgeries, included were 39 patients with 41 complex ICA aneurysms that were treated between 1998 and 2016. For the series of flow diversions, 62 patients with 76 ICA aneurysms were included from 2014 to 2019. In the treatment-oriented series, we analysed the internal carotid artery in segments, as this dictates the selection of treatment strategy. All the imaging studies and medical records were reviewed for relevant features in relation to aneurysms, complications and patient outcomes.

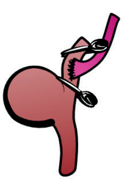
Results

The ICA was the most frequent location for GIAs in the cerebral arteries (39%) and most of these aneurysms were located specifically in the cavernous ICA segment (42%). Half of all GIAs presented mainly with symptoms of mass effect (50%). The cavernous GIAs were only rarely ruptured (10%) in contrary to the supraclinoid GIAs (36%). In general, wall calcification and intraluminal thrombosis were more seldom diagnosed in ruptured than in unruptured

GIAs. In treatment of the complex ICA aneurysms with bypass procedures, the strategic goal of aneurysm treatment was achieved in 95% of cases (occlusion, 83%; flow modification, 12%). With flow diversion of the ICA aneurysms, 61% of aneurysms were occluded at 6-month follow-up and 69% at the latest follow-up. In both groups of treatment, the cavernous aneurysms became occluded slightly more often than the aneurysms in the supraclinoid region. Posttreatment large-scale strokes were rare (3–6%), but minor complications were seen more often. The pretreatment cranial nerve dysfunctions improved only moderately at best (cranial nerve-specific improvement rate of up to 60%). Respectively in groups of bypass and flow diversion, 74% and 85% of patients with unruptured aneurysms had favourable outcome at the latest follow-up. In both groups, only 25% of patients having unruptured aneurysms and presenting with poor functional status improved significantly to having a favourable outcome.

Conclusions

The ICA is the most common location for GIAs and patients often present with symptoms of mass effect. Indirect treatment of complex ICA aneurysms with bypass procedures or flow diversion is feasible. Major treatment-related complications are rare, but minor complications occur at a non-negligible rate. Cranial nerve dysfunctions improve only in a proportion of patients. Lately, flow diverters have taken over the treatment of many complex ICA aneurysms, but the best treatment strategy should be assessed on a case-by-case basis, taking into consideration the burden of complex features of these ICA aneurysms. ❦



Tiivistelmä
(abstract in Finnish)

Tavoitteet

Kompleksiesilla kallonsisäisillä aivovaltimopullistumilla eli aneurysmilla on ominaisuuksia, jotka tekevät aneurysmien hoidosta vaikeaa. Jättianeurysmat (≥25 mm) ovat harvinainen kompleksien aneurysmien alaryhmä, ja hoitamattomana niillä on erityisen huono ennuste. Kokonsa takia jättianeurysmat tulevat esille usein aivohermojen toimintahäiriöitä aiheuttaen. Tässä retrospektiivisessä tutkimuksessa tavoitteemme oli seikkaperäisesti kuvailla sisemmän kaulavaltimon (internal carotid artery, ICA) alueella sijaitsevien jättianeurysmien anatomisia ominaisuuksia. Kompleksien aneurysmien hoitamiseksi tarvitaan usein epäsuoria menetelmiä aneurysman sulkemiseksi. Tämän takia analysoimme myös aivovaltimo-ohitusleikkausten sekä virtausohjureiden (flow diverter) hoidolliset tulokset sisemmän kaulavaltimon alueella sijainneiden aneurysmien osalta.

Menetelmät

Kaikki tutkimukseen sisällytetyt potilaat olivat olleet hoidossa HUS Helsingin yliopistollisessa sairaalassa, ja potilastiedot haettiin aneurysmarekisteristä. Yhteensä 125 potilaalla oli todettu 129 erillistä jättianeurysmaa (50 aneurysmaa sisemmän kaulavaltimon alueella) vuosien 1987 ja 2007 välillä. Aivovaltimo-ohiteleikkauksessa olleita potilaita oli yhteensä 39 ja heillä oli todettu 41 aneurysmaa, jotka hoidettiin vuosien 1998 ja 2016 välillä. Virtausohjurilla hoidettuja potilaita oli yhteensä 62 ja vastaavasti heillä oli diagnosoitu 76 aneurysmaa, jotka hoidettiin vuosien 2014 ja 2019 välillä. Hoitomenetelmiin keskittyneissä potilassarjoissa analysoimme sisemmän kaulavaltimon aneurysmat segmenteittäin, koska aneurysman sijainti määrittää hoitostrategian valintaa. Kaikki kuvantamistutkimukset sekä potilastiedot analysoitiin aneurysmiin, hoidon komplikaatioihin ja hoitotuloksiin liittyvien olennaisten tietojen osalta.

Tulokset

Sisempi kaulavaltimo on yleisin sijainti jättianeurysmille aivovaltimoiden alueella (39%), ja useimmat näistä aneurysmista sijait-

sevat edelleen kavernöottisen valtimosegmentin alueella (42%). Puolet kaikista jättianeurysmista oli diagnosoitu pääasiallisesti paineoireiden vuoksi (50%). Kavernöottiset jättianeurysmat olivat vain harvoin puhjenneita (10%), mutta kovakalvon sisäpuolitse sijainneet aneurysmat olivat vuotaneet useammin (36%). Jättianeurysman seinämän kalkkeutuneisuutta tai verihyytymää aneurysman sisällä nähtiin harvemmin vuotaneissa kuin vuotamattomissa aneurysmissa. Kompleksien aneurysmien hoidossa aivovaltimo-ohitusleikkauksilla saavutettiin strateginen tavoite 95% tapauksista (aneurysman sulkeutuminen, 83%; virtausolosuhteiden muutos, 12%). Virtausohjureilla toteutetussa hoidossa 61% aneurysmista oli sulkeutunut kuuden kuukauden seurantahetkellä ja kaikkiaan 69% viimeisten seurantakäyntien kohdalla. Molempien hoitomenetelmien kohdalla kavernöottiset aneurysmat sulkeutuivat hieman kovakalvon sisäpuolitse sijainneita aneurysmia useammin. Toimenpiteiden jälkeiset laaja-alaiset aivoverenkiertohäiriöt olivat harvinaisia (3–6%), mutta vähäisempiä komplikaatioita nähtiin useammin. Toimenpiteitä edeltäneet aivohermojen halvausoireet kohenivat vain kohtalaisesti (aivohermokohtaisen oireen lievittyminen enimmillään 60% tapauksista). Vuotamattoman aneurysman omanneiden, ja aivovaltimo-ohitteella tai virtausohjurilla hoidettujen potilaiden kohdalla vastaavasti 74% ja 85% potilaista oli toimintakyvyltään itsenäisiä viimeisen seurantakäynnin ajankohdalla. Potilaista, joilla oli vuotamaton aneurysma, ja jotka olivat jo sairaalaan tullessa huonokuntoisia, vain 25% toipui itsenäiseen elämään.

Johtopäätökset

Sisempi kaulavaltimo on yleisin sijainti jättianeurysmille ja näillä potilailla on usein aneurysman aiheuttamia paineoireita. Epäsuora aneurysmien hoito aivovaltimo-ohitteilla tai virtausohjureilla on toteuttamiskelpoista. Vakavat hoitoon liittyvät komplikaatiot ovat harvinaisia, mutta vähäisempiä komplikaatioita todetaan merkittäviä määriä. Viime vuosina virtausohjureilla on hoidetty yhä enemmän komplekseja aneurysmia, mutta paras hoitomenetelmä tulisi valita tapauskohtaisesti ja punniten erilaisten kompleksien ominaisuuksien yhdistelmien aiheuttamaa kokonaishaastetta. ❦

Introduction

Among neurosurgical challenges, the small subgroup of complex intracranial aneurysms represents one of the biggest problems for vascular neurosurgeon.[1–5] As the name implies, there have been no simple solutions for treating these lesions.

The internal carotid artery is the most common location for intracranial aneurysms.[6–10] Consequently, complex aneurysms of various etiologies are often diagnosed in this segment. Especially giant aneurysms (minimum diameter of 25 mm) are characterized by multiple complex attributes. However, due to the rarity of these lesions, relatively little is known about their anatomical and morphological features in relation to smaller aneurysm counterparts.[11,12]

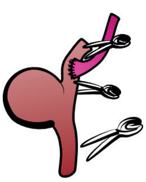
In addition to the risk of causing stroke in the form of subarachnoid hemorrhage, complex aneurysms may present with ischaemic attacks or tumor-like symptoms.[6,13] Due to their size, giant aneurysms often compress cranial nerves in their vicinity.[14] If these aneurysms are left untreated, the general prognosis is comparable to terminal cancer at poorest.[6,15]

Neurosurgical treatment methods have developed vastly during the last two centuries. From times of an adventurous neurosurgeon stepping into the unknown, a modern neurosurgeon is equipped with diagnostic and surgical aids and tools that have advanced tremendously. The cumulative worldwide knowledge and experience of treating these lesions has provided some guidance. This has led to a situation wherein more complex aneurysms are nowadays manageable. On the other hand, requirements for quality and outcome of treatment have progressed in conjuction with patient's expectations.

Two main avenues of treatment are available.

Direct microsurgical treatment necessitates visualization of the lesion, and this is achieved by accessing the deep intracranial space under a microscope. During the last decades, endovascular treatment via catheterization of arteries has provided a much less invasive alternative to reach an aneurysm. Still, the direct treatment of complex aneurysms only seldom yields constant results and major complications can be encountered.

Indirect aneurysm treatment focuses on obliteration or repair of the parent artery from which the aneurysm originates. The advantage of this strategy is that the complexity of the target aneurysm often becomes secondary as the approach is more like a blockade than a direct hit. Parent artery occlusion combined with microsurgical bypass procedure, i.e. distal revascularization of the occluded artery carrying the aneurysm, and endovascular stent-like flow diverters are the two main types of indirect treatment.[16–19] Bypass procedures are performed only in dedicated neurovascular centers (only a single center in Finland), so the publications are limited. Flow diversion is one of the newest endovascular treatment methods, and thus, more reports on treatment of especially complex aneurysms are needed. ❦



Review of the literature

2.1 INTRACRANIAL ANEURYSMS

2.1.1 DEFINITION OF INTRACRANIAL ANEURYSMS

Intracranial aneurysms (IAs) are pathologic outpouchings of cerebral arteries. They are typically located at branching points of arteries. As the caliber of intracranial arteries is only a few millimeters at the widest, also the common intracranial aneurysms have similar small dimensions. The prevalence of IAs in the population is 2–3%.[10,20]

2.1.2 RISK FACTORS FOR DEVELOPING ANEURYSMS

Intracranial aneurysms are considered to be acquired lesions caused mainly by a combination of inflammatory and hemodynamic stress at the arterial wall.[21] Reported risk factors for developing IAs are female sex, family history of IAs, smoking, hypertension, heavy alcohol use and, in young adults, cocaine use (Table 1).[22–26] Few primarily hereditary connective tissue conditions may confer increased risk for IA development while the autosomal dominant polycystic kidney disease (ADPKD) has the strongest association.[27,28] Aneurysms may accompany various other intracranial vascular pathologies, e.g. arteriovenous malformations and Moyamoya disease.[29–31]

2.1.3 SUBARACHNOID HEMORRHAGE

2.1.3.1 Incidence of subarachnoid hemorrhage

Typical small IAs are silent asymptomatic lesions and become symptomatic only when the aneurysm wall abruptly ruptures leading to subarachnoid hemorrhage (SAH), a specific form of stroke. The general incidence of SAH in the population is approximately 9 per 100.000 person-years, and the incidence has been declining for the past decades.[36,37] On the contrary to previously reports, the incidence of SAH in Finland is no higher than in other countries.[37] SAH causes substantial excess mortality as 27–44% of all patients die despite modern treatment.[38,39]

2.1.3.2 Risk factors for aneurysm rupture

At present, many unruptured IAs are diagnosed in brain imaging studies carried out because of unrelated symptoms.[20] For patients with unruptured IAs, the annual average rate of rupture is estimated to be 1%.[8,32] However, the patient-specific risk factor bur-

Table 1
Reported risk factors for aneurysm development and rupture.

For aneurysm development[22–28]	For aneurysm rupture[6,8,32–35]
Female sex	Female sex
Smoking	Age inversely
Hypertension	Smoking
Heavy alcohol use	Hypertension
(Cocaine use)	Aneurysm size over 7 mm
Family history of IAs	Aneurysm growth
Hereditary predisposition (e.g. ADPKD)	Aneurysm location
	Irregular aneurysm shape

den affects the individual total risk. Reported risk factors for aneurysm rupture overlap with those predisposing to initial aneurysm formation; female sex, smoking, hypertension, patient age inversely as well as aneurysm size over 7 mm, growth, location and irregular shape (table 1).[6,8,32–35]

2.1.4 DIAGNOSTICS

2.1.4.1 Unruptured aneurysms
The ‘gold standard’ to diagnose vascular pathologies is invasive digital subtraction angiography (DSA) with high spatial resolution. Computed tomography angiography (CTA) may be superior to DSA in treatment planning, but the smallest aneurysms (<3–5mm), or aneurysms beside bony base of the skull may escape detection.[40–42] To further minimize risks of ionizing radiation and catether-related complications, three-dimensional time-of-flight magnetic resonance angiography (3D-TOF-MRA) gives good diagnostic performance for IA detection in low-risk patients.[43] Together, CTA and MRA have a combined sensitivity of 76–98% and specificity of 85–100%.[44]

2.1.4.2 Ruptured aneurysms
In patients suffering of SAH, the accumulation of blood is well visualized in non-contrast computed tomography (CT) during the first six hours after onset.[45,46] With symp-tomatic high-risk patients having clean CT later than six hours after ictus, lumbar puncture and cerebrospinal fluid (CSF) analysis is used to confirm possible presence of degradation products of blood and hemoglobin. CTA is the primary modality for detection of ruptured aneurysms in emergency departments.[47,48] In CTA negative cases with diffuse SAH, DSA may reveal atypical aneurysms in a small proportion of patients.[49]

2.1.5 TREATMENT

2.1.5.1 The premicrosurgical era
In 1785, the Hunterian ligation of an artery was first performed by Scottish surgeon John Hunter for a peripheral aneurysm in the lower extremity (Table 2).[50–53] Then in the early 1800s, ligation of the cervical common carotid artery was first applied by Cooper.[54] In 1885, Horsley operated on a patient thought to have a brain tumour, but a gi-

ant internal carotid artery aneurysm was revealed; both cervical carotid arteries were ligated, and the patient experienced a good recovery.[55] In 1911, after abrupt artery occlusions, Matas described the temporary compressive occlusion of artery in order to assess the distal collateral reserve.[56] In 1931, Dott was the first surgeon to expose a ruptured midde cerebral artery aneurysm and wrap it in a piece of muscle.[57] In 1932 by Olivecrona and in 1935 by Dandy, the carotid artery trapping technique was introduced.[58,59] Later in the following decades, Mount and Crutchfield among others, reported on clamps, which allowed gradual occlusion of the cervical carotid artery to achieve control on, and reduce the rate of otherwise common ischaemic complications.[60–62] The basic principle of Hunterian ligation is still used in modern neurosurgery.

2.1.5.2 The microsurgical era

To be prepared for intracranial aneurysm surgery, preoperative diagnostics had to be developed further. In 1927, Moniz introduced the concept of arterial angiography which made the diagnosis of intracranial aneurysms by imaging possible.[63] Already before in 1911, Cushing had developed "the silver clip" for occluding vessels in tumor surgery.[64] However, it was Dandy in 1937, who became the first neurosurgeon to perform a planned surgical clip ligation of an intracranial aneurysm.[65] In 1957, Kurze was the first to introduce the operating microscope in order to better visualize structures. After 1966, Yasargil popularized the microscope in aneurysm surgery.[66,67] Since, the optics and software of microscopes have progressed vastly; e.g. in 2003, indocyanine green video angiography (ICG-VA) was applied to neurovascular surgery in order to visualize blood flow in arteries.[68] Also, real-time image-guidance or heads-up display (HUD) navigation may be used in complex lesions.[69] Lately, separated camera and screen units (exoscopes) have entered the market.[70]

2.1.5.3 The revascularization era

After the historical technique of Hunterian ligation and occlusion of arteries, it took over 150 years of technical development to achieve the capabilities for revascularization. In 1963, Woring was first to publish on extracranial-to-intracranial (EC-IC) cerebral artery bypass, but Yasargil's experience in 1967 again popularized the idea.[71,72] In Yasargil's case, superficial temporal artery-to-middle cerebral artery (STA-MCA; "low flow") bypass revascularized region of ischaemic brain caused by artery occlusion.[72] In 1971, Lougheed utilized a saphenous vein graft (SVG) in "high-flow" type bypass after the idea was already being applied to coronary artery disease.[73,74] Since then, many neurosurgeons (e.g. Sundt, Sekhar, Spetzler and Lawton) further refined the bypass indications, strategies and techniques during the last decades; new bypass donor and recipient sites (e.g. intracranial-to-intracranial [IC-IC] bypass), graft types, anastomoses as well as anesthesia and monitoring modalities have emerged.[75–88] Also in 1993, the first patient was treated with the excimer laser–assisted nonocclusive anastomosis (ELANA) technique which was developed for the purpose of performing anastomoses without temporary artery occlusion.[89] The further developedment lead to concept of a seamless ELANA (SELANA) which has not yet succeeded in clinical trials.[90] In 2018, Lawton published the idea of categorizing bypasses by generations, variations and anatomical locations in order to standardize the different strategies.[91]

2.1.5.4 The endovascular era

Endovascular (i.e. via vessel lumen) treatments represent the most recent decades of technological advances in aneurysm treatment.[92] In 1964 Luessenhop and Velasquez performed the first catheterization of intracranial arteries.[93] In 1974, Serbinenko intro-

Table 2
Developmental steps in neurosurgical treatment techniques.

Premicrosurgical era	Microsurgical era	Bypass era	Endovascular era
1785; Hunterian ligation **1885;** carotid ligation for ICA aneurysm			
	1911; "silver clip" **1927;** angiography		
1931; wrapping **1932 – 1935;** trapping	**1937;** aneurysm clipping		
1950s onwards; vascular clamps	**1957 – 66;** microscope		
	late 1960s; pterional craniotomy	**1963 – 67;** EC-IC bypass	**1964;** catetherization of intracranial arteries
		1971; bypass grafts **1970s onwards;** new recipient and donor sites, IC-IC bypass	**1974;** balloon occlusion
			1980s; glue-like embolic materials
		1993; ELANA	**1990s;** coiling **1996;** stenting with cardiac stents **1997 onwards;** BAC and SAC
	2003; ICG-VA		**2004;** cerebrovascular stents
	2010s onwards; modern exoscopes		**2010s onwards;** flow diversion

duced the balloon catheterization for selective diagnostic and treatment purposes.[94] During the 1970s and 1980s, the endosaccular aneurysm balloon occlusion gained popularity, but treatment resulted in high rate of complications.[92] During the same time, experimentation was done with glue-like embolic material.[95,96] In 1991, Guglielmi's version of detachable coils and electrothrombosis took its place in the forefront of endovascular treatment.[97,98] In 1996, Feldman was the first to perform carotid artery stenting with a coronary stent.[99] Then, in 1997, Moret proposed the "remodeling technique" of balloon-assisted-coiling (BAC) to achieve denser packing of coils in wide-necked aneurysms.[92] Stent-assisted-coiling (SAC) was developed at approximately the same time, still with cumbersome coronary stents which necessitated balloon inflation for deployment.[100,101] Not until 2004, the first self-expanding stent for neurovascular indications was introduced.[102] Coming to the 2010s, parent artery flow diverters, and endosaccular flow disruptor devices were invented.[103,104]

2.1.5.5 Present armamentarium

The modern neurosurgeon is supplied with a wide variety of microsurgical and endovascular treatment methods for aneurysm occlusion. The two main types of direct aneurysm treatment, however, still are microsurgical clipping and endovascular coiling. As the complexity of lesion increases, other endovascular modalities such as BAC, SAC or flow disruptors are considered devices among others. If treatment of target aneurysms is not feasible with these direct methods, parent artery occlusion with or without bypass procedures or flow diverters may be considered.

2.1.5.6 Decision-making in unruptured aneurysms

The main goal of treatment in unruptured aneurysms is to prevent aneurysm rupture and SAH. The clinician estimates the patient-specific rupture risk of the target aneurysm, and scoring systems exist to aid in this process. For example, PHASES scoring combines factors based on six prospective trials of unruptured aneurysms.[105] Another recently published, simplified, scoring system based on prospective follow-up of a Finnish cohort introduces four parameters for rupture risk scoring; age, smoking status (not included in PHASES score), IA size and location.[106]

Then, aneurysm rupture risk should be weighted against the treatment-related risks to further give recommendations whether to treat the aneurysm, and with which modality. The largest studies to date (e.g. ISUIA) have compared the microsurgical clipping and endovascular coiling in unruptured aneurysms. In general, the results encouraged to utilization of endovascular coiling, but discussion on the long-term outcomes of different modalities continues.[6,107–110] Meta-analyses of unruptured aneurysms report a poor outcome of 6.7% (including mortality of 1.7%) in surgically treated patients and 4.7% (including mortality of 1.8%) in endovascular cases.[111,112] According to ISUIA, large or giant aneurysms share the poorest outcomes (25–34% of cases), with the rate exceeding 40% in giant aneurysms of the posterior circulation.[6]

In low-risk aneurysms for which active treatment is not considered justified, conservative treatment of risk factors is important. Cessation of smoking and treatment of hypertension are the measures a patient can take to decrease the risk of aneurysm growth and rupture.[113,114] Currently, the significance of acetylsalicylic acid as a preventive medication is investigated.[115,116] Also, follow-up imaging of unruptured aneurysms is usually needed in younger, working age patients as 9% of aneurysms show growth according to a meta-analysis.[117]

In higher risk aneurysms, obliteration of lesion is pursued. The availability of treatment methods, as well as the capabilities of different neurosurgical units vary.[118] For optimal surgical outcome, the neurosurgeon should be experienced,[119] the patient should be young and in good general fitness,[6,110,120] the aneurysm should be straightforward to approach and there should be a clear aneurysm neck for a clip placement. On the other hand, endovascular treatment is much less invasive, and usually favoured especially for older patients.[6] Also, certain surgically complicated, difficult-to-reach or eloquent regions, e.g. aneurysms near base of the skull, or in the posterior cerebral circulation, are nowadays mainly territory of endovascular treatment.[6] However, with endovascular methods, risk of aneurysm recurrency is higher and therefore necessitate follow-up imaging studies.[121,122]

2.1.5.7 Decision-making in ruptured aneurysms

After initial aneurysm rupture, and defined by clinical deterioration, 14% of patients suffer rebleeding already before reaching the hospital.[123] Of these patients surviving at least 24 hours, 22% experience rebleeding during the next four weeks with case fatality rate of 51%.[124] At one year, 65% of patients with ruptured but untreated aneurysms have died.[125]

Among patients surviving to hospital after SAH, the clinical prognosis is effected largely by age and neurological status, which is graded usually either on Hunt & Hess or WFNS scales.[126–131] Thus, ruptured aneurysms are considered for treatment as long as the presenting neurological status is not too poor.

The patients suffering from aneurysmal SAH are monitored routinely in the intensive care unit for neurological, respiratory and cardiovascular functions. Obliteration of a ruptured aneurysm is recommended to take place early, within 72 hours after onset of symptoms.[132] A few larger studies have compared the clipping and coiling of ruptured aneurysms (ISAT[7,133–135]; BRAT[136,137]; CARAT[138]). Again, there is some controversy regarding the clinical outcomes in long-term, but coiling seems to be associated with more re-treatments and re-ruptures although the absolute numbers are relatively small. European and American guidelines recommend coiling over clipping in ruptured aneurysms if both treatment options are considered equally effective, but interdisciplinary discussion between neurosurgeons and neurointerventionalists should be a standard protocol to find the best patient-specific solution.[107,139] However, these results may not be generalized to complex aneurysms.[140]

Also secondary complicating problems related to SAH, such as excessive accumulation of CSF (hydrocephalus) or delayed ischemic events due to arterial constriction (vasospasm) typically occur within the first days or weeks.[141,142]

2.2 COMPLEX ICA ANEURYSMS

2.2.1 DEFINITION OF COMPLEXITY

Approximately 33–42% of intracranial aneurysms are located in ICA.[6–10] Complex aneurysms represent a subset of IAs which have attributes complicating the treatment and occlusion possibilities with conventional surgical or endovascular methods. An estimated 5–10% of intracranial aneurysms have complex features. There is no definitive consensual agreement of these attributes and many reports of different aneurysms considered as complex have been published (Table 3).[1–5,143] The attributes defining complexity are often related to the size, shape, location, branching arteries or collateral circulation, and other morphological features. Hanel and Spetzler listed following features; 1) giant size (≥25mm); 2) difficult location; 3) previous treatment; 4) presence or absence of collateral circulation; 5) intraluminal thrombosis; 6) wall calcification.[1]

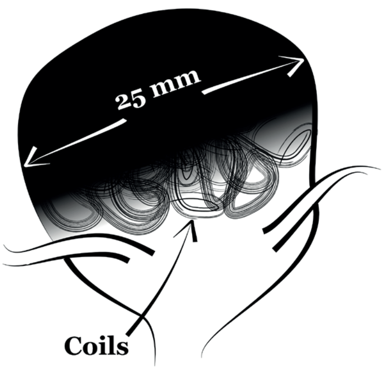
2.2.1.1 Giant aneurysms

Giant intracranial aneurysms (GIAs) are de-

Table 3
Features of aneurysms regarded as complex.

Feature
Giant size (≥25 mm)
Shape and morphology
- Fusiform
- Dolicoectatic
- Serpentine
- Blood blister-like aneurysm
- Dissecting aneurysm
- Pseudoaneurysm
- Wide aneurysm neck
- Intraluminal thrombosis
- Wall calcification
Difficult location
Incorporated artery branches
Recurrent aneurysms

Figure 1
Recurrent, previously coiled GIA having intraluminal thrombosis (black area) and two major artery branches originating from the wall.



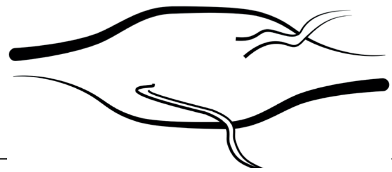
fined as aneurysms of all shapes with a minimum diameter of 25 mm (Figure 1). They represent less than 5% of all intracranial aneurysms and are most often located in the ICA.[8,11,110] It is not exactly known why certain aneurysms reach giant size, but growth of smaller IAs to such sizes has been documented.[144] Microvascularization and inflammation in intraluminal thrombus may result in repeated intramural microhemorrhages, and predispose to aneurysm enlargement. Serpentine aneurysms are a rare subtype of partially thrombosed GIAs with patent vascular channel coursing through the aneurysm mass and thrombus.[151] GIAs in particular tend to present with symptoms of tumor-like mass effect due to their size.[14,145,152,153]

2.2.1.2 Fusiform aneurysms and dolicoectasia
Fusiform aneurysms are circumferential, nonsaccular dilatations of artery segments (Figure 2). In contrary to saccular aneurysms, they do not have any defined aneurysm neck area. They are rare aneurysms, estimated to represent 1% of all intracranial aneurysms, and have a tendency to develop in the posterior cerebral circulation.[11,145,155] Atherosclerosis is one possible predisposing factor.[145] In comparison, dolicoectasia refers to an extensive pathology of an artery segment having morphological components of both elongation ("dolico") and distension ("ectasia").[156]

2.2.1.3 Other aneurysms without neck
Blood blister-like, dissecting and pseudoaneurysms have different etiologies, but share common features such as tears in the arterial wall and morphology of hemispheric bulges at nonbranching artery sites. All these aneurysm types represent less than 1–3% of all intracranial aneurysms.[157–163]

Blood blister-like aneurysms (BBA) are found almost invariably in the ICA with presentation of SAH (Figure 3). The suggested etiology is dissection of artery wall.

Figure 2
Fusiform aneurysm without identifiable neck. Small perforator arteries complicating treatment.



BBAs are prone to rupture when surgically approached, as only a thin sheet of adventitia covers the aneurysm. Exact diagnostic criteria of these lesions have not been defined.[160,164–168]

Spontaneus intracranial dissecting aneurysms are far less common than cervical artery dissections and the location of symptomatic lesions is more often in the posterior cerebral circulation than in the anterior circulation. Disruption of internal elastic lamina seems to be a common histologic finding in these lesions. A morphological feature in imaging studies is usually a segmental stenosis with subsequent dilatation of the affected artery. Presentation may be ischemic symptoms or SAH.[169–173]

Pseudoaneurysms have only a thin fibrous wall without any true vascular layers and as such, the etiology is usually artery wall injury due to trauma. Pseudoaneurysms of the ICA are typically located in the petrous or cavernous ICA near the base of the skull.[174–178]

2.2.1.4 Wide-necked aneurysms

Wide-necked aneurysms are most often defined as aneurysms having neck size ≥4mm or dome-to-neck ratio of <2 but the definition varies (Figure 4).[179] The wider the aneurysm neck is, the more problematic the occlusion with clipping is as complex clip configurations may be needed while nearby perforator arteries are endangered.[180–182] In endovascular treatment, difficulties arise with endosaccular treatment modalities; e.g. the coils tend to herniate from the aneurysm and do not properly maintain the 3D structure.[183,184]

2.2.1.5 Intraluminal thrombosis

Intraluminal thrombosis is generally found in 2% of aneurysms, but more often in larger aneurysms, and in up to 39% of GIAs (Figures 5–6).[8,11,15,185–187] A clinical classification scheme of thrombus morphology has been proposed by Lawton et al.[188] Giant thrombosed aneurysms mimic tumor masses and thrombosis is associated with more

Figure 3
Blood blister-like aneurysm.

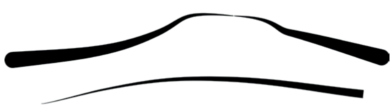
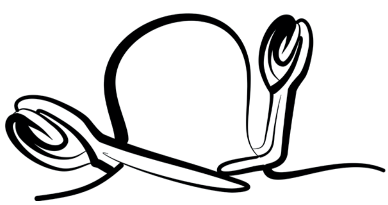


Figure 4
Wide-necked aneurysm requiring multiple clips for occlusion.



extensive radiological perianeurysmal parenchymal oedema.[189] To gain surgical access to these lesions, removal of thrombus may be needed (thrombectomy).[188] In thrombosed aneurysms, surgical treatment is reported to have better angiographic occlusion rates and less re-treatments in comparison to endovascular coiling, results mainly influenced by coil compaction into unstable thrombus mass.[185]

2.2.1.6 Wall calcification

Microscopic calcification of the aneurysm wall is detected in up to 78% of histological samples, but macroscopically only in less than 2% of imaged aneurysms (Figures 7–8).[8,190] Larger aneurysms (>10 mm) seem to more often have macroscopic calcification and up to 31% of GIAs are reported to present with such hardened shells.[11,17,191,192] Calcification of the aneurysm neck area may cause problems with the surgical clip positioning or clip blade closure and lead to clip slippage, or predispose to plaque emboli.[17,192–195] In comparison to endovascular approaches, surgical clipping of calcified aneurysms is a significant source of morbidity in unruptured aneurysms.[196]

2.2.1.7 Difficult location

Proximally, the cavernous or paraclinoid ICA segments (C4–5) near the base of the skull are more difficult to safely approach by surgical means due to the presence of bony projections and neurovascular structures traversing the packed region. Distally, the supraclinoid ICA (C6–7) has major branching arteries and small perforators along its course vulnerable to cause ischaemic complications.[4,197–201]

2.2.1.8 Incorporated arteries

Artery branches or perforators may be incorporated in the aneurysm dome or neck (Figure 9). The lenticulostriatal perforators are packed in the vicinity of the ICA bifurcation. These branches usually need preserva-

Figure 5
Intraluminal thrombosis.

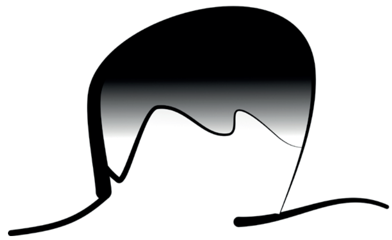


Figure 6
Axial MRI plane showing a left-sided GIA with extensive intraluminal thrombosis (black area).

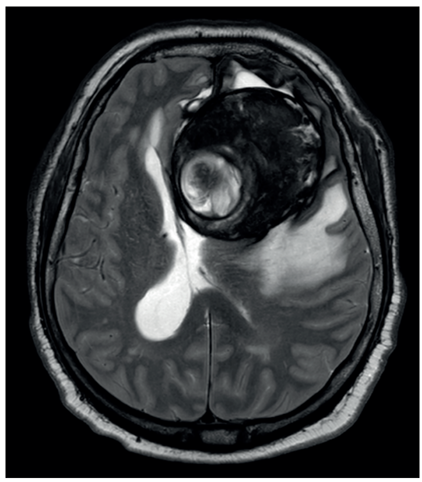
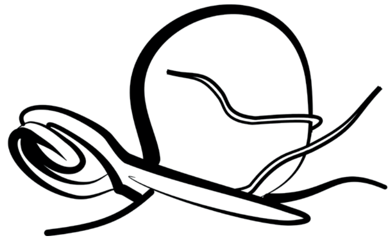


Figure 7
Calcified neck complicating clipping.

Figure 8
Axial CT plane without contrast showing left-sided GIA with wall calcification (white rim).

Figure 9
Perforators complicating clipping.



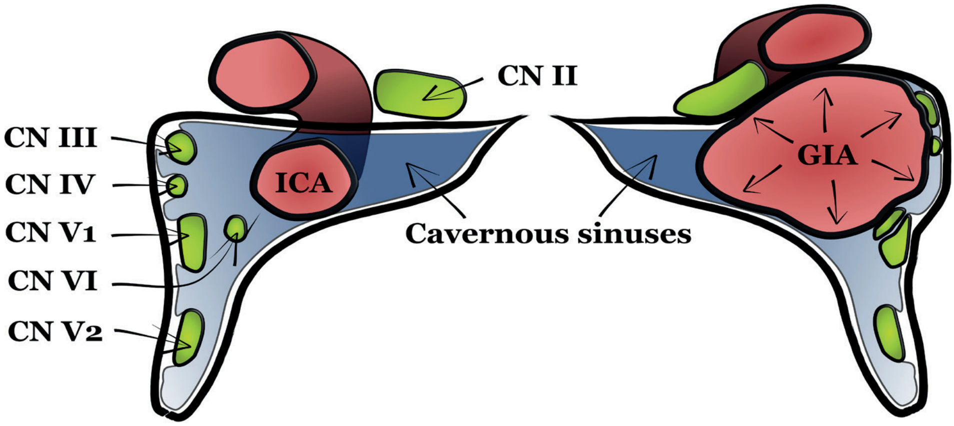
tion of patency in order to avoid ischaemic complications. On the other hand, the same branches may lead to persistent aneurysm remnants and residual filling if not occluded. Such factors present challenges in forming aneurysm occlusion strategies.[180,202–206] Sometimes bypass procedures targeted only to the branching arteries may allow the direct attack on aneurysm.[207]

2.2.1.9 Recurrent aneurysms
After aneurysm clipping, recurrence or regrowth of aneurysms is reported to occur in up to 3% of cases, and in as high as 14% of partially clipped aneurysms with initial residual filling.[122,137,208,209] With endovascular coiling, one fifth of aneurysms reopen during the follow-up according to a review study.[121] Retreament is 6.9 times more likely to be needed in aneurysms treated with endovascular coiling in comparison to surgical clipping.[210] Re-treatment of recurrent aneurysms may be challenging due to the presence of foreign material after original treatment (clips, coils etc.), scar formation after an extravascular surgical approach or distorted morphological features of recurred aneurysm.[211]

2.2.2 PRESENTATION OF COMPLEX ICA ANEURYSMS

2.2.2.1 Rupture and hemorrhage
Tendency to rupture varies among different types of complex aneurysms and large morphology-specific epidemiologic studies are generally lacking due to rarity of these lesions. The rupture rate of intradural GIAs is exceptionally high, up to 40–50% in five years, and if not treated, 18% of ruptured GIAs rebleed during the first two weeks with associated mortality of 33%.[6,15] In a series of ruptured GIAs, the most common site for aneurysms was the paraclinoid ICA.[15] Among fusiform aneurysms, a rupture rate of 3% per year is reported for posterior circulation wherein fusiform morphology is more common.[212] Ruptured blood blister-like or dissecting ICA aneurysms represent each less than 1% of all SAH cases.[163,172] The rare case of rupture of extradural, cavernous ICA aneurysm would typically lead

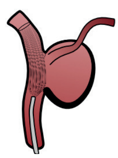
Figure 10
Coronal plane at the level of cavernous sinuses. On the right side, GIA at the carvenous ICA segment is causing compression on cranial nerves.



to development of carotid-cavernous fistula or epistaxis instead of SAH.[213,214]

2.2.2.2 Thromboembolism and ischaemia
To be considered as source of thromboembolism, the location of aneurysm in artery tree should anatomically match the clinical appearance of symptoms, and other common etiologies should be excluded (e.g. cervical carotid stenosis, cardiogenic embolus). Approximately 3% of patients with intracranial aneurysms present with thromboembolic symptoms, 40% of aneurysms seeding emboli are located in the ICA and most common clinical symptoms are motor deficits.[13] Even though radiological thrombi are more often encountered in larger aneurysms and GIAs, also small aneurysms (<10 mm) may seed emboli resulting in ischemic attacks.[215–217] Zhang et al. reported 20 patients with complex aneurysms (17%) presenting with ischaemic strokes in their surgical series.[218]

2.2.2.3 Cranial nerve dysfunctions
Cranial nerve dysfunctions (CNDs) are caused by compressive or ischemic etiologies.[219] Even small aneurysms may cause cranial nerve (CN) compression in two particular artery branching sites due to proximity of these structures. First, unruptured paraclinoid aneurysms near the ophthalmic artery may compress the optic nerve (CN II) in up to 38% of cases.[220,221] Second, isolated oculomotor palsy (CN III) is common finding in presentation of posterior communicating artery (Pcom) aneurysms affecting up to 34% of cases.[222–224] Due to their size and reach, large or giant aneurysms in the ICA may cause different combinations of vision deficit and ophthalmoplegia in addition to trigeminal nerve (CN V) involvement.[14,153,225–229] GIAs located in the cavernous or paraclinoid segment usually cause uniocular field loss due to optic nerve compression, and more superior aneurysms tend to cause biocular field defects due to lateral chiasma compression.[230] More lateral mass effect of cavernous GIAs seem to cause extraocular muscle palsies (oculomotor, CN III; trochlear, CN IV; abducens



nerve, CN VI) more often than medial mass which is explained by the relation of cranial nerves traversing the lateral border region of cavernous sinus (Figure 10).[153] Symptomatic compression of facial nerve (CN VII) due to internal carotid artery aneurysm is a rarity.[231–234]

2.2.2.4 Other symptoms of mass effects

Patients with GIAs may report nonspecific symptoms which are potentially related to mass effect (e.g. headache, dizziness etc). Hydrocephalus is a rare, but a specific possible complication of GIAs in the internal carotid artery. In such cases, the aneurysm is typically directed posteriorly and obstructs the third ventricle.[235–237] Pituitary gland dysfunction due to compression by an aneurysm is described mainly in case reports.[238,239]

2.3 TREATMENT-RELATED ANATOMY

2.3.1 CLASSIFICATIONS OF ICA SEGMENTS

In 1938 Fischer divided the internal carotid artery into five segments (C1-5) in order to describe patterns of arterial displacement by mass effect of intracranial tumors.[240] The segment numbering was in counterdirection in relation to arterial flow, starting from the carotid terminus. The segments were not constrained by anatomical compartments, thus reducing the accuracy.

Then, in 1981 Gibo proposed the division of the whole ICA into four segments starting from the cervical common carotid artery bifurcation and numbered in the direction of arterial flow (C1–4); the C4 segment was further divided into the ophthalmic segment, the communicating segment and to the most distal choroidal segment.[241] These subsegments of C4 give off intradural perforating arteries with relatively constant sites of termination.

The presently most commonly used classification was published in 1996 by Bouthillier et al (Figure 11).[201] They named seven different ICA segments (C1–7). The order of segments is again in the direction of arterial flow, and practical anatomical borders of different segments were honoured.

Later development of endovascular procedures and endoscopic, transsphenoidal neurosurgery has motivated a proposal of new anatomical classifications to better serve these subspecialties. However, these classifications are not widely used.[242,243]

Figure 11

ICA segments according to the Bouthillier's classification. C1, cervical; C2, petrosal; C3, lacerum; C4, cavernous; C5, clinoid; C6; ophthalmic; C7 communicating.

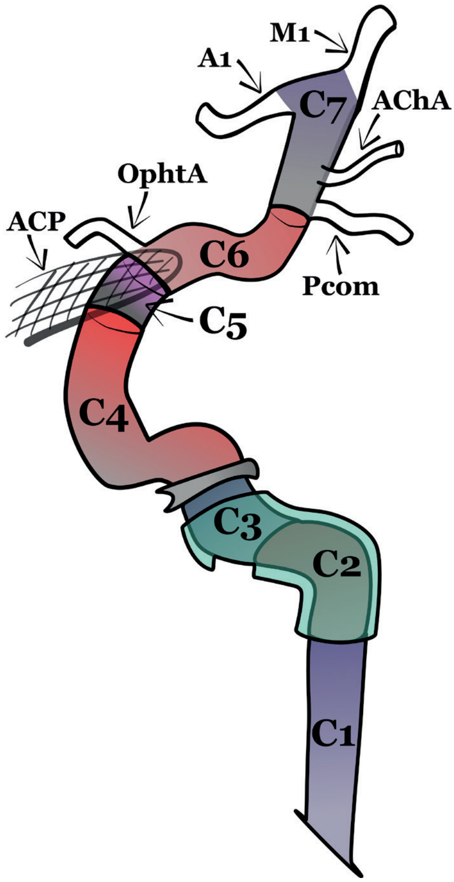
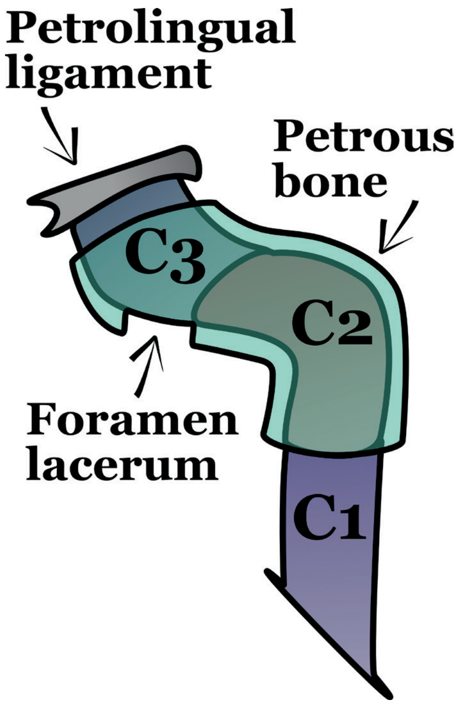


Figure 12
The cervical (C1), petrous (C2) and lacerum (C3) segments of the ICA. Pseudoaneurysm at the petrous segment (arrow).



2.3.2 EXTRACRANIAL AND EXTRADURAL SEGMENTS

2.3.2.1 The cervical segment of the ICA (C1)
The cervical segment of the ICA extends from the common carotid artery bifurcation located at the cervical level between the second and fourth cervical vertebrae, to the external orifice of the carotid canal at the base of the skull (Figure 12).[201,244] Postganglionic sympathetic nerves surround the cervical ICA, and the carotid sheath covers the bundle of cervical segment along with the internal jugular vein laterally and the vagus nerve posterolaterally. This segment only rarely gives of branches.[244,245]

2.3.2.2 The petrous segment of the ICA (C2)
The cervical segment changes to the petrous segment when it enters the base of the skull at the petrous temporal bone anterior to the internal jugular vein and medial to the styloid process. The petrous ICA has three divisions; the vertical segment, the genu- and the horizontal segment (Figure 12). The petrous segment within this carotid canal ends at the posterior edge of the foramen lacerum, a bony opening covered with fibrocartilaginous tissue. The vidian, as well as small periosteal branches, and more seldom the caroticotympanic artery may arise from this segment. Various neuro-otological structures are located in the vicinity; the greater and lesser superficial petrosal nerves, the cochlea, the tympanic cavity and the geniculate ganglion.[177,201,246,247]

2.3.2.3 The lacerum segment of the ICA (C3)
The lacerum segment of the ICA begins at the posterolateral margin of the foramen lacerum (Figure 12). The foramen lacerum consists of a foramen on the extracranial surface, which is surpassed but not pierced by the ICA, and of a canalicular portion. The canalicular portion has an open roof through which the ICA exits. The lacerum segment ends at the superior margin of the petrolingual ligament which runs between the anterior sphenoid lingula and the posterior petrous apex. In this segment, the ICA courses first upwards, then forms the lateral loop and ascends in the vertical canal towards the posterior cavernous sinus. The greater superficial petrosal nerve traverses anterior to the ICA.[201,248]

2.3.3 INTRACRANIAL AND EXTRADURAL SEGMENTS

2.3.3.1 The cavernous segment of the ICA (C4)
The cavernous segment consists of the ICA between the superior margin of the petrolingual ligament and the proximal dural ring (Figures 13–14).[201] The proximal dural ring is formed by the inner dural layer separated from dura propria at the level of the inferior

FIGURE 13
The cavernous (C4) and clinoid (C5) segments of the ICA. Aneurysm at the cavernous segment.

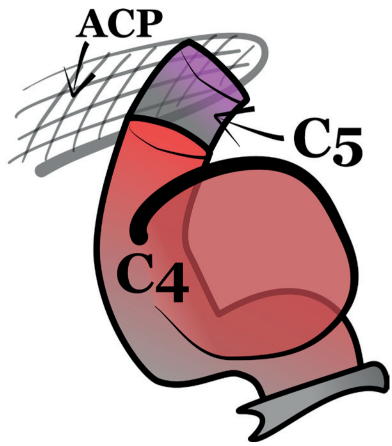
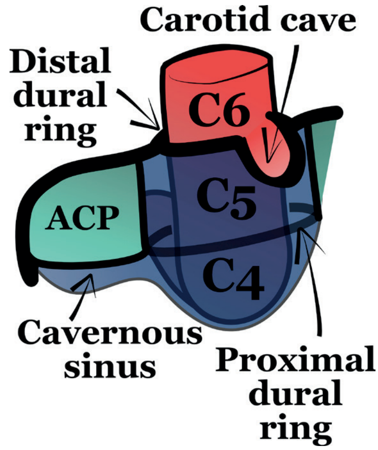


FIGURE 14
The proximal and distal dural rings. The clinoid segment (C5) communicates with the cavernous sinus. Aneurysm is located in the carotid cave.



surface of the anterior clinoid process (ACP). The proximal dural ring does not merge into the adventitia of the ICA, thus, it is not a tight barrier between compartments (Figure 14). The proximal dural ring also separates the oculomotor nerve from the ICA, and this specific part of the ring is called the carotid-oculomotor membrane (COM).[249,250] The diameter of the cavernous segment of the ICA varies between 3.3–5.4 mm.[251] During its course in the cavernous segment, the ICA first traverses vertically, forms the medial loop, courses horizontally and then forms again the anterior loop (genu).[201] Two main branches originating from the cavernous ICA are the meningohypophyseal trunk often arising from the superior aspect, and the inferolateral trunk arising from the inferior aspect. Capsular artery branches are only seldom met, and a persistent primitive trigeminal artery is a rarity.[252]

2.3.3.2 The clinoid segment of the ICA (C5)
The clinoid segment of the ICA is located beside the bony ACP (Figures 13–14). It begins at the proximal dural ring and continues to reach the distal dural ring.[201,249] This ICA segment is covered in a loose sheath of inner dural layer, which is proximally continuous with the cavernous sinus roof. Only the distal dural ring tightly merges with the adventitia of the ICA and forms the border of the intra- and extradural spaces (intradural aneurysms may cause SAH). The clinoid segment has a wedged shape and continues only for an average of 5 mm. Typically, there are no branching arteries at the clinoid segment. To surgically expose this region, anterior clinoidectomy, i.e. drilling of the bony prominence, is needed.[253]

2.3.4 INTRACRANIAL AND INTRADURAL SEGMENTS

2.3.4.1 The ophthalmic segment of the ICA (C6)
The proximal limit of the ophthalmic ICA segment is the distal dural ring which limits the intradural space.[201] Here, on the ventromedial side of the dural ring, a dural pouch or evagination called the carotid cave may

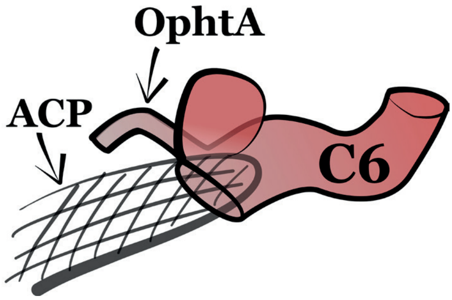
occasionally be present (Figures 14–15).[254] Its distal limit is the proximal edge of the posterior communicating artery (Pcom). The diameter of the ophthalmic segment of the ICA varies between 2.4–4.1 mm. The carotid artery enters the carotid cistern, a space filled by CSF, and runs in a posterior, superior and slightly lateral direction.[255] The ophthalmic artery (OphtA), the first branch of this segment, usually originates anterior to the tip of the ACP and from the rostromedial ICA, and then courses on the inferior surface of the optic nerve. The diameter of the OphtA is approximately 1.3–1.5 mm.[256] The ophthalmic artery may rarely arise from the clinoid segment of the ICA or from the middle meningeal artery.[249,257] Single or multiple superior hypophyseal arteries (SHA) originate from the proximal half and posteromedial surface of the ophthalmic ICA segment.

2.3.4.2 The communicating segment of the ICA (C7)

The communicating segment is the terminal segment of the ICA beginning from the proximal edge of the origin of Pcom and ending at the ICA bifurcation below the anterior perforated substance (Figure 16).[201,255] From there, the ICA divides into the anterior (ACA) and middle cerebral arteries (MCA). The first major branch arising from the posteromedial surface of the communicating segment is the Pcom forming the lateral border of the circulus of Willis. The diameter of the Posterior Communicating Artery (Pcom) ranges between 0.3–1.6 mm.[251] The Pcom may be absent in 1% of cases wherein perfusion of the posterior circulation is supplied by the vertebrobasilar arteries.[251] The second branch is the anterior choroidal artery (AChA), usually located closer to the Pcom than the bifurcation of the ICA, and originating also from the posteromedial aspect of the ICA.[255] The diameter of the AChA is between 0.1–0.6 mm.[251] The AChA may originate from the middle cerebral artery or the Pcom in less than 1% of cases.[258]

Figure 15

The ophthalmic segment (C6) of the ICA. Aneurysm is located near the branching site of the OphtA.

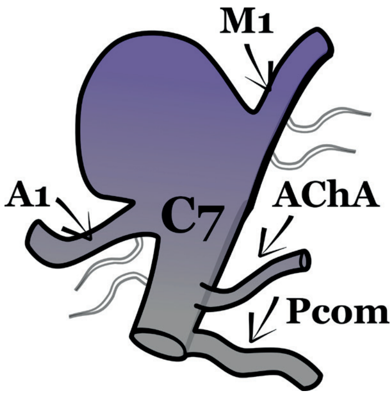


2.3.5 VASCULAR ANATOMY FOR BYPASS PROCEDURES

2.3.5.1 Artery pedicles and donor sites

In situ artery pedicles, e.g. superficial temporal artery (STA) branches, represent distal arteries and are classically regarded as low-flow bypasses (flow rates of <50 mL/min). Artery pedicles are usually anastomosed without grafts. The STA is the most commonly used artery pedicle (Figure 17). It has a diameter of approximately 2 mm, and is considered suitable for bypasses if the minimum diameter is 1 mm.[259,260] The proximal STA traverses in front of the auricle and divides further to the frontal and parietal branches. If both STA branches are anastomosed simultaneously, high-flow rates may be achieved ("double-barrel technique").[72,207,261] The proximal STA trunk has been reported as a "higher-flow" donor site as well.[262,263] The occipital artery (OA) is usually reserved for posterior circulation bypasses, but may be used to revascularize the MCA region if the STA is hypoplastic or damaged.[264] The posterior auricular artery (PAA) is located between the STA

Figure 16
The communicating segment (C7) if the ICA. Small perforator arteries are visualized. Aneurysm is located at the ICA bifurcation.



and the OA and emerges behind the auricle. The prevalence of the PAA extending to the temporoparietal region is approximately 6%, and in such cases, it may be a substitute for the STA.[265]

Donor sites in the cervical region (common, internal or external carotid arteries [CCA; ICA; ECA]) are used for high-flow bypasses (>50 mL/min) in combination with interpositioned grafts.[2,73] The internal maxillary artery (IMA), the largest terminal branch of the ECA, courses to the infratemporal fossa and may be used as a donor artery with the aid of a short interposition graft ("moderate-to-high-flow"; 20–60 mL/min).[266–268] The proposed advantages of utilization of the IMA is that cervical dissection is avoided and the needed graft length is shorter.[268] The first branch of the ECA, the superior thyroid artery, is also mentioned as a donor site.[269] Even contralateral donor sites may be used with long interposition grafts ("bonnet bypass").[260]

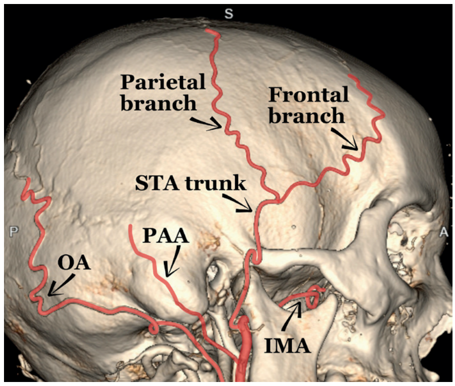
Intracranial arteries can also act as donor sites; very case specific intracranial-to-intracranial (IC-IC) bypasses with or without grafts may be considered.[77,86,143,270,271] In comparison to EC-IC bypasses, their advantage is a single site of exposure, although the technique is more difficult. One would also risk two intracranial arteries if the bypass fails. For example of almost historical value in treatment of cavernous ICA aneurysms nowadays, the petrosal ICA segment exposed through Glasscock's triangle has served as a donor site.[86,272] Though typically not applicable to ICA aneurysms, the intracranial bilateral arteries that approach each other in the midline, e.g. the anterior cerebral artery (ACA) or the posterior inferior cerebellar artery (PICA), are good examples of IC-IC "in situ side-to-side" bypasses without grafts.[273]

2.3.5.2 Recipient sites
The recipient site is determined by the artery occlusion strategy, and by the corresponding region of revascularization. Especially at the distal ICA and the proximal MCA, the lenticulostriatal perforators should not be compromised if anastomosis is performed. Distal MCA segments (M4; diameter of 1.2.–1.4 mm) are common recipients for artery pedicles, and the more proximal MCA (e.g. M2; diameter of 1.8 mm) or the supraclinoid ICA for graft anastomoses.[207,260] The more superficial the recipient site is, the more comfortable the exposure and working space is for the surgeon to accomplish the anastomosis. Approach to the proximal recipient sites at the ICA require extensive splitting of the Sylvian fissure and retraction of the frontal and temporal lobes, and still the procedure is performed in the depths of a deep cone-shaped corridor.

2.3.5.3 Grafts
The surgeon's experience and preference mostly affect which type of bypass graft is

selected. The most commonly used saphenous vein graft (SVG) is harvested from the medial side of the lower thigh or upper leg. SVGs have intraluminal valves permitting only unidirectional flow (valves may be excised), they have thinner walls than intracranial arteries and are more prone to kinking.[274,275] Graft flow varies between 70 and 250 mL/min.[2,276,277] A valveless radial artery graft (RAG) of the forearm provides slightly smaller flow rates of 40 to 150 mL/min.[2,277] In some reports, the RAG is categorized as "intermediate- or medium-flow" bypass.[270,278,279] The Allen's test together with Doppler ultrasound is typically used to assess the ulnar collaterals before harvesting the radial artery.[84] Due to the arterial wall type, vasospasm is a problem that may arise postoperatively.[78,83,274,276] However, RAG may increase in caliber during the follow-up which is not seen in SVGs.[276] If used for EC-IC bypasses, the length of these grafts would span 18–20 cm from the carotid and 7–9 cm from the STA trunk or IMA to the MCA segments.[263,268] Also, reports on grafting of STA, OA, lingual artery, superior thyroid artery, descending branch of the lateral circumflex femoral artery and anterior tibial artery are published.[271,280–283]

Figure 17
Right-sided lateral view of three-dimensional CTA reconstruction demonstrating various artery pedicles; STA, IMA, OA and PAA.



2.3.6 CAVERNOUS SINUS

Paired cavernous sinuses, the venous junctions of multiple veins, are located bilaterally near the anatomical center of the head. The sella turcica, the pituitary gland and the sphenoidal air sinuses are found in between. On both sides, the cavernous sinus has a shape similar to that of a boat with its bow facing anteriorily. The superior orbital fissure defines the anterior edge, and the posterior border is defined by the dorsum sellae together with entrance point to Meckel's cave. To specify, Meckel's cave is a dural and subarachnoid cavern communicating with the posterior fossa. The cavernous sinuses envelope the cavernous segment of the ICA inside the dural leaflets and isolate the artery into the extradural space. The paired cranial nerves course inside the sinuses and near the lateral walls on both sides. In order from superior to inferior, the cranial nerves are as follows; the oculomotor (CN III), the trochlear (CN IV), the ophthalmic division of the trigeminal nerve (CN V1) and the abducens nerve (CN VI). The abducens nerve (CN VI) has a more medial location in relation to the other aforementioned nerves. It traverses from the posterior fossa through Dorello's canal to reach the cavernous sinus, and then courses medial to the ophthalmic nerve (CN V1) and lateral to the cavernous ICA. Multiple cavernous sinus triangles, potential surgical windows to cavernous region pathologies, are defined by the areas in between the traversing cranial nerves (e.g. clinoidal, oculomotor, supratrochlear and infratrochlear triangle [Parkinson's]). Also more basally, the so called middle fossa triangles are limited by nerve divisions of the trigeminal nerve (CN V1–3).[252,284]

2.3.7 THE ANATOMY OF ENDOVASCULAR APPROACHES

Endovascular interventions of aneurysms are performed via peripheral arteries and by introducing microwires and catheters into cerebral vasculature arising from the aortic arch. The most common access site has been the femoral artery in the groin. Distally after the inguinal ligament, the external iliac artery continues as the common femoral artery (diameter of 4 – 9 mm) and then bifurcates to the superficial (3 – 10 mm) and deep femoral arteries (3 – 8 mm). However, the noncompressable region of the external iliac artery above the inguinal ligament, and continuation of the retroperitoneal sheath around the common femoral artery below the ligament, are proposed as risk factors for developing retroperitoneal hematoma after artery puncture.[285–287] Also, pseudoaneurysms are reported to form more often with other puncture sites of the groin than the common femoral artery.[288] Due to these potential complications as well as positive experience shared by cardiologists, transradial (radial artery; 2 – 3 mm) access at forearm or wrist has recently gained popularity also among neurointerventionists.[289,290] Radial artery puncture may be done either right- or left-sidedly, even a more distal puncture at the anatomic snuffbox is feasible, and different endovascular devices are compatible with the smaller artery caliber.[291–294]

2.4 TREATMENT OF COMPLEX ICA ANEURYSMS

2.4.1 DIRECT MICROSURGICAL TREATMENT

2.4.1.1 Clipping

Direct clipping of complex aneurysms is challenging and depends on the burden of different morphological attributes listed previously.[17,192,295–304]

The surgical approach commences with the planning of a bone flap (craniotomy). Various craniotomy types are available. Frontotemporal pterional craniotomy was popularized by Yasargil and is the most common type to reach anterior cerebral circulation including ICA aneurysms (Figure 18).[17,158,163,305] Other approaches have been developed to provide different angles and extensions of exposure (e.g. supraorbital, orbitozygomatic and “mini” versions).[1,17,306,307]

After splitting the lateral Sylvian fissure, exposure of the aneurysm is particularly difficult at the proximal cavernous or paraclinoid segments wherein the structures of the base of the skull obscure the approach, and additional removal of bone and related microstructures is often needed (e.g. intra- or extradural anterior clinoidectomy, optic nerve unroofing, distal dural ring and falciform ligament sectioning) [Figure 19].[192,220,249,304] Nearby neurovascular structures should be meticulously protected to avoid complications.[220,304,308,309] At the supraclinoid ICA, artery branches and perforators may be attached or incorporated in the aneurysm wall.[144,203,204,310]

Temporal clip occlusion of parent artery (proximal and/or distal control, temporary

Figure 18

Right-sided pterional craniotomy to the bifurcation of the ICA wherein an aneurysm is located. The optic chiasm is seen beside in yellow.

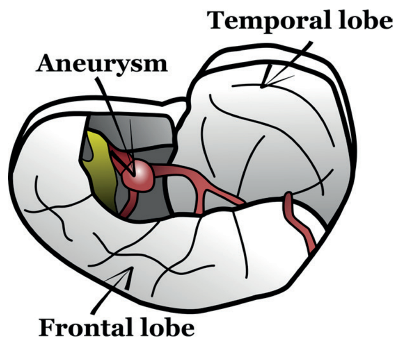
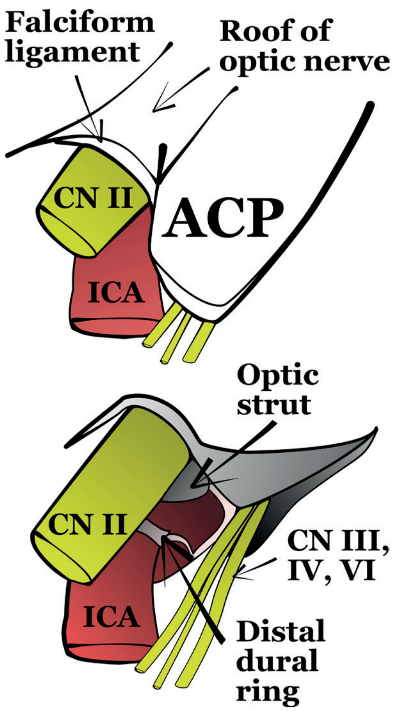


Figure 19
Right-sided view from above to clinoid region. Above; ICA and CN II are covered by skull base structures. Below; anterior clinoidectomy, optic nerve unroofing, distal dural ring and falciform ligament sectioning are done. Consequently, the clinoid (C5) and the proximal ophthalmic (C6) ICA segments as well as the optic strut are exposed.



trapping) is used to soften the aneurysm dome and to enable safer and easier aneurysm dissection and neck exposure. Typically longer parent artery occlusion times are needed for complex aneurysms, e.g. GIAs.[298] Retrograde suction decompression techniques, orifice blocking with an endovascular balloon and even resection of giant or thrombosed aneurysms ([endo]aneurysmectomy) may be applied.[181,188,302,311–314] It is also possible to temporarily arrest the systemic blood circulation for the same effect. Adenosine-induced cardiac arrest, rapid ventricular pacing or the most demanding option, hypothermic circulatory arrest, may change few complex and unclippable aneurysms to clippable.[17,315–317]

Neck clipping itself may be complicated by aneurysm orientation, a wide neck, incorporated branches, a calcified neck or morphologies without a clear neck; fusiform, blister-like, dissecting or pseudoaneurysms.[17,163,318] In recurrent aneurysms, the previously placed clips and scar formation after surgical dissection or endovascular embolization material may obscure the anatomy.[319] Different clip shapes and configurations are usually needed for exact neck occlusion or to reconstruct the affected artery segment; e.g. straight, curved, angled, "T-bar", "mini" or fenestrated clips in tandem, stacked or perpendicular configurations (e.g. Yasargil® Aneurysm Clip System, B. Braun Melsungen AG, Melsungen, Germany) [Figure 20].[163,192,203,320–322] Vascular clamps may be used to temporarily occlude a wide aneurysm neck region to pilot clip application, and special clip types are proposed for attacking calcified and thickened aneurysm necks ("booster clip", "compression clip").[322–324] Even after clipping, vascular clamps may be used to force clip blades to close.[195]

Intraoperative monitoring (IOM) of sensory and/or motor tracts is suggested to reduce the number of ischaemic complications during aneurysm clipping, but the benefit and effect on long-term outcome is questionable.[300,325–329] Indocyanine green and fluorescein videoangiography (ICG- and FL-VA) give a real-time video view of artery and aneurysm patency status after clipping.[68,330,331] Also, as for primary diagnostics, an intraoperative DSA study is optional.[332] For postoperative imaging after clipping, CTA is a commonly applied modality, but DSA gives superior accuracy in cases of complex aneurysms or foreign material (clips, coils etc.).[333]

Figure 20
Aneurysm clipping with fenestrated clips which encircle an artery branch.

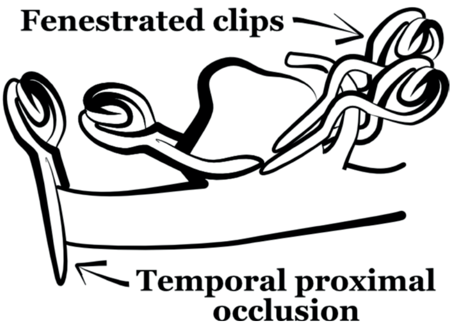
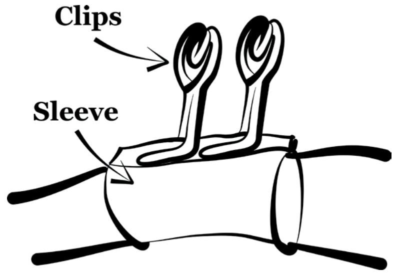


Figure 21
Wrapping technique with Gore-Tex® sleeve and clips.



2.4.1.2 Wrapping
The wrapping technique is typically used as a "last resort" and only in situations wherein an aneurysm is not directly clippable (e.g. fusiform, blood blister-like or dissecting morphology) and endovascular treatment is not feasible (Figure 21). Wrapping is performed by constructing a protective sleeve around the aneurysm or pathologic artery segment. Coating material is nowadays mainly polytetrafluoroethylene (Gore-Tex®; W. L. Gore & Associates, Flagstaff, Arizona, USA) to reduce tendency of granuloma formation related to e.g. cottonoid sponges, but also autologous tissue in the form of muscle or fascia has been used.[158,159,172,173,334,335]

2.4.2 DIRECT ENDOVASCULAR TREATMENT
2.4.2.1 Endovascular coiling
With standard endovascular coiling, the aneurysm dome is filled with platinum coils to form a three-dimensional occlusive mass, which leads to thrombosis (e.g. Guglielmi Detachable Coil; Stryker Neurovascular; Fremont, CA, USA). The giant, wide-necked or circumferentially enlarged aneurysms are challenging or impossible as targets due to problems with coil packing and likelihood of recurrent filling after coil compaction, migration or thrombus resolution.[121,336–338] Hydrogel coated coils in comparison to bare platinum coils are reported to reduce aneurysm recurrence rates, but the benefit is controversial.[339–341] Coiled aneurysms are routinely followed with serial DSA or MRA imaging.[342,343] The most frequenly used classification scheme for occlusion grade of coiled aneurysms is one proposed by Raymond and Roy (Raymond-Roy Occlusion Classification [RROC] or Montreal Scale) as follows; complete occlusion (class I), residual neck (class II) and residual aneurysm (class III).[344] Later, a modification to RROC was proposed with two separate subclasses; IIIa and IIIb. The class IIIa aneurysms have contrast opacification within coil interstices and IIIb aneurysms between coil mass and aneurysm wall. While IIIa may improve spontaneously to total occlusion, the class

IIIb was associated with larger aneurysms and poorer occlusion rates in long-term.[345]

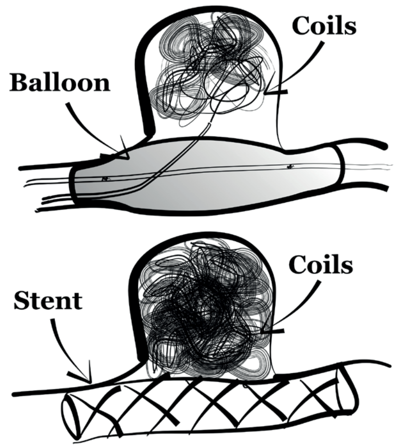
2.4.2.2 Balloon- (BAC) and stent-assisted coiling (SAC)

The purpose of balloon- or stent-assisted coiling is to aid in denser coil packing and in prevention of coil herniation to parent artery especially in large and wide-necked aneurysms (Figure 22).[184,346–351] Among others, self-expendable Neuroform EZ® or Atlas™ stents may be used in SAC (Stryker Neurovascular, Fremont, CA, USA). During these procedures, either an endovascular balloon is inflated temporarily to remodel the coil mass, or a stent acts as a permanent scaffold in the parent artery. The balloon may also aid in "jailing" the microcatheter into the aneurysm neck during coiling, whereas coiling through stent poruses is also possible. If iatrogenic aneurysm rupture occurs, an inflated balloon seals the site rapidly. Both assistive techniques are more challenging to perform at artery bifurcations.[337] Thrombogenicity is drawback of the SAC technique, and periprocedural antiplatelet medication is needed.[346,349] It is worth mentioning that specific assistive devices for coiling of artery bifurcation aneurysms are also available, but published series are small.[352,353]

2.4.2.3 Endosaccular flow disruption

Endosacculars flow disruptors are considered as "intraluminal flow diverters" (Figure 23). These devices have a porous and hollow three-dimensional form which consequently promotes aneurysm thrombosis (e.g. WEB® Embolization System, MicroVention, Aliso Viejo, CA, USA).[354–361] The official indications are saccular, small-to-large-sized (≤10 mm) and wide-necked (≥4 mm) aneurysms at main artery bifurcation sites like the ICA terminus.[355–358] Lately, off-label treatments of sidewall aneurysms of ICA trunk have been reported.[359,360] Conventional coiling, stenting or parent artery flow diversion may be combined with these devices.[357,359]

Figure 22
Balloon- and stent-assisted coiling of wide-necked aneurysms.



2.4.2.4 Onyx embolization

Onyx® (ethylene vinyl alcohol copolymer; Micro Therapeutics, Irvine, CA, USA) is a liquid embolic material dedicated for endovascular embolization (Figure 24). It forms a cast with an initial semi-liquid component centrally which may be expanded with further injections.[311,362–367] Similar to BAC, the aneurysm neck may be protected with a balloon during serial injections. The Onyx® cast has been combined with coiling or stents to improve occlusion rates. Giant, wide-necked and recurrent aneurysms, even pseudo- and blood blister-like aneurysms, have been treated with this technique.[311,362–367]

2.4.3 INDIRECT MICROSURGICAL TREATMENT

Indirect microsurgical treatment targets the parent artery wherefrom the aneurysm originates. The aim is to occlude the pathologic artery segment, and thus, obliterate the aneurysm. The strategy makes many of the complex aneurysm features secondary [Figure 25].

Figure 23
Endosaccular flow disruptor (e.g. WEB® device)

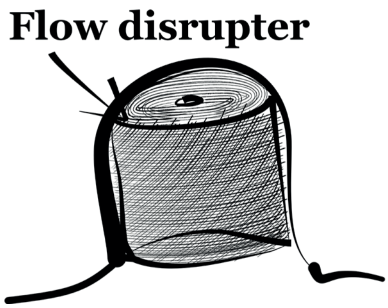
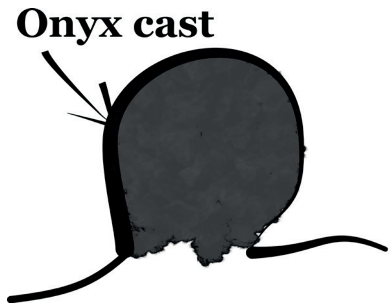


Figure 24
Aneurysm with Onyx® cast.



2.4.3.1 Assessment of collateral circulation

In order to safely proceed with parent artery occlusion, physiological and functional imaging studies are needed to assess the reserve of intracranial collateral circulation. With intracranial ICA aneurysms, classically the cervical carotid artery proximal to the aneurysm is temporarily occluded with an endovascular balloon (balloon test occlusion; BTO).[94,368] Selective BTO at the site of planned permanent occlusion reduces false negative results.[207,369] The risk of BTO for permanent neurological defects is low (0.3–0.4%) but non negligible.[370,371]

During the test, the patient is awake and neurological status is observed for any deterioration. The effect and sensitivity of BTO may be enhanced with a hypotensive challenge (blood pressure decreased 20 mmHg or 25% of mean arterial pressure). With contralateral injection, the DSA study is assessed for anatomical or time-related abnormalities of contrast filling. Appearance of asymmetrical delays in venous phase filling of the hemispheres has improved predictive values.[372] Parent artery occlusion is not safe, if neurological deterioration or insufficiency of radiological collateral flow is seen.

Other diagnostic and imaging methods may give additional information in uncertain cases, and reduce false negative results; transcranial Doppler (TCD), electroencephalography (EEG), CT or MR perfusion imaging, positron emission tomography (PET) or single-photon emission computed tomography (SPECT).[368,373–377]

2.4.3.2 Parent artery occlusion

If BTO confirms the presence of brisk collateral circulation, one may proceed with permanent parent artery occlusion (PAO) [Figure 26]. The complex petrous or cavernous aneurysms without major artery branches are classical targets for proximal CCA or ICA occlusion in the cervical region.[17,144,368,378–381] Previously, gradual occlusion with clamps or tourniquets was common.[382] Nowadays, abrupt endovascular occlusion methods are often applied (coils or balloon; rarely plugs, WEB® or liquid embolic material).[144,270,379,380,383–386] Occlusion may be extended to aneurysm trapping if needed due to retrograde aneurysm filling.[385,387] Distal occlusion only is an optional strategy in selected cases if risking e.g. proximal perforators is then avoided.[16,388] Immediately after distal occlusion, the resulting pressure variations in the aneurysm are in the range of normal daily activities, and should not increase the risk to aneurysm rupture.[389]

2.4.3.3 Bypass procedures

The strategy and level of ICA occlusion determines boundary conditions and flow demand for revascularization (Figure 27). The preoperative findings in BTO may demonstrate the need for either a high- or low-flow bypass.[279] In general, if a patient becomes symptomatic during BTO, then high-flow bypass is needed. If moderate collateral flow is present and only minor angiographic defects are seen, a low-flow bypass may be sufficient.[5,207] In addition, intraoperative flow rates may be measured with a microvascular ultrasonic flow probe. If measurements are done with and without temporary occlusion of the parent artery, the reduction in flow rate may be matched with proper donor artery accordingly.[279,390] On the other hand, a universal approach with high-flow bypass even without a preoperative BTO is proposed.[16,274] The need for distal revascularization may be obvious when occluding the most complex aneurysms incorporating major artery branches (e.g. carotid bifurcation aneurysms), but exact preoperative assessment is usually impossible and creative solutions are then needed, often in form of multiple bypasses to provide flow sequestration.[391]

During the bypass procedure, e.g. EC-IC bypass, standard neurosurgical practices are employed to expose the intracranial anastomosis site. The donor artery or grafts are dissected and harvested. The cut flow value of a donor artery may be measured with a microdoppler device to assess its suitability (i.e. rate of free flow from cut end). Then, heparinized saline solution is used to wash blood from the donor vessel to pre-

Figure 25

Right-sided pterional approach showing a GIA at the ICA bifurcation. Due to the aneurysm size, exposure of the aneurysm neck is challenging. Thus, indirect occlusion strategy is chosen instead of direct attack. Black circle marks the potential recipient artery for a bypass procedure.

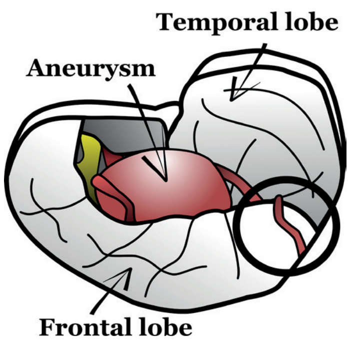


Figure 26

Examples of PAO.

vent thrombosis. After temporary clip occlusion of the recipient site, the recipient artery is incised and irrigated. The conventional bypasses are sutured under high magnification either in an end-to-side or an end-to-end fashion (Figure 28). Interrupted or continuous 10–0 nylon sutures are typically used in the MCA and larger sutures (e.g. 8- to 6-0) at the cervical carotid.[260] To minimize risk of ischaemia during the temporary occlusion, an additional protective STA-MCA bypass may be first constructed distal to the target site.[4,392] Alternatively, this additional bypass may be used for measuring blood pressure in the middle cerebral artery to alert of low flow situations.[393,394]

The ELANA technique differs substantially from the aforementioned conventional technique of constructing an anastomosis. It involves first reflecting the graft artery's cut end over a platinum pilot ring, fixating the ring with sutures, and then suturing the anastomosis in the recipient wall without temporary artery occlusion (Figure 29). After this, an endoluminal laser device is introduced to the artery confluence via the graft, and the recipient artery wall is perforated finishing the anastomosis (arteriotomy).[89]

After finishing the bypass, a microdoppler device is used again for the final flow measurements.[278,279] A cut flow index (CFI; ratio of bypass flow to donor artery's cut flow [free artery ending]) of ≥0.5 predicts long-term bypass patency.[395] In addition, intraoperative ICG angiography may be used to confirm parent artery and bypass patencies.[68,278] A problem with the measuring and monitoring of arterial flow and patency is that it does not alert if the perfusion in more proximal and nonvisualized, deep perforator arteries are endangered. As with surgical clipping, intraoperative monitoring may assist in identifying these critical events during the procedure.[278] Even awake bypass procedures have been reported to enable clinical testing for neurological deficits.[396]

Figure 27
Simplified illustration of EC-IC bypasses; double barrel STA-M4 bypass and ECA-graft-ICA (C7) bypass.

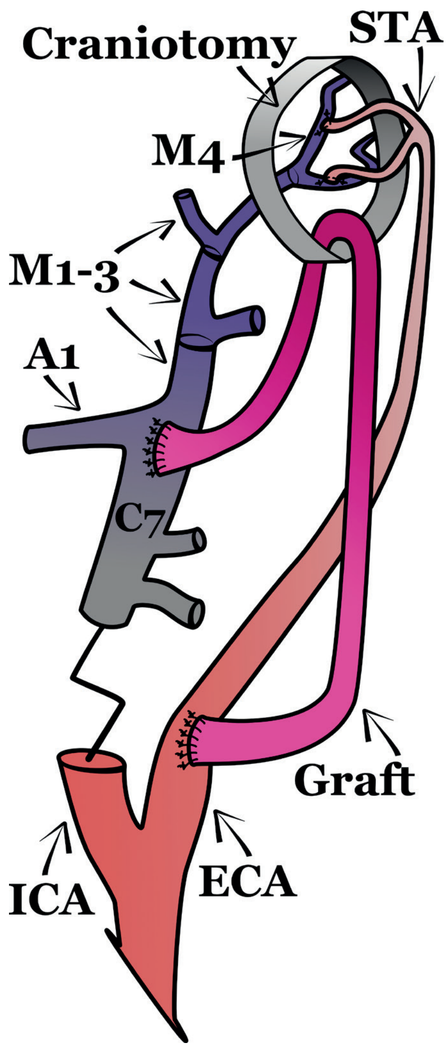


Figure 28
Conventional anastomosis with interrupted sutures. Temporary clip occlusion of the donor artery.

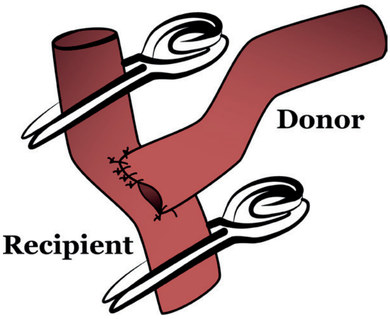
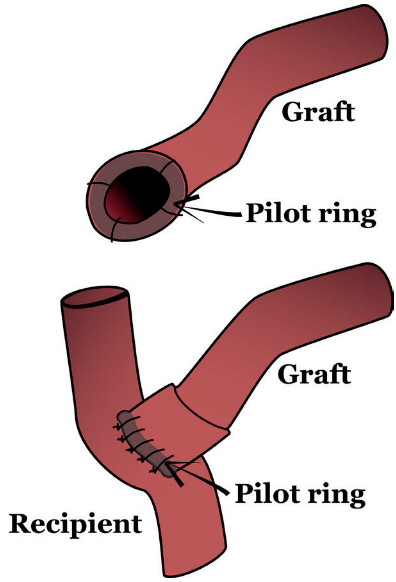


Figure 29
ELANA anastomosis with platinum pilot ring. After suturing, the recipient artery wall is perforated with laser device.



Postoperative imaging modalities are similar to those used in clipping technique. To prevent bypass thrombosis, acetylsalicylic acid is often administered postoperatively, but peri- or intraoperative anticoagulation or heparinization is typically avoided to prevent hemorrhagic complications.[270] Temporary induction of postoperative hypertension may be used to support cerebral perfusion.[270]

2.4.4 INDIRECT ENDOVASCULAR TREATMENT

2.4.4.1 Flow diversion

A flow diverter (FD) is an endovascular stent-like device with denser coverage in comparison to conventional stents (e.g. Pipeline™ Flex Embolization Device; PED; Medtronic Neurovascular, Irvine, CA, USA).[397] The device diverts the main flow vector away from the aneurysm into the parent artery (Figure 30). Diminished flow within an aneurysm leads to delayed thrombosis and ultimately the device is covered with a neointimal vascular layer. The porosity of the stent is made high in an effort to minimize the risk of side branch or perforator occlusions nearby the aneurysm.

Originally the PITA and PUFS trials encouraged the widespread utilization of FDs in unruptured and proximal large or wide-necked ICA aneurysms.[18,19] Up to 90% of ICA aneurysms were estimated to be technically treatable with FDs.[398] Since, many new FD devices have emerged and off-label indications have vastly expanded to cover different complex aneurysm morphologies of the whole ICA up to its bifurcation. Examples are available on the flow diversion of different morphologies of aneurysms as follows; small or giant, fusiform, blood blister-like, dissecting, pseudoaneurysms, aneurysms with incorporated branches, recurrent, tandem as well as ruptured aneurysms.[399–407] New small-caliber devices have been developed for accessing distal branches beyond the circulus of Willis.[408] Coiling may also be used as an adjunctive measure in large aneurysms.[409]

The major drawback of the procedure is the necessity of long-term dual antiplatelet therapy (DAPT) for prevention of in-stent thrombosis and thromboembolic complications. Typically, acetylsalicylic acid and clopidogrel are combined for a 6-to-12-months period at minimum, but other options are available for patients having resistance to clopidogrel.[406,410,411] In ruptured aneurysms, DAPT causes challenges if other surgical interventions are needed (e.g. placement of external ventricular drain in case of hydrocephalus) and raises concerns about the risk of rebleeding.[403,412]

Radiologic treatment results are controlled with series of DSA or MRA studies spanning at least a couple of years. During the follow-up, the aneurysm occlusion rates are defined with various scales dedicated for flow diversion (e.g. O'Kelly-Marotta [OKM] or modificated RROC).[344,413]

2.5 TREATMENT OUTCOMES IN COMPLEX ICA ANEURYSMS

2.5.1 DIRECT TREATMENT

2.5.1.1 Direct surgical treatment

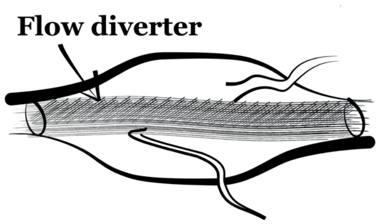
Direct clipping has historically been the gold standard of aneurysm treatment. Especially giant aneurysms, which often share multiple complex attributes, are estimated to be technically clippable in half of cases, but generalizations should be made cautiously.[17,414] The very heterogeneous nature of complex ICA aneurysms makes comparison of different surgical series very difficult. Most series including direct aneurysm clipping are mixtures of various aneurysm morphologies in different locations, unruptured and ruptured aneurysms, or other surgical treatment strategies in addition to clipping. Especially large aneurysms without a clear neck (e.g. fusiform morphology) are nearly impossible lesions to obliterate with clipping.[131] Series describing clipping of giant ICA aneurysms report morbidity and mortality rates of 1–44% and 0–15% respectively.[17,192,295–304] Regarding complex ICA aneurysms, especially giant aneurysm size together with increasing patient age are associated with higher risk for poor outcome after direct surgery.[6,17,111,120,131]

Wrapping can be done in cases wherein other treatment methods are not feasible, but nowadays flow diversion ("endoluminal wrapping") is usually considered as the first option. Small case series of different pathologies, e.g. fusiform or blood-blister like aneurysms, are reported with low treatment-related morbidity or mortality.[334,335] However, two larger series of ruptured aneurysms report high rates of rebleedings (17%) up to three years after primary treatment.[173,415] Due to their size, GIAs are rarely technically feasible targets for wrapping.

2.5.1.2 Direct endovascular treatment

For coiling to be technically possible, the aneurysm has to have a dome wherein to pack the coils. This prerequisite already excludes many aneurysm morphologies. The most common procedural complication of coiling is a thromboembolic event, occurring in 5–10% of cases and with the highest risk in ruptured wide-necked (21%) or large aneurysms (28%).[183,338,416,417] In addition, pro-

Figure 30
Flow diverter in a fusiform aneurysm.



truding coil loops from the aneurysm sack increase the risk.[418] A review by Parkinson in 2008 reported a major neurological morbidity rate of 24% and mortality rate of 9% for coiled GIAs. After coiling, up to 55% of GIAs reopen during the follow-up, and few even late after confirmation of initial occlusion.[121,336,419,420] More specifically for large or giant ICA aneurysms, high long-term recurrence (31–49%) and retreatment (26–42%) rates have been reported.[338] Large or giant (>10 mm), partially coiled aneurysms tend to harbor bleeding risk of 3.5% in the long-term.[417]

Balloon- and stent-assisted coiling techniques were developed to enhance coiling results in wide-necked aneurysms. A meta-analysis comparing SAC to bare coiling showed a favourable reduction in aneurysm recurrence rate in favor of SAC (16% vs. 34%) without an increase in complications.[348] Also, SAC may yield better angiographic results and less re-treatments in comparison to BAC.[184] However, a series of 41 large or giant ICA aneurysms treated with SAC showed higher rates of retreatment (22%) and aneurysm mass effect exacerbation (24%) in comparison to parent artery occlusion or flow diversion.[349] Also, a prospective, randomized study of large and giant aneurysms reported substantially lower aneurysm occlusion rates for SAC when compared to flow diversion (25% vs. 75%).[350] Then, another meta-analysis of very large aneurysms (>20 mm) reported similar occlusion rates for SAC and flow diversion (73% and 72%). The same data showed a high rate of ischaemic complications for SAC (30%) which may reflect the technical challenges in treating the largest aneurysms.[351] Altogether, the role of BAC and SAC is controversial.

Treatment with endovascular flow disruption is possible only for a limited number of aneurysms matching the dimensions of the device. As postprocedural thromboembolic complications have been reported, the routine use of prophylactive antithrombotics should be considered. Few series reported morbidity ranging between 0–10% with no reported mortality.[357,359,361]

Onyx embolization is rarely used in aneurysms but may not be forgotten. The main problem is that the material is nonadhesive, making distal embolization or parent artery occlusion possible complications.[311,362–367] Also, recurrent filling of cast and aneurysm wall interface has occured in up to 36% of GIAs treated with Onyx.[367,421] Treatment related morbidity of 8–16% and mortality of 3–18% have been reported.[362,367]

All things considered, the direct endovascular methods translate poorly to the treatment of the most complex aneurysms, the GIAs.

2.5.2 INDIRECT TREATMENT

2.5.2.1 Parent artery occlusion

Drake published a series of 135 patients harboring giant ICA aneurysms which were treated with PAO. During the years, occlusion techniques evolved from surgical suturing to endovascular balloon deployment. Excellent radiological and clinical outcomes were achieved in 98% of cases with petrous or cavernous aneurysms.[144] Similar results have been reported elsewhere.[378,379,383,422] However, supraclinoid aneurysms in particular may remain filled by major artery branches (OphtA, Pcom, Acom) or perforators, but partial aneurysm thrombosis and flow reduction is often a sufficient goal in such cases.[144,379]

A recent meta-analysis focused on "very large" (>20 mm) aneurysms and compared different endovascular treatment methods. The report showed favourable results for PAO in comparison to reconstructive treatment methods (coiling, BAC/SAC, flow diversion) in unruptured aneurysms; the occlusion rate was higher (93% vs. 73%), recanalization was infrequently seen (5% vs. 40%) and the morbidity rate was lower (9% vs. 15%). Improvement of aneurysm mass effect was seen more often as well (77% vs. 50%). In ruptured aneurysms, morbidity was slightly higher in the PAO than in the coiling group (29% vs. 20%).[351]

Of special notion, formation of de novo aneurysms elsewhere in the cerebral arteries due to changed flow dynamics after PAO is a rarely reported phenomenom.[423]

Thus, at least for proximal ICA aneurysms, simple PAO may yield good results.

2.5.2.2 Bypass procedures

As with surgical clipping, published reports on complex ICA aneurysms treated with bypass procedures are very heterogeneous and direct comparison is difficult. The occlusion as well as revascularization strategies vary substantially. No randomized trials are available, but the concept of revascularization is well acknowledged.[424]

Depending on the strategy, aneurysm occlusion rates range between 77%–100%.[17,274,297,304] Reported bypass patency rates of different pedicles (e.g. STA) and grafts (e.g. SVG, RAG) are 73–98% in the long-term, while most bypass occlusions occur during the first postoperative week.[270,304,425–430]

The published reports on bypass surgery from the last 10 years report morbidity and mortality rates of 0–26% and 0–13% respectively (Table 4). [2,4,5,17,192,218,267,270,274,282,297,304,393,396,429,431] The most common cause for morbidity is postoperative stroke due to the occlusion of an artery branch or perforator in addition to early bypass occlusions.[4,17,218,426] Location of an aneurysm near the ICA bifurcation seems to be associated with higher risk for perforator-related infarction.[4]

Some reports included also ruptured aneurysms, but the subgroup analyses are often lacking.[4,5,270,298,429] In a nationwide report from U.S., the mortality rate was higher in ruptured (21%) than in unruptured aneurysms (8%) treated with bypass procedures, but the case volume per surgeon was low. Especially vasospasm and related changes in cerebral perfusion may complicate the treatment with bypasses after SAH.[5,163]

Regarding the ELANA technique, van der Zwan et al. recently reported of no advantage in outcomes when compared to conventional bypass techniques.[431]

2.5.2.3 Flow diversion

Flow diversion was already initially dedicated for complex ICA aneurysms. The major series reported rates of 0–20% for morbidity and 0–5% for mortality, while occlusion rates reached 66–93% during the follow-up (Table 5).[18,19,205,304,309,349,402,406,409–411,432–438] The most recent nationwide prospective cohort study (DIVERSION) included 477 consecutive aneurysms of all locations and showed permanent morbidity rate of 6% and mortality rate of 1%. Larger aneurysm size was a risk factor for complications.[432] Another recent prospective trial (SCENT) focused on large or giant ICA aneurysms (including the distal ICA) and reported similar rates of morbidity and mortality.[411]

Contrary to this, Kallmes et al. reported higher morbidity (23%) and mortality (6%) rates for unruptured GIAs of the anterior circulation.[436] Also in 2017, a randomized Canadian study (FIAT) raised concerns on the safety of flow diversion as it was early cessated due to a high proportion of complications and deaths.[439]

Other studies analyze the causes of morbidity and mortality. According to a meta-analysis in 2013, and a separate pooled analysis in 2017, ischaemic strokes (6%), SAH (4%) and ICH (2–3%) occur at non-negligible rate, and more often in large aneurysms.[401] This is supported by other studies including larger aneurysms.[349,409] Post-procedural rate of aneurysm ruptures after one month is 2%, and up to 6% in GIAs of the anterior circulation.[401,436] Usage of multiple coaxial flow diverters may dispose to hemorrhagic events, and the fusiform aneurysm morphology to ischaemic events.[440,441] Also, late ischemic complica-

Table 4
Published surgical series including EC-IC bypass procedures for complex ICA aneurysms with focus on the last ten years.

Author	Year	ICA aneurysms	Morbidity	Mortality
Nussbaum et al.[5]	2019	33/126	4%	3%
van der Zwan et al.[431]	2019	25/36	25%	6%
Zhang et al.[218]	2019	69/115	17%	9%
Ota et al.[4]	2018	91/159	34%	1%
Abdulrauf et al.[396]	2017	30	7%	0%
Ban et al.[270]	2017	35/62	8%	0%
Straus et al.[282]	2017	44/130	26%	0%
Wang et al.[267]	2017	23/32	15%	0%
Matsukawa et al.[393]	2016	67	10%	0%
Kalani et al.[429]	2014	27/56	15%	11%
Kim et al.[304]	2014	20	20%	0%
Ishishita et al.[274]	2013	38	0%	0%
Sughrue et al.[17]	2011	62/141	9%	13%
Sekhar et al.[2]	2008	90	1%	0%
Sharma et al.[297]	2008	151	NA	9%
Cantore et al.[192]	2008	68/99	3%	8%

tions may occur despite adequate regime of DAPT.[442]

In ruptured aneurysms, postprocedural rebleeding rate is 4% according to a meta-analysis, and risk is highest during the first 72 hours.[403] In another meta-analysis, the larger aneurysm size (≥20 mm) was associated with highest rate (n=4, 57%).[407] The same rebleeding rate of large aneurysms was seen also in a recent case series (n=3, 60%).[407]

Regarding occlusion rates of aneurysms, other complicating factors have been reported; e.g. size, intraluminal thrombosis, branches originating from the aneurysm wall and location at the Pcom or AChA origin may predispose to lower rates.[205,206,443,444] Adjunctive coiling may increase aneurysm occlusion propability, but in a meta-analysis there was no clear effect.[18,205,351] An ongoing prospective multicenter study ARETA (Analysis of Recanalization after Endovascular Treatment of Intracranial Aneurysms) will probably shed new light in stability and aneurysm recurrence rates of flow diversion.[347]

Table 5

Published series on flow diversion with focus on large prospective studies and case series of complex ICA aneurysms.

Author	Year	ICA aneurysms	Occluded	Morbidity	Mortality
Chen et al.[406]	2019	18/19	78%	0%	0%
Gory et al.[432] (DIVERSION)	2019	NA/477	80%	6%	1%
Martinez et al.[410] (PFLEX)	2019	47/50	82%	0%	0%
Meyers et al.[411] (SCENT)	2019	180	66%	6%	2%
Pierot et al.[433] (SAFE)	2019	86/103	73%	3%	2%
Yan et al.[349]	2019	61	70%	11%	5%
Bender et al.[205]	2018	367/445	82%	9%	1%
Mokin et al.[402]	2018	45	88%	19%	2%
Oishi et al.[434]	2018	100	69%	4%	1%
Silva et al.[309]	2018	70	89%	16%	0%
Adeeb et al.[409]	2017	32/50	77%	20%	0%
Kallmes et al.[435] (ASPIRe)	2016	185/207	75%	7%	2%
Kallmes et al.[436]	2015	311	NA	9%	4%
Möhlenbruch et al.[437]	2015	23/29	73%	9%	0%
Kim et al.[304]	2014	24	81%	12%	0%
Becske et al.[19] (PUFS)	2013	107	87%	5%	1%
De Vries et al.[438]	2013	32/49	83%	3%	0%
Nelson et al.[18] (PITA)	2011	28/31	93%	6%	0%

Altogether, even while being a “Swiss Army knife” for many complex aneurysms, the pros of flow diversion do not come without costs.

2.5.3 IMPROVEMENT OF CRANIAL NERVE DYSFUNCTIONS

According to a review report, preprocedural CNDs seem to improve more often with surgical clipping than with endovascular coiling. With surgery, the mass effect on cranial nerves may be reduced immediately by clipping, and in larger aneurysms, by aneurysmectomy. With endovascular treatment, the cessation in aneurysm pulsatility, and gradual reduction in aneurysm size have been proposed as possible mechanisms.[219]

With paraclinoid aneurysms, new postoperative visual deficits or cranial nerve dysfunctions occur due to surgical manipulation in 13–29% of cases.[220,304,308,309,445] On the other hand, coiling of large paraclinoid aneurysms may result in progressive, but potentially transient visual loss due to perianeurysmal inflammation or enlargement.[446–448]

Only a few reports focus on bypass surgery and recovery of CNDs; improvement rates of 30–85% are reported.[225,304,428] The improvement of visual disturbances seems to be worse than that of ophthalmoplegia.[225]

Flow diversion reportedly results in improvement of preprocedural CNDs in 40–94%.[304,309,434,449–451] On the other hand, flow diversion may cause slight ophthalmic modifications in extensive ophthalmic examinations, but the rate of clinically relevant complications is low at 3%.[452,453] A recent comparative meta-analysis of paraclinoid aneurysms treated with clipping, coiling or flow diversion found superior trends for flow diversion in symptom relief and safety regarding vision outcomes.[221] ❦

Aims of the study

1. To define the clinical, anatomical and morphological features of giant intracranial aneurysms based on radiographic imaging studies.

2. To describe and assess the principles, complications and outcomes of bypass surgery for complex internal carotid aneurysms.

3. To assess the complications and outcomes in relation to aneurysm features in endovascular flow diversion for complex internal carotid aneurysms.

Patients, materials and methods

These studies are based on the Helsinki Intracranial Aneurysm Database. The database consists of over 9000 patients with diagnosed intracranial aneurysms referred to the Helsinki University Hospital (HUS), Finland. Under HUS, Helsinki Neurosurgery serves the largest population in the nation, approximately 1.8 million people. For cerebral bypass procedures, Helsinki Neurosurgery has the national responsibility of all Finnish patients (population of 5.5 million people). Endovascular procedures for aneurysms, including flow diversion, are performed in all five university hospitals in Finland (Helsinki, Kuopio, Oulu, Tampere and Turku University Hospitals).

4.1 PUBLICATION I: ANATOMY AND MORPHOLOGY OF GIANT ANEURYSMS

4.1.1 PATIENTS AND IMAGES

Publication I is based on a retrospective case series of 125 consecutive patients diagnosed with 129 single or multiple giant intracranial aneurysms. To evaluate the radiolocial features, only GIAs diagnosed from 1989 onwards were included due to more constant availability of imaging records. When the study was launched, the database included cases up to year 2007. Only CT and DSA imaging modalities were used during the first ten years of the study period. The modern modalities, CTA, MRI and MRA studies, were available in various combinations for 78 patients.

4.1.2 IMAGE AND CLINICAL ANALYSIS

An experienced neurovascular radiologist and neurosurgeon (Riku Kivisaari) assessed all the imaging studies for relevant features. The diameter of saccular GIAs were defined by the dome maximum, and the diameter of fusiform aneurysms by the length of affected artery segment. Other measurements such as parent artery diameter, aneurysm width and neck size were assessed. Radiological intraluminal thrombosis was diagnosed from the CT or MR studies. The presence of thrombus was also indirectly supported by mismatch in size of intraluminal filling in angiographic studies and aneurysm size in native studies. Wall calcification was diagnosed from CT studies. In addition to radiological data, all clinical records were reviewed.

4.1.3 STATISTICAL ANALYSIS

The data was analyzed with statistical software (IBM SPSS Statistics; IBM Corp., Armonk, New York, USA). Due to the rarity and consequently relatively small number of GIAs, only descriptive statistical analyses were carried out.

4.2 PUBLICATION II: BYPASS SURGERY FOR COMPLEX ICA ANEURYSMS

4.2.1 PATIENTS AND IMAGES

Publication II is based on a retrospective case series of 39 consecutive patients with 41 complex ICA aneurysms which were treated with various occlusion strategies in combination with bypass procedures. The first cerebral bypass was performed in our department in 1998. During our study period of 1998–2016 and among all the 255 bypass cases performed, conventional bypasses with manual suturing represented 224 cases and the ELANA technique was applied in the remaining 31 cases. As experience and capability developed with conventional techniques, ELANA was abandoned in 2010. Among all these cases, we found altogether 41 complex ICA aneurysms (two patients with bilateral aneurysms). Other not included indications for bypass procedures were aneurysms of different locations or cerebrovascular pathologies such as Moyamoya.

Again, multiple overlapping combinations of imaging modalities were available. All the patients had a preoperative DSA study and BTO was done in 25 patients to assess collateral circulation. Preoperative CTA or MRA study was available in 26 and 35 patients respectively, and CT/MR perfusion studies in eight cases. CT/CTA or MRI/MRA were used for verification of postprocedural bypass patency and for the assessment of possible complications after operation and during the follow-up. Outpatient visits for clinical assessment ensued after treatment at 3-to-6-months and then according to patient-specific assessment.

4.2.2 IMAGE AND CLINICAL ANALYSIS

The imaging data was always primarily analyzed by an experienced neuroradiologist, and additional measures were later performed if needed. Location of aneurysms, morphological type and relevant operative radiographic features were identified from imaging studies. The diameter of saccular aneurysms was defined by the dome maximum, and the diameter of fusiform aneurysms by the length of affected artery segment. Branches originating from the aneurysms were identified. Radiological intraluminal thrombosis was diagnosed from the CT or MR studies and wall calcification from CT studies. Aneurysm occlusion status and patency of bypass were assessed from follow-up studies. Clinical patient records were reviewed for treatment strategies, clinical outcome and improvement of cranial nerve dysfunctions.

For analysis, ICA aneurysms were devided into three subgroups of anatomical locations; 1) the cavernous segment with no major artery branches; 2) the supraclinoid segment with artery branches (OphtA, Pcom, AChA); 3) the ICA bifurcation with major anterior (ACA) and middle cerebral artery branches (MCA).

4.2.3 STATISTICAL ANALYSIS

The data was analyzed with statistical software (IBM SPSS Statistics; IBM Corp., Armonk, New York, USA). Only descriptive statistical analyses were performed due to the rarity and low number of cases in our series.

4.3 PUBLICATION III: FLOW DIVERSION FOR ICA ANEURYSMS

4.3.1 PATIENTS AND IMAGES

Publication III is based on a retrospective case series of 62 consecutive patients with

ICA aneurysms which were treated with endovascular flow diversion. In our department, the first flow diversion of an ICA aneurysm was performed in February 2014. Last patient included in the study was treated in January 2019.

Various flow diverter devices were used; Pipeline™ Embolization Device (PED; Medtronic Neurovascular, Irvine, CA, USA), Surpass Streamline® Diverter (Stryker Neurovascular, Fremon, CA, USA), Fred® (Microvention, Aliso Viejo, CA, USA) and Derivo® Embolization Device (Acandis, GmbH, Pforzheim, Germany). PED was the most commonly used device due to its versatility. Surpass Streamline® is a more rigid stent and is preferred in cases of simple parent artery anatomy. Our conventional regime for periprocedural antiplatelet medication included clopidogrel (75–150 mg) daily for 3–6 months and acetylsalicylic acid (100–250mg) for up to 24 months.

Multiple overlapping imaging strategies were used. In addition to procedural DSA, 49 patients had a separate preprocedural diagnostic DSA study in records. CT and MRI were assessed for possible postprocedural complications. Our routine follow-up consists of DSA study at 3-to-6-months (all patients) and subsequent DSA at 12-to-24-months (35 patients). Also, outpatient visits for clinical assessment ensue after treatment at 3-to-6-months and then in conjuctiong with follow-up, imaging. During the follow-up. the aneurysm occlusion status was defined by the O'Kelly-Marotta grading scale.[413]

4.3.2 IMAGE AND CLINICAL ANALYSIS

The imaging data was always primarily analyzed by an experienced neuroradiologist, and possible additional measures were later supplemented. The location of aneurysms, morphological type and procedural data were identified from (pre)procedural DSA studies. The diameter of saccular aneurysms was defined by the dome maximum, and the diameter of fusiform aneurysms by the length of the affected artery segment. Other attributes such as aneurysm width and patency of FD-covered parent artery side branches were assessed. Radiological intraluminal thrombosis was diagnosed from the CT or MR studies and wall calcification from CT studies. The status of aneurysm occlusion as well as parent or branch artery patency were assessed from follow-up studies. To assess clinical outcome and improvement of cranial nerve dysfunctions, all the relevant clinical records were reviewed.

For analysis, ICA aneurysms were devided into two subgroups of anatomical locations; 1) the cavernous segment with no major artery branches; 2) the supraclinoid segment including the ICA bifurcation with side branches (OphtA, Pcom, AChA, ACA, MCA).

4.3.3 STATISTICAL ANALYSIS

The data was analyzed with statistical software (IBM SPSS Statistics; IBM Corp., Armonk, New York, USA). Due to novelty of flow diversion, only a small number of treated ICA aneurysms were possible to include in the study, and thus only descriptive statistical analyses were performed. ❦

Results

5.1 ANATOMY AND MORPHOLOGY OF GIANT ANEURYSMS (PUBLICATION I)

Spanning the study period of 19 years, 4018 patients with 5839 intracranial aneurysms were recalled from the aneurysm database. Altogether 129 giant aneurysms (2%) were diagnosed in 125 patients (3%). Of these patients, three (2%) had bilateral GIAs in the ICA, and one of these patients had a third GIA located in the basilar trunk. Additional smaller aneurysms were diagnosed in 35 patients (28%).

The mean age of these 125 patients was 53 years and a slight majority of them were female (n= 66, 53%). Altogether 63 (52%) patients presented with symptoms of aneurysm mass effect; CNDs (n=28, 22%), epilepsy (n=13, 10%), hemiparesis (n=4; 3%), obstructive hydrocephalus (n=2, 2%) or other nonspecific symptoms such as headache (n=16, 13%) [Table 6]. Regarding strokes, approximately one third of patients had a ruptured aneurysm leading to SAH (n=42, 34%) and 10 patients (8%) had experienced thromboembolic ischemia.

5.1.1 ANATOMICAL DISTRIBUTION OF GIANT ANEURYSMS

5.1.1.1 Giant aneurysms

Altogether 50 aneurysms (n=39%; 38 unruptured, 12 ruptured) were located in the ICA. The number of aneurysms varied in other regions as follows; middle cerebral artery (MCA; n=41; 32%; 24 unruptured and 17 ruptured), anterior cerebral artery (ACA; n=6; 5%; 3 unruptured and 3 ruptured) and vertebrobasilar and posterior cerebral artery aneurysms (VB-PCA; n=32; 25%; 22 unruptured and 10 ruptured).

Table 6
Presenting symptoms in GIA patients (n=125).

Symptom	n (%)
Mass effect	63 (50%)
- Cranial nerve dysfunction	28 (22%)
- Epilepsy	13 (10%)
- Hemiparesis	4 (3%)
- Hydrocephalus	2 (2%)
- Nonspecific, e.g. headache	16 (13%)
(Co)incidental	16 (13%)
SAH	42 (34%)
Thromboembolic ischaemia	10 (8%)

Table 7
Location of giant ICA aneurysms and relation to rupture status (n=50).

ICA aneurysms	All 50 (39%)	Ruptured 12 (24%)
Cervical ICA (C1)	1 (1%)	0
Cavernous ICA (C4)	21 (16%)	2 (10%)
Ophthalmic ICA (C6)	10 (8%)	2 (20%)
Communicating ICA (C7)	18 (36%)	8 (44%)
- Pcom	9 (7%)	3 (33%)
- AChA	1 (1%)	0
- Bifurcation of the ICA	8 (6%)	5 (63%)

5.1.1.2 Giant ICA aneurysms
In order of frequency, ICA aneurysms were diagnosed in extradural cavernous (C4; n=21; 42%), intradural communicating (C7; n=18; 36%) and ophthalmic (C6; n=10, 8%) segments. Cervical ICA was a rare location as only one traumatic aneurysm was found (Table 7).

5.1.1.3 Ruptured giant ICA aneurysms
Twelve giant ICA aneurysms were ruptured (24%) [Table 7]. A slight trend of increasing aneurysm rupture rate from proximal towards distal ICA segments was seen. Of proximal cavernous aneurysms, 10% were ruptured (n=2), and in the ICA bifurcation the rate was higher 63% (n=5). Altogether, almost half of aneurysms in the communicating ICA segment (C7) were ruptured (n=8, 44%).

5.1.2 MORPHOLOGY OF GIANT ICA ANEURYSMS

5.1.2.1 Morphological features of giant ICA aneurysms
The majority of giant ICA aneurysms were saccular (n=43, 86%) [Table 8]. Slightly more aneurysms were located in the right ICA or had a smooth and regural aneurysm wall (both; n=27, 54%). Wall calcification was seen in 19 (38%) and intraluminal thrombosis in 20 cases (40%). None of the ICA aneurysms were associated with anatomical variations of arteries.

5.1.2.2 Measurements of giant ICA aneurysms
Maximum diameter of ICA aneurysms ranged from 25 to 57 mm (Table 8). The mean diameter of saccular and fusiform aneurysms was 30 and 36 mm correspondingly. Mean parent artery diameter, i.e. diameter of ICA, ranged from 3 to 6 mm.

Table 8
Morphology of giant ICA aneurysms (n=50).

Shape	n (%)
Saccular	43 (86%)
Fusiform	6 (12%)
Traumatic, dissecting	1 (2%)
Wall appearance	
Smooth wall	27 (54%)
Irregular wall	22 (44%)
Calcification and thrombosis	
Wall calcification	19 (38%)
Intraluminal thrombosis	20 (40%)

Table 9
Measurements of giant ICA aneurysms; saccular and fusiform aneurysms (n=50).

Saccular (n=43)	mean (range) [mm]
Maximum diameter	30 (25 – 57)
Maximum dome width	25 (12 – 52)
Maximum neck width	12 (4 – 28)
Parent artery width	4 (2 – 6)
Fusiform (n=7)	
Maximum diameter	36 (27 – 45)
Maximum dome width	14 (8 – 18)
Parent artery width	3 (2 – 5)

5.1.3 REGIONAL AND MORPHOLOGICAL TRENDS OF GIANT ANEURYSMS

Most of the ICA aneurysms were saccular (86%) in contrast to the VB-PCA region wherein approximately one third of aneurysms had fusiform shape (34%). The mean diameter of saccular and fusiform aneurysms in the ICA was slightly smaller than in the other major regions (30 vs. 33-40 mm; 36 vs. 41–53 mm). Among different regions, the proportion of ruptured aneurysms (24%) was lowest in ICA (MCA, 41%, ACA, 50%; VB-PCA, 31%). All ruptured GIAs had more infrequently wall calcification (24% vs. 38–67%) or intraluminal thrombosis (33% vs. 40–67%) than all aneurysms in general.

5.2 PRESENTATION OF TREATMENT GROUPS (PUBLICATIONS II-II)

5.2.1 BYPASS PROCEDURES

In the series of 39 patients with 41 ICA aneurysms treated with bypass procedures, bilateral mirror aneurysms were found in two patients (5%) [Table 10]. None of the patients presented with acutely ruptured aneurysms. Aneurysm mass effect caused CNDs in a majority of cases (n=29; 74%). Aneurysms were giant-sized in 26 patients (63%). Ten patients (31%) had history of treatment regarding the target aneurysm.

5.2.2 FLOW DIVERSION

Altogether 62 patients with 76 ICA aneurysms received treatment with flow diversion (Table 10). Adjacent tandem aneurysms were diagnosed in 11 patients (18%) and mirror aneurysms in four patients (6%). Four patients (6%) presented with SAH and twelve patients presented with CNDs (19%). Aneurysm had reached giant size in seven cases (11%). Other complex features were as follows; 22 recurrent or unsuccessfully treated aneurysms (29%), six fusiform aneurysms (8%), seven dissecting or pseudoaneurysms (9%) and eight aneurysms with a side branch originating from the aneurysms wall (11%).

Table 10

Presentation of patients and morphology of ICA aneurysms treated with bypass procedures or flow diversion.

Patients	**Treatment with bypass procedures n (%)**	**Treatment with flow diversion n (%)**
No.	39	62
Mean age [yrs]	50	54
Presentation		
Symptoms of CNDs	29 (74%)	12 (26%)
SAH	0	4 (6%)
Aneurysms		
No.	41	72
- Cavernous	23 (56%)	18 (25%)
- Supraclinoid	12 (29%)	} 56 (75%)
- ICA bifurcation	6 (15%)	
Tandem aneurysms [pt.]	0	11 (18%)
Mirror aneurysms [pt.]	2 (5%)	4 (6%)
Specific complex features		
Giant aneurysm (≥25 mm)	26 (63%)	7 (11%)
Fusiform aneurysm	14 (34%)	6 (8%)
Dissecting aneurysm	0	5 (7%)
Pseudoaneurysm	0	2 (3%)
Side branches	NA	8 (11%)
Recurrent aneurysm	10 (31%)	22 (29%)
Ruptured aneurysm	0	4 (5%)
Wall calcification	18 (44%)	9 (13%)
Intraluminal thrombosis	23 (56%)	7 (10%)

5.3 TREATMENT OF COMPLEX ICA ANEURYSMS (PUBLICATIONS II-III)

5.3.1 BYPASS PROCEDURES

5.3.1.1 Bypass procedures for cavernous aneurysms

Bypass procedures were needed in the treatment of 22 patients having cavernous ICA aneurysms (Table 11) [Figure 31]. One patient had bilateral mirror aneurysms at this segment. Most of the aneurysms were giant in size (n=14, 61%).

Altogether 25 EC-IC bypass procedures were performed including the one case with bilateral aneurysms and re-treatments in two separate cases. Due to a lack of branching arteries in the cavernous segment, the straightforward occlusion strategy of PAO was usually pursued (n=20, 87%).

As these aneurysms and occlusion sites had a proximal location, the preoperative assessment for revascularization often led to a choice for a high-flow bypass (n=16; 78%). This reflects also the heavy reliance in the ELANA technique for constructing the anastomosis (n=14, 61%) [Figure 32]. Moderate-to-high-flow bypass was chosen in two cases (9%; double barrel STA-MCA) and low-flow bypass in five cases (22%; STA-MCA) [Figure 33].

5.3.1.2 Bypass procedures for supraclinoid aneurysms

In our series, treatment of 12 supraclinoid ICA aneurysm necessitated revascularization (Table 11). Half of these aneurysms were giant in size (n=6, 50%). Eight cases had a single or multiple branching arteries originating from the aneurysm dome in order of frequency; Pcom (n=5; 42%), OphtA (n=4; 33%) and AChA (n=3; 25%).

Among these 12 patients, altogether 13 EC-IC bypass procedures were performed including one re-treatment. The supraclinoid segment with branching or perforator arteries reflected the chosen occlusion strategies; simple PAO (n=8, 58%; one PAO performed not until the re-treatment for occluded bypass was done), clipping (n=1; 8%; intraoperative finding allowed aneurysm neck clipping after completion of bypass) and trapping (n=1; 8%; proximal balloon and distal clip occlusion). In two cases of recurrent aneurysms, previous PAO without revascularization had led to a situation wherein the aneurysm at the level of Pcom had persistent retrograde filling through this artery. Endovascular occlusion of the Pcom was the chosen occlusion strategy in both cases (17%).

The revascularization strategies varied as follows; high-flow bypass with SVG in five cases (42%), moderate-to-high-flow bypass in one case (8%; STA-SVG-MCA) and low-flow in six cases (50%; STA-MCA). Due to more superficial location of anastomosis site, the ELANA technique was applied on-

FIGURE 31
Anteroposterior DSA study showing an aneurysm in the cavernous ICA segment (C4). The communicating ICA segment (C7) is seen distal to the aneurysm.

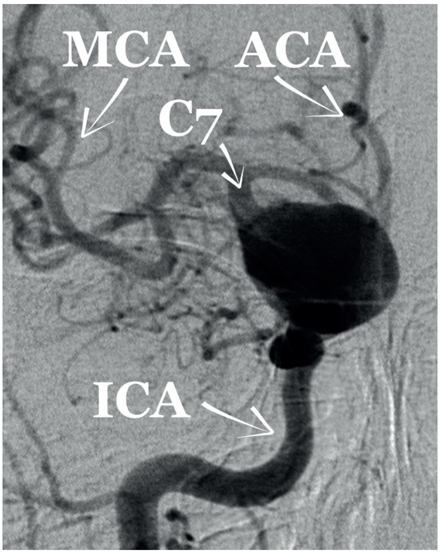


Figure 32
Lateral view of merged cerebral and cervical DSA studies demonstrating a high-flow bypass. Distal anastomosis was performed with ELANA technique (platinum pilot ring magnified).

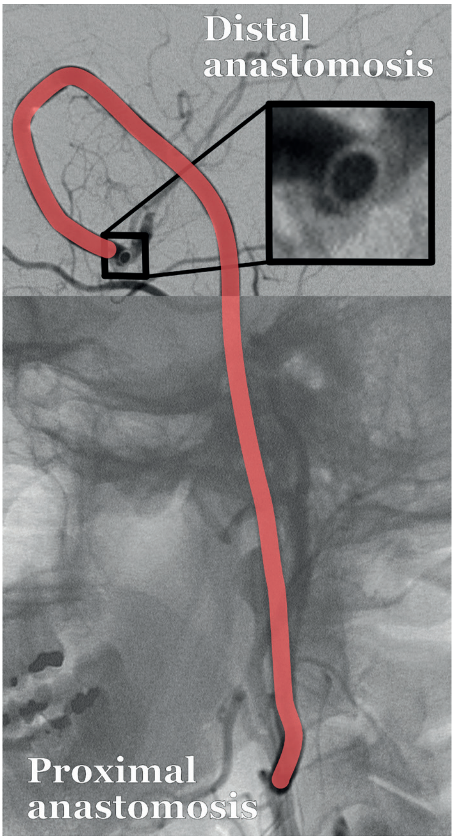
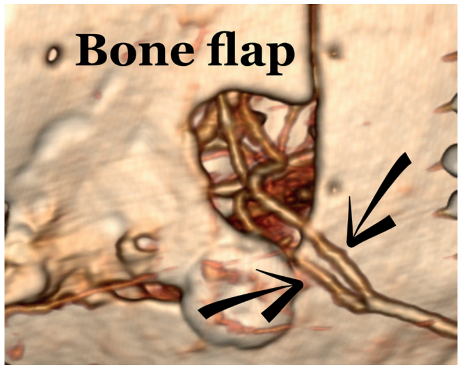


Figure 33
Lateral 3D-CTA reconstruction showing a double barrel bypass with two STA branches (arrows) traversing the craniotomy.



ly in two cases (17%) while the recipient sites were then M1 or M2 segment of the middle cerebral artery.

5.3.1.3 Bypass procedures for aneurysms in the ICA bifurcation

Five patients were diagnosed with aneurysms in the ICA bifurcation with incorporation of the M1 and A1 branches (Table 11) [Figure 34]. One of these patients harboured bilateral mirror aneurysms of this segment. All of the aneurysms had giant size.

The six aneurysms were all treated with EC-IC bypass procedure. Due to complexity in aneurysms of this region, the occlusion strategies varied substantially as follows; trapping (n=2), clip reconstruction (n=1), proximal occlusion (n=1) and Crutchfield apparatuses (vascular clamps) in case of mirror aneurysms.

Single high-flow bypass with graft was chosen in two cases, moderate-to-high-flow bypass in another two cases (double barrel STA-MCA) and low-flow bypass in one case (STA-MCA). A strategy of combined high- and low-flow bypasses was accomplished in one particular aneurysm. In this case, the aneurysm and ICA bifurcation was reconstructed and compartmentalized with clips in order to form two isolated regions of blood flow. The distal compartment included the ACA and MCA regions (STA-MCA bypass), and the proximal compartment included the prominent Pcom and AChA (ECA-RAG-M2 bypass) [Figure 35].

5.3.1.4 Re-treatment with bypass procedures

Three patients were re-treated due to intraoperative bypass occlusion (n=2) or persistent filling of supraclinoid aneurysm after

Figure 34
Anteroposterior DSA study showing an aneurysm in the communicating ICA segment (C7). The cavernous ICA segment (C4) is seen proximal to the aneurysm.

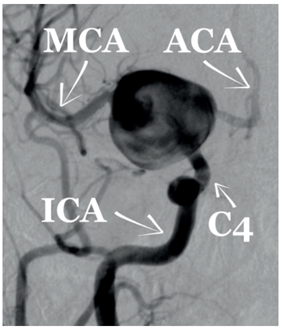
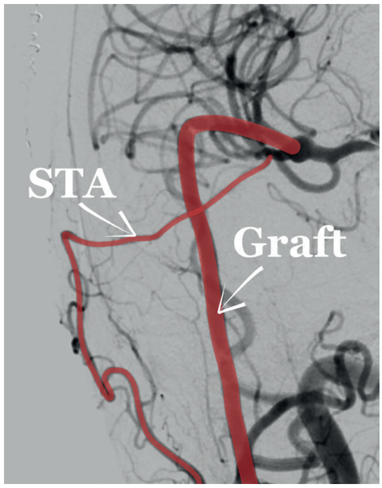


Figure 35
Anteroposterior view of DSA study showing the combination of low- (STA) and high-flow (graft) bypasses.



distal occlusion (n=1) [Table 11; Figure 36]. In all these cases a new ECA- or STA-MCA bypass was reconstructed with an interpositioned saphenous vein graft. However, two of the reconstructed bypasses occluded; one during early follow-up (≤7 days) and another at later follow-up.

5.3.2 FLOW DIVERSION

5.3.2.1 Flow diversion for cavernous aneurysms

Flow diversion was the chosen treatment modality in 16 patients having 18 cavernous ICA aneurysms (Table 12). Three patients harboured multiple adjacent tandem aneurysms (19%). One third of aneurysms were giant-sized (n=6; 25%). Taken together, eighteen flow diverter deployments were performed including re-treatments of two patients. The first patient receiving treatment with a flow diverter in our department, and the only such case recognized thus far, had the flow diverter device migrated and dislodge partly into the aneurysm dome. Re-operation in this case with another flow diverter was unsuccessful.

5.3.2.2 Flow diversion for supraclinoid aneurysms

Altogether 48 patients with 56 supraclinoid ICA aneurysms were treated with flow diversion (Table 12). Eight patients had tandem aneurysms (18%). Only one aneurysm was giant-sized (n=1; 2%) but the other 23 aneurysms (39%) were regarded as large (≥10 mm). Almost half of the aneurysms were recurrent (n=21, 44%) with history of clipping and/or coiling. Also various other complicating features were noted (Table 13). To treat the aneurysms, 56 flow diversion procedures were executed. This number includes treatment of cases with bilateral mirror aneurysms (8%) and re-treatment in four instances (4%).

5.4 OUTCOME OF TREATMENT (PUBLICATIONS II-III)

5.4.1 ANEURYSMS AND ARTERIES

5.4.1.1 Bypass procedures: aneurysms

The latest angiographic follow-up showed occlusion rates of 91% for cavernous aneurysms (n=21), 83% for supraclinoid aneurysms (n=10) and 50% for aneurysms locat-

Table 11
Aneurysm occlusion strategies and bypass types for ICA aneurysms (n=41).

Occlusion type	Cavernous n (%)	Supraclinoid n (%)	ICA bifurcation n (%)
Proximal	19 (83%)	7 (58%)	3 (50%)
- Endovascular	6 (26%)	3 (25%)	-
- Crutchfield clamp	1 (4%)	-	2 (33%)
Distal	1 (4%)	-	-
Side branch (Pcom)	-	2 (17%)	-
Trapping	3 (13%)	1 (8%)	2 (33%)
Neck clipping	-	1 (8%)	-
Clip reconstruction	-	-	1 (17%)*
Bypass type			
High-flow	16 (78%)	5 (42%)	3 (43%)*
- ELANA	14 (61%)	2 (17%)	-
Moderate-to-high flow	2 (9%)	1 (%)	2 (29%)
Low-flow	5 (22%)	6 (50%)	2 (29%)*
Re-treatment	2 (9%)	1 (8%)	-

*Two separate bypasses for compartmentalized aneurysm.

ed in the ICA bifurcation (n=3). Altogether three aneurysms did not respond to treatment in radiologic respect (7%). The causes were incomplete trapping in one case and intentional incomplete occlusion with Crutchfield clamp in two cases.

5.4.1.2 Bypass procedures: bypass patency

Two bypasses (5%) became occluded intraoperatively (one case of ELANA). These led to subsequent reoperations. Early bypass occlusions (≤7 days) were diagnosed in seven cases (17%; five cases of ELANA; one reoperated bypass). During the late follow-up, occlusion of the bypass was seen in five patients (12%) without clinical sequela (another reoperated case included). The majority of all occluded bypasses were perfomed with SVG (n=13, 93%).

5.4.1.3 Flow diversion: aneurysms

Among the four initially ruptured supraclinoid aneurysms, CTA confirmed the obliteration of two aneurysms during the same

Figure 36
Anteroposterior view of merged pre- and postprocedural (black box) DSA studies showing addition of proximal coil occlusion due to persistent aneurysm filling. The previously performed trapping had failed, and antegrade blood flow through the aneurysm and into the OphtA had continued.

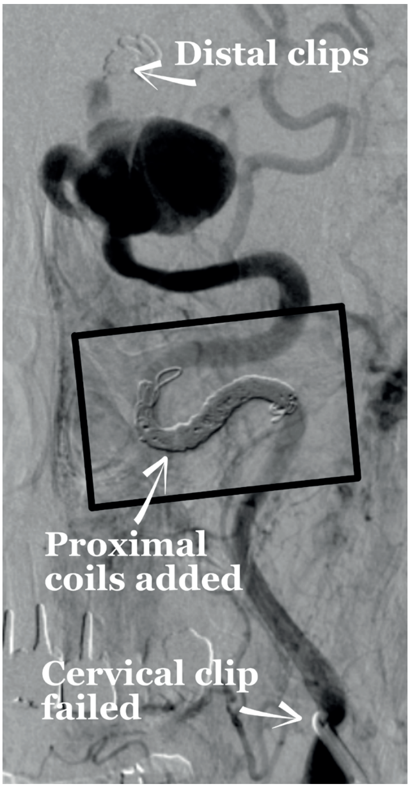


Table 12
Flow diversion for ICA aneurysms.

Devices	Cavernous n (%) 18 (25%)	Supraclinoid n (%) 56 (75%)
Surpass Streamline®	12 (67%)	17 (75%)
- With coils	-	1 (2%)
- With Atlas™ stent	-	1 (2%)
- Multiple devices	-	1 (2%)
Pipeline™	6 (33%)	28 (50%)
- Multiple devices	3 (17%)	3 (5%)
Fred®	-	9 (16%)
Derivo®	-	2 (4%)

hospitalization (<2 weeks). The third aneurysm re-ruptured on the 10th postprocedural day and led to a case fatality. The fourth ruptured aneurysm was partially filling at routine 6-month follow-up but has not re-ruptured during 17-months of total follow-up.

The first routine angiographic follow-up visits at 3-to-6 months showed that altogether 36 of the 59 patients (61%; excluded are two case fatalities and one case had follow-up elsewhere) had occluded aneurysms (cavernous aneurysms, 69%; supraclinoid aneurysms, 58%) [Table 13]. During later follow-up, additional five patients (8%) achieved aneurysm occlusion.

Thus, a total occlusion rate of 69% was found in our series (n=41/59). However, 9 of the 18 patients with residual aneurysms did not reach follow-up angiograms beyond the first 6 months. Three aneurysms in three patients (5%) had not responded to treatment at latest follow-up (OKM grade A; including one case of migrated device and one case of mirror aneurysm filling through patent channel in between the device and artery wall).

Re-treatments with additional FDs were performed in six cases (10%) for variable indications; rerupture, device migration or residual filling (Table 14).

5.4.1.4 Flow diversion: patency of devices and branches

Asymptomatic, slight stenosis of flow diverter stent (n=8/55, 15%) or stenosis of parent artery beside the flow diverter (n=5, 9%) were seen in follow-up DSA studies. In one another case, in-stent stenosis progressed to an asymptomatic occlusion of distal ICA, but the anterior communicating artery provided good crossflow. The need for prolonged usage of antiplatelet medication was assessed on a case-by-case basis.

During the follow-up, only clinically silent occlusions of flow diverter -covered ICA side branches were noted; OphtA (n=3, 6%), Pcom (n=10, 20%), AChA (n=1, 3%) and A1 segment (n=2, 18%). The distal landing zone of the flow diverter was in the M1 segment of the MCA in 11 cases (19%). Of these, one case developed an ICH and deep ischemia immediately after procedure.

5.4.2 ISCHAEMIC COMPLICATIONS

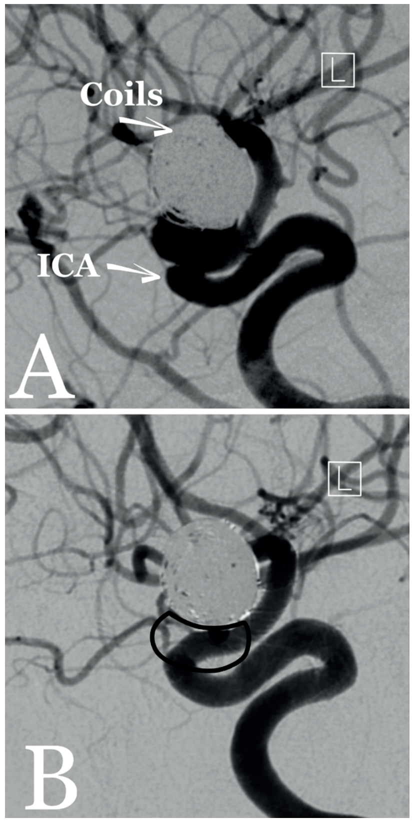
5.4.2.1 Bypass procedures

During the early postoperative period (≤7 days), symptomatic ischaemic lesions were encountered in six cases of cavernous aneurysms (27%), in four cases of supraclinoid aneurysms (33%) and in three cases of aneurysms in the ICA bifurcation (50%). This yelds a rate of 33% for symptomatic patients (n=13). In addition, four patients (10%) had only radiologic ischemic findings (Table 15). Both, ischaemia of perforator and main trunk regions were seen, but the most frequent specific location was the capsular region (n=8). Low-molecular-weight heparin (LMWH) was commonly combined to postprocedural ASA if ischaemic lesions were encountered (n=8; 47%).

Among all the 13 cases with symptomatic ischaemia, six cases of concurrent early bypass occlusions were diagnosed (cavernous aneurysms treated with the ELANA technique). However, only one full-blown hemispheric infarction was seen implying that robust collateral circulation was available in other five cases. Another three cases of early (≤7 days) and five cases of late, but clinically silent bypass occlusions were diagnosed.

FIGURE 37

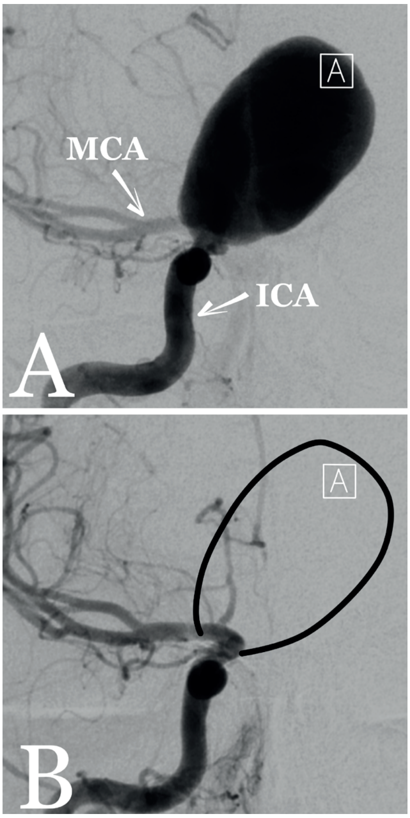
Lateral pre- (A) and postprocedural (B) DSA studies of a previously coiled and recurrent aneurysm in the ICA. Treatment with flow diverter lead to aneurysm occlusion (B). Black line designates the area where the aneurysm was (B).



5.4.2.2 Flow diversion

After flow diversion, there were 10 patients (16%) with early diagnosed (≤24 hours) symptomatic ischemia. All flow diverters were patent and patients were on routine periprocedural antithrombotic medication. Another two cases (3%) experienced clinically silent ischemia (Table 15). Ischemic complications were associated with treatment of cavernous (n=3) and supraclinoid aneurysms (n=9) at the same rate (19%). In the majority of patients (n=8, 67%), multiple lesions were

Figure 38
Anteroposterior view of pre- (A) and postprocedural (B) DSA studies of a GIA at the ICA bifurcation. Treatment with flow diverter lead to aneurysm occlusion (B). Black line designates the area where the aneurysm was (B).



located in various cerebral lobes or regions. Overrepresentation of ischemic complications was seen in cases with two implanted flow diverters (n=4/7, 57%).

5.4.3 HEMORRHAGIC COMPLICATIONS

5.4.3.1 Bypass procedures

Local contusions related to parenchymal manipulation or retraction were seen near deeper anastomosis sites (n=7, 18%) [Table 16]. Other frequently associated findings were the utilized ELANA technique (n=6, 86%) and consequently used peroperative systemic heparinization (n=4, 57%). However, only two cases experienced related symptoms. Another three cases (7%) needed removal of postoperative epi- or subdural hemorrhages. There were no intracerebral or subarachnoid hemorrhages requiring intervention.

5.4.3.2 Flow diversion

Major hemorrhagic complications occurred in three cases (5%) [Table 16]. Those included SAH following treatment of an unruptured aneurysm and after treatment of initially ruptured aneurysm (n=2, 3%). One case was diagnosed with ICH (2%). All hemorrhagic complications were associated with supraclinoid aneurysms.

Due to femoral artery puncture, two cases of retroperitoneal hematomas requiring surgical removal were diagnosed (3%). Also, procedured-related were three cases of pseudoaneurysms (5%) and two cases of arterial dissections (3%).

5.4.4 CRANIAL NERVE DYSFUNCTIONS

5.4.4.1 Bypass procedures

At presentation, 29 patients (74%) had preoperative CNDs, and six aneurysms located only in cavernous ICA were associated with combined dysfunctions of multiple nerves (Table 17). Treatment caused new postoperative CNDs in nine patients (23%). Abducens nerve dysfunction (CN VI; n=15, 38%) was the most common finding among preoperative CNDs and oculomotor nerve dysfunction (n=6, 67%) among postoperative CNDs. Among preoperative CNDs, CN II and III dysfunctions improved at rates of 22% and 25% respectively. The CN IV–VI dysfunctions improved at a higher rate of 40–50%. Among the postoperatively occurred CNDs, majority of the CN III dysfunctions improved (83%). Later strabismus surgery corrected two cases of abducens nerve palsies.

5.4.4.2 Flow diversion

At pretreatment phase, 12 patients (19%) had CNDs related to aneurysm mass effect (Table 17). Most of these aneurysms were at least large-sized (≥10mm; n=11, 92%). After treatment, two patients developed new CNDs related to treatment of very large cavernous aneurysms (≥20 mm; 2%). Cavernous aneurysms most frequently caused CN III or VI dysfunctions (both; n=5, 63%) and supraclinoid aneurysms CN II dysfunction (n=3, 75%). During the follow-up, eight patients (67%) experienced improvement. Vision deficits (CN II) improved at rate of 60%. Among the motor ocular nerves, CN III and VI showed highest recovery rates of 40–50%. Improvement of symptoms was seen only in cases with totally occluded aneurysms.

5.4.5 FUNCTIONAL OUTCOME

5.4.5.1 Bypass procedures

In the series of bypass procedures, the mean follow-up length was 51 months (range 0–201; 0 for three foreigners and for two cases of death [one case fatality; one unrelated death]). Altogether 31 patients (79%) presented with good (≤2) and eight patients (21%) with poor modified Rankin Scale score (mRS; ≥3). At discharge phase, 17 patients (44%) had worse mRS score than at presentation. However, only four patients (10%) with postoperative complications ended up in the poor outcome group for long-term. Of the patients initially presenting with poor mRS score, two patients (5%) recovered into good outcome group (Table 18).

5.4.5.2 Flow diversion

In the series of flow diversion, altogether 54 patients (87%) with unruptured aneurysms presented with a good mRS score. Of these good grade patients, three patients were classified in the poor outcome group for long-term (one case of ischemic complication, one case of ICH, and one case fatality due to aneurysm rupture two weeks

TABLE 13
Flow diversion and aneurysm occlusion rates at first DSA follow-up in association to various features (n=59).

Aneurysms [patients]	Occluded n (%)
All	36 (61%)
- Cavernous	11 (69%)
- Supraclinoid	26 (58%)
Presentation [aneurysms]	
SAH	2 (50%)
Recurrent	11 (48%)
Morphology [aneurysms]	
Saccular	31 (63%)
Fusiform	1 (20%)
Dissecting	2 (40%)
Pseudoaneurysm	2 (100%)
Side branch	4 (50%)
Size [aneurysms]	
≥9 mm	23 (61%)
10-24 mm	17 (63%)
≥25 mm	6 (86%)
Multiplicity [patients]	
Multiple aneurysms	6 (50%)
Tandem aneurysms	5 (63%)
Mirror aneurysms	1 (25%)
Flow diverter [patients]	
Surpass Streamline®	21 (60%)
Pipeline™	15 (56%)
Fred®	7 (78%)
Derivo®	0
Multiple flow diverters	3 (43%)

Table 14
Re-treatment with flow diversion (n=6).

Cause	Time to re-treatment	Time from re-treatment to latest follow-up	OKM grade change
Rerupture	11 days	6 days	Case fatality
FD migration	8 months	33 months	A ▶ A
FD migration	17 months	7 months	B ▶ D
Persistent filling	22 months	6 months	B ▶ C
Increased filling	24 months	6 months	A ▶ B
Persistent filling	44 months	6 months	B ▶ B

Table 15
Ischaemic complications and related segmental location of treated aneurysms.

<table>
<tr><th>Aneurysm location</th><th>Bypass procedures n (%)</th><th>Flow diversion n (%)</th></tr>
<tr><td>Cavernous</td><td>8 (36%)</td><td>3 (19%)</td></tr>
<tr><td>Supraclinoid</td><td>6 (50%)</td><td rowspan="2">} 9 (19%)</td></tr>
<tr><td>Bifurcation</td><td>3 (50%)</td></tr>
<tr><td>Symptomatic</td><td>13 (33%)</td><td>10 (16%)</td></tr>
<tr><td>Case fatalities</td><td>1 (3%)</td><td>-</td></tr>
</table>

Table 16
Hemorrhagic complications.

Minor hemorrhage	Bypass procedures n (%)	Flow diversion n (%)
Contusion	7 (18%)	-
Symptomatic	2 (5%)	-
Major hemorrhage		
SAH	-	2 (3%)
ICH	-	1 (2%)
Extra-axial hemorrhage	3 (8%)	-
Retroperitoneal	-	2 (3%)
Symptomatic	3 (8%)	5 (8%)
Case fatalities	-	2 (3%)

Table 17
Cranial nerve dysfunctions and improvement during the follow-up.

CNDs [patients]	Bypass procedures n (%)	Flow diversion n (%)
At presentation	29 (74%)	12 (19%)
Occurred after treatment	9 (23%)	2 (3%)
Improvement [nerves]		
Vision (CN II)	22%	60%
Motor (CN III, IV, VI)	up to 50%	up to 50%

after eventless treatment). Four patients (6%) with unruptured aneurysms presented with a poor mRS score, and of these, one patient had favourable functional outcome in long-term. Two patients presenting with SAH had a good outcome score at follow-up (mRS score ≤2 at 6–12 months). One patient suffering SAH had a fatal outcome due to aneurysm re-rupture (Table 18). ❦

Table 18

Functional outcome of patients with unruptured aneurysms presented with modified Rankin Scale score groups (good outcome, ≤2; poor outcome, ≥3). Four patients suffering of SAH and who received treatment with flow diverters were excluded due to different initial prognosis.

	Bypass procedures n (%)		Flow diversion n (%)	
Time point	**Good mRS ≤2**	**Poor mRS ≥3**	**Good mRS ≤2**	**Poor mRS ≥3**
At presentation	31 (79%)	8 (21%)	54 (93%)	4 (7%)
At discharge	20 (51%)	19 (49%)	49 (84%)	9 (16%)
At latest follow-up	29 (74%)	10 (26%)	52 (90%)	6 (10%)

Discussion

6.1 ANATOMY AND MORPHOLOGY OF GIANT ICA ANEURYSMS

Our anatomic series of 129 GIAs consists of consecutive patients over a time period of 19 years. With this, we aimed at minimizing selection bias which is inevitably present in the treatment-focused case series published on such rare lesions as GIAs. For the same reason, prospective studies would be very slow to perform.

6.1.1 PRESENTATION

In our series, among all major artery regions the ICA was the most common location for giant aneurysms (n=50, 39%). The finding is supported by earlier studies, but no large epidemiologic reports on exact anatomical location are available.[11,15,17,192] Most GIAs in the ICA presented with symptoms of mass effect and CNDs due to multiple cranial nerves traversing the region to reach orbita.[14,153,192] Probably for the same reason, ICA aneurysms were diagnosed already at slightly smaller size than aneurysms in the other major artery regions. Expected low number of ruptured GIAs in the cavernous segment were seen, which is related to their location in the extradural space.[6,14,229] On the other hand, almost half of GIAs in the supraclinoid region presented with rupture.

6.1.2 MORPHOLOGY

A majority of GIAs in the ICA were saccular (86%). Depending on the complex combination of inflammation, degeneration, location in arteries and flow dynamics, aneurysms may take a saccular or fusiform configuration. However, in the ICA, there are multiple major artery branching sites which are favorable locations for the saccular shape. Also, the bony base of the skull and the location of the ICA between the intra- and extradural compartments may provide external support and steer the aneurysm development towards the saccular shape instead of longer pathologic segments of fusiform morphology. Then, regarding aneurysms with wall calcification and/or intraluminal thrombosis, we saw a protective trend against rupture. A similar finding is reported in one study focusing on GIAs.[11] However, intraluminal thrombosis may predispose to embolization, and has not been a protective factor against rebleeding of GIAs.[13,15] Most patients presenting with thromboembolic symptoms in our series had radiologic thrombosis in the aneurysm sack (n=6, 60%).

6.2 TREATMENT OF COMPLEX I CA ANEURYSMS

6.2.1 BYPASS PROCEDURES

General comparison to other surgical series of bypass procedures for complex ICA aneurysms is difficult as case-specific aneurysm occlusion strategies vary. Some previous studies report occlusion rates ranging from 77% to 100%, the latter reached with uniformly performed aneurysm trapping.[17,274,297,304] In our series, 83% of aneurysms became obliterated after various combinations of occlusion and revascularization strategies. The goal of reduction in aneurysm flow was achieved in an additional 12% of cases. Depending on the specific location of the ICA aneurysms, different anatomical attributes should be included in formulation of treatment strategy.

6.2.1.1 Strategy for cavernous ICA aneurysms

For aneurysms in the cavernous segment without major branching arteries, the simple PAO alone is a straightforward strategy. Without revascularization, simple PAO may yield aneurysm occlusion rates of up to 100%.[383,422] In our series, aneurysm occlusion rate of 91% (n=21) was ultimately achieved for cavernous aneurysms. We did the PAO immediately after intraoperative confirmation of the bypass patency. However, flow diversion is nowadays considered as primary treatment modality for this artery segment. The significance of bypass procedures would be in cases wherein other treatment methods have failed and PAO is needed but not tolerated without revascularization.

6.2.1.2 Stragery for supraclinoid ICA aneurysms

For supraclinoid aneurysms, the branching arteries (OphtA, Pcom) may retrogradely fill the aneurysm, or even one another. Due to these branches, proximal PAO may yield more uncertain occlusion results. AChA branch is crucial to protect, but superior hypophyseal artery (SHA) divisions are relatively safe to sacrifice.[454] With aneurysm trapping, more risks are taken for ischaemic complications. However, we achieved a good aneurysm occlusion rate of 83% in supraclinoid aneurysms of which the majority were treated with PAO. With PAO, the disrupted flow pattern seemed to ultimately lead to aneurysms thrombosis. In such cases, the progressive aneurysm thrombosis did not cause symptomatic occlusions of branch arteries.[17] Of special notion, targeted endovascular coiling of Pcom resulted in similar deep ischaemic lesions in two cases of our series. Therefore, a more exact clip ligation may be preferred to protect the Pcom perforators.

6.2.1.3 Strategy for aneurysms in the ICA bifurcation

Complex aneurysms in the ICA bifurcation were the most heterogenous group. The same strategic principles of treatment for supraclinoid aneurysms are valid. In addition, lenticulostriatal perforators or artery of Heubner may be incorporated in the aneurysm. Robust crossflow through the anterior communicating artery may permit occlusion of the ipsilateral A1 segment. Diffuse collaterals from the ECA may perfuse the MCA region having an effect on magnitude of revascularization needed. In our series, trapping was possible in two cases leading to exclusion of aneurysm. As a secondary strategy, proximal occlusion and resulting flow reversal may be sufficient to trigger aneurysm thrombosis. Third, and most challenging option is remodeling and compartmentalization of aneurysms. In such cases, multiple bypasses may be needed for each compartment.

6.2.1.4 Bypass patency

Previous studies report bypass patency rates of various grafts or pedicles ranging 73–98% while most occlusions occur during the first postoperative week.[270,304,425–430] In our series, patency rate at the latest follow-up was 68% (n=30). Among the nine early bypass occlusions in our series, only six patients experienced ischemic complications, and only one full hemispheric infarction was seen. Thus, robust and protective collateral circulation had to be present in these cases and may have itself contributed to easier occlusion tendency. Late bypass occlusions are usually clinically silent events and positive sign of development of extensive collateral perfusion. We saw five such late bypass occlusions in our series.[426,430]

6.2.2 STRATEGY OF FLOW DIVERSION

The internal carotid artery is a good target for flow diversion due to its proximal location and large caliber. Tortuosity in the carotid siphone or atherosclerotic changes may raise technical challenges in device deployment. Also, very wide-necked aneurysms or longer pathologic segments may be problematic for treatment with a single device necessitating coaxial constructions. However, when this aneurysm complexity increases, obliteration rates decrease and procedure-related complication risks become higher.[206,436,444] Prolonged dual antiplatelet therapy is necessary as late ischemic complications may occur, which limits the use of FDs when treating ruptured aneurysms.[403,442] The majority of the aneurysms in our series were either giant, recurrent or shared other morphological features regarded as complex.

6.2.2.1 Ruptured aneurysms

In ruptured ICA aneurysms, we consider flow diversion only after other treatment methods are found not feasible, thus narrowing the cases to mainly ruptured dissecting or blister aneurysms. In our series, three such aneurysms became occluded or were filling less (75%), which is comparable to numbers previously reported (88%).[402] The fourth aneurysm re-bled reflecting the complicated nature of delayed aneurysm occlusion after flow diversion (case fatality).[402] As opposed to using clopidogrel in cases of ruptured aneurysms, we administered postprocedural low dose tinzaparin instead (LMWH). This was due to easier reversibility (e.g. for external ventricular drain [EVD] placement or aneurysm rebleeding) and to cover the need for venous thromboembolism prophylaxis. Further analysis of this medication regimen was impossible because of low number of cases, but a meta-analysis reported no major differences between various other antiplatelet therapy protocols.[403]

6.2.2.2 Occlusion rate

The long-term complete occlusion rates for all ICA aneurysms treated with FDs are 57–95%, and 62–91% for cohorts of large or giant ICA aneurysms.[309,400,411,455–461] However, aneurysm features, treatment protocols and availability of follow-up seem to vary substantially. In our series, the rate of patients with completely occluded aneurysms at first 6-month follow-up was 61% (n=36/59) including patients treated for multiple aneurysms. The cumulative occlusion rate is known to slow down with time.[400] We saw only five additional patients (8%) reaching total aneurysm occlusion during the later follow-up. So, our confirmed total occlusion rate was 69% which is in line with previous findings. Late aneurysm recurrences are rare after successful treatment with flow diversion.[462] We did not see any late recurrences but in two cases (3%) the residual filling expanded. In our opinion, long-term follow-up of partially occluded aneurysms is justified.

6.2.2.3 Outcome-related features

In our series, there was a small difference in occlusion rates of cavernous (69%) and supraclinoid (58%) aneurysms in favor of the cavernous group without side branches. As reported before, incorporated side branches or fusiform morphology of aneurysms seem to have negative effect on occlusion rates.[206,463] This is best explained by the special flow dynamics. Although we saw occlusion rates lower-than-average for recurrent aneurysms, and higher-than-average for giant aneurysms, there are also reports on contradicting trends.[461,464] Flow diversion has particular advantage in treatment of multiple tandem aneurysms as one device may be sufficient, and we achieved acceptable patient-specific occlusion rates in such cases.[404] Bilateral aneurysms behave as independent aneurysms as expected, and we tend to treat these in separate sessions.

Regarding the various devices for flow diversion, none has proved to be absolutely superior. For example, similar occlusion rates for matched case cohorts is reported for PED and Fred®.[460] Our slightly better results with Fred® probably reflect the small case number and case complexity. Two coaxial devices with more extensive coverage did not seem to increase the probability of aneurysm occlusion in our experience.

Perioperative antiplatelet medication is essential in flow diversion. To our knowledge, there are no studies supporting superiority of specific medication regimen. We had higher occlusion rates in cases treated with prasugrel instead of clopidogrel. However, it has been shown that prasugrel has similar safety and efficacy profile in comparison to clopidogrel.[465]

6.2.2.4 Re-treatment

The very case-specific re-treatment rate was 10% among all the aneurysms in our series of flow diversion. Re-treatment of residual aneurysms with additional flow diverters is planned case-by-case. Our first line strategy for promoting thrombosis in residual aneurysms is stepwise tempering of dual antiplatelet therapy (DAPT) and watchful waiting. Earlier re-intervention is usually justified in primarily ruptured or enlarging residual aneurysms.

6.2.2.5 Late flow diverter and side branch patency

After the treatment, in-stent stenosis is an issue that may arise.[466–468] In our series, none of the patients (15%) developed related symptoms, but late follow-up imaging (≥24 months) was not available for the majority of cases. Longer follow-up studies may yield more information in the future.

Covering the ICA branches with flow diverters is reported generally safe, but angiographic artery occlusions may occur; OphtA (5–11%), Pcom (11–43%), AChA (0–1%) and ACA (0–100%).[469–471] OphtA coverage may cause minor ophthalmic modifications or transient ischaemic attacks regardless of OphtA patency status.[452] Pcom or AChA occlusions seem to rarely cause any late ischemia (0%).[472–474] Around the ICA bifurcation, and in the case of lenticulostriatal branch coverage, having protective effect from long enough DAPT is important.[202] In our series, the ICA side branch occlusion rates of different arteries varied (3–20%) during the follow-up, but no symptomatic or radiologic ischemia was seen. It seems that this delayed nature of branch occlusions gives sufficient time for collateral arteries to develop.[475]

6.2.3 POSTPROCEDURAL ISCHAEMIA AND HEMORRHAGE

6.2.3.1 Bypass procedures

Previous studies on bypass procedures for aneurysms often report only permanent morbidity with rates ranging 0–26%.[2,4,5,17,192,218,267,270,274,282,297,304,393,396,429,431] Among our series of bypass procedures, one third of the patients (n=13) had symptomatic ischaemic complications. The radiologic findings were mainly thromboembolic or local watershed-type of infarctions regardless of bypass status. Only one case suffered a full hemispheric infarction after early occlusion of the bypass. Other entities, the minor hemorrhagic contusions, were heavily associated with the ELANA technique which requires longer time of surgery, static retraction[476] and frequent heparinization. Then, the extra-axial hematomas necessitating surgical removal were diagnosed infrequently (7%) and at similar rate as in previous reports (1-10%).[5,304,428,429] Despite these different complications, only four patients deteriorated from good to poor functional status in long-term. Thus, relatively mild deficits or good clinical recovery from such lesions was commonly seen. Currently in bypass procedures, we prefer conventional and superficial anastomoses which require less invasive cranial exposures leading to less manipulation and less brain retraction. Also, instead of systemic administration, heparinized solutions are used only locally for graft and recipient irrigation.

6.2.3.2 Flow diversion

Ischaemic strokes related to flow diversion occur at rate of approximately 6% according to a meta-analysis from 2013, and separate pooled analysis from 2017.[401] In addition, clinically silent radiologic lesions are very common in routinely performed post-procedural diffusion-weighted MRI (51%).[477] In our series of flow diversion, there were ten symptomatic patients with radiologic ischaemia (16%). The radiologic findings in these patients were typically scattered embolic, or perforator-related strokes with no radiologic vessel occlusions. The overpresentation of ischaemia in cases wherein coaxial flow diverters were deployed (57%) may be explained with the lengthier procedures and by the extensive prothrombotic surface deployed.[477] Very wide or diffuse aneurysm necks may require this strategy of multiple devices although single device would be preferable. Then, regarding hemorrhages, SAH (4%) and ICH (2–3%) occur also at nonnegligible rates and more often in large aneurysms.[401] For primarily ruptured aneurysms, the rebleeding risk after flow diversion is reported to be approximately 4%.[403] We saw postprocedural hemorrhages of all three above-mentioned types, and both cases of SAH resulted in case fatalities. The endovascular intervention per se and local changes in flow dynamics may predispose to SAH, and inevitable antiplatelet medication further complicates hemorrhages. In addition, as endovascular procedures are performed using remote puncture sites, we saw two cases of surgically evacuated retroperitoneal hematomas related to femoral artery puncture in the groin. Flow diversion using a transradial instead of a transfemoral approach is reported to be technically possible and safe, and a shift towards this approach in neurointerventions may be justifiable to increase safety.[293]

6.2.4 CRANIAL NERVE DYSFUNCTIONS

Among publications on bypass surgery or flow diversion for ICA aneurysms, there are only a few reports focusing on improvement of CNDs. The rates of improvement after bypass surgery vary between 30–85% and after flow diversion between 40–94%.[144,221,225,304,309,428,434,449–451] Correspondingly in our two series, 45%–67% of patients experienced improvement in favor of flow diversion. At best, recovery rates of specific nerve dysfunctions, i.e. vision or single ocular motor nerves, was moderate at 50–60%. The results reflect more the heterogeneosity and small number of cases than differences of treatment methods. However, total aneurysm occlusion seemed to be a prerequisite for improvement after flow diversion, and this finding may favor pursuing more definitive surgical occlusion in certain cases of difficult and progressive CNDs.[450] On the other hand, the occurrence of new postprocedural CNDs was more often related to bypass procedures (23%) than to flow diversion (3%). In the bypass group, direct nerve manipulation during intracranial ICA anastomosis (ELANA technique) and early exacerbation of mass effect after aneurysm thrombosis at cavernous segment may have explained the overpresentation. We have currently abandoned the ELANA technique and prefer distal MCA recipient sites with easier exposure. The lower rate of new CNDs after flow diversion may be related to fewer number of giant aneurysms in the series (n=9), but the literature also reports this as a rare phenomenom.[449,456] Then, regardless of chosen treatment type, time to treatment seems to be an especially important factor in improvement of CNDs.[225,449] Patients may tolerate well the slowly worsening sight or diplopia which leads to delays in seeking treatment and to less favorable outcomes.

6.2.5 FUNCTIONAL OUTCOME

When treating complex aneurysms, the selected cases, treatment strategies and execution have a major effect on outcome. In some previous reports, the rate of good functional outcome for bypass procedures varies between 78–100% and for flow diversion between 68–96%.[4,5,270,282,304,400,402,404,428,429,431,455] In our two series, the proportion of patients with good outcome ranged from 74% (bypass procedures) to 87% (flow diversion). A more important observation was that only a few patients presenting with good functional status end up in the poor outcome group in long-term (5–10% of cases). In the bypass group, however, many patients experience treatment-related functional decline, but then improve to or near their initial status at later follow-up. This temporal deterioration would be disadvantageous in older or critically ill patients with less compensatory capacity for recovery. On the other hand, patients presenting with unruptured aneurysms but already in poor functional status, only seldom achieved independency again regardless of treatment method (25% of cases in both treatment groups). In such cases, the less invasive "flow diversion first" policy may be justifiable if applicable. In general, ischemic or hemorrhagic complications were the major factors having a negative effect on the functional outcome and explained the case fatalities. In bypass surgery, a combination of meticulous pre- and perioperative assessments and surgical technique are reflected in the outcome. With the more straightforward technique of flow diversion, the major cerebrovascular complications seem to occur in more unpredictable fashion which leads to difficulty in naming any case-specific pre-emptive measures.

6.3 FUTURE PERSPECTIVES

6.3.1 GIANT INTRACRANIAL ANEURYSMS

Relatively little is known about probably the most complex aneurysms, giant intracranial aneurysms, and the information is based mainly on smaller treatment-oriented case series.[11,12,17,144,297] The main problem is the rarity of these lesions. To attack this problem, a multicenter registry was launched in Charité Hospital, Germany (Giant Intracranial Aneurysm Registry).[478] Few anatomical or treatment-related reports are already published.[152,153,189] In 2016, the same group also did a comparative meta-analysis of clinical outcomes between surgical and endovascular treatment of GIAs. As bit of a surprise, the exact treatment method did not seem to have an effect.[120] Such results reflect the heterogeneousity of GIAs and treatment again, and justify more research on the topic to find the most effective and safest solutions for patients harbouring these dismal lesions. Quickly evolving digitalization in the modern society may provide better and more efficient tools for researchers to collaborate globally in future.

6.3.2 TRENDS IN THE TREATMENT OF COMPLEX ANEURYSMS

After introduction of flow diversion, inevitably more GIAs and other complex aneurysms are treated with endovascular means, and the technique has taken over aneurysms from bypass procedures. However, in the broader picture, a recent nationwide analysis from the U.S. showed that the proportion of patients who underwent a bypass procedure for treatment of unruptured aneurysms has been relatively stable before and after the introduction of flow diverters in 2011 (0.4–0.6% of cases). Thus, there is still an obvious need for neurosurgeons subspecializing in bypass surgery. The report showed also that bypasses were lately performed only in teaching hospitals which emphasizes the expertise, experience and technical skills nowadays needed. Due to the low volume of bypass procedures in general, the centralization of these surgeries to a single university hospital in Finland has been justifiable.

Then more specifically, Michael Lawton, a reputated vascular neurosurgeon, recently gave his expert opinion on the status and future of open microsurgery and bypasses.[143] Proximal ICA aneurysms in the cavernous or paraclinoid segments are nowadays treated mainly with flow diversion and this is reflected in reduction of high-flow bypasses during the last years. Still, the distal cerebral arteries, regions whereto flow diversion or other endovascular methods do not yet reach, are potential territories for bypasses. However, the supraclinoid ICA segment is a "midway region" and shares some aforementioned complicating anatomic features regarding flow diversion. There, revascularization offers an extra dimension of flexibility to attack the target aneurysm if flow diverters are considered unsuitable, or they fail.[282,479] Both techniques are important tools in the neurosurgeon's armamentarium, but further studies are needed to clarify indications of different treatment methods and shed more light in long-term results.[304,480,481]

6.3.3 DEVELOPMENT OF TREATMENT METHODS

In practice, performing a functional bypass represent one of the most challenging neurosurgical tasks and involves many aspects of dexterity. To achieve the needed level of performance in increasingly complicated cases, laboratory training is needed and these training environments should be advanced.[282,482,483] Also, the concept of seamless anastomosis, SELANA, is an interesting step forwards though it has been disappointing in clinical settings thus far.[90] A semiautomatic construction of bypass and anastomosis may be reality in future.

In endovascular procedures, the learning curve in manual skills is steeper, and usually not the limiting factor in procedures. Thus, flow diversion may be performed at similar volume as other endovascular treatment methods. Lately, the development of endovascular treatment has heavily focused on different devices. Particularily in flow diversion, two major components may be advanced further. First, the flow diverters should adapt to the delicate conditions when distal, small caliber arteries and more fragile lesions are treated. Second, development of device coatings to minimize the need for antiplatelet medication, or to eliminate the risk of in-stent stenosis would be useful.[484] In addition to implantable devices, also robotics are already being developed and introduced for neuroendovascular device deployment purposes.[485,486] As the automatization improves, even remotely performed endovascular procedures may become possible.[475]

6.3.4 COSTS OF TREATMENT

The cost of treatment is significant topic in health care economics. In complex surgeries, such as bypass procedures, the facility costs (e.g. time in the operation room and longer hospitalization) are main causes of expenses.[304,487] The implantable devices and other supplies form the majority of expenses in endovascular treatment (e.g. coils and flow diverters).[487] In treatment of GIAs, it is estimated that major cost reduction would be achieved with cheaper prices of endovascular devices.[488] However, modern treatment protocols rely more and more on technology, and this goal may be difficult to achieve. ❦

Conclusions

I. The internal carotid artery is the most common location for giant intracranial aneurysms, which commonly present with symptoms related to mass effect. In contrary to giant aneurysms in the supraclinoid segment, aneurysms in cavernous segment share low risk of rupture. In giant aneurysms, the lack of wall calcification or intraluminal thrombosis seemed to correlate with an increased rupture rate. No relevant anatomical variations were associated to carotid giant aneurysms. Multiplicity of giant aneurysms is a rare finding, but in such cases, they tended to involve bilateral carotid arteries.

II. Bypass surgery of complex carotid aneurysms is a feasible treatment method. The specific treatment strategy is constructed on the basis of segmental aneurysm location. The cavernous aneurysms became occluded slighty more often than the supraclinoid aneurysms or the aneurysms in the ICA bifurcation. Major complications leading to long-term functional decline are rare. Preoperative cranial nerve dysfunctions recover only moderately. Lately, flow diverters have taken over many carotid aneurysms, but bypass procedures continue to provide solutions in cases wherein other treatment methods are not feasible or fail.

III. Flow diversion is a feasible treatment method for cavernous and supraclinoid carotid aneurysms including those with complex features. Various complex aneurysm features may prevent or slow down the aneurysm occlusion process in long-term. The cavernous aneurysms became occluded slighty more often than their supraclinoid counterparts. Major complications leading to long-term functional decline are rare. Preprocedural cranial nerve dysfunctions recover moderately at best but require the complete occlusion of the aneurysm. The unique reconstructive nature of flow diversion makes it an important tool for the modern vascular neurosurgeon. ❦

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Among neurosurgical challenges, the small subgroup of complex intracranial aneurysms represents one of the biggest problems for vascular neurosurgeon. Giant intracranial aneurysms are a rare subgroup of complex aneurysms with a particularly poor natural history. Due to their large size, these tumor-like aneurysms often present with cranial nerve dysfunctions. In this retrospective study, we aimed to provide a comprehensive description of the anatomical features of giant aneurysms in the internal carotid artery (ICA). As the name implies, there have been no simple solutions for treating complex aneurysms. They are often difficult to approach directly, necessitating indirect treatment strategies. We therefore analysed a case series of bypass surgery and flow diversion in relation to the execution and outcomes in different segments of the ICA.

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