Univerzita Karlova v Praze

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Autoreferát disertační práce

Mozková aneurysmata - modality léčby a přirozený průběh.

Bezpečnost a efektivnost léčebných strategií aneurysmat na a. cerebelli inferior posterior.

Intracranial Aneurysms – Treatment Options and Natural Course.

Safety and Efficacy of Treatment Strategies for Posterior Inferior Cerebellar Artery Aneurysms.

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Disertační práce bude nejméně pět pracovních dnů před konáním obhajoby zveřejněna k nahlížení veřejnosti v tištěné podobě na Oddělení pro vědeckou činnost a zahraniční styky Děkanátu 1. lékařské fakulty.

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ABSTRAKT

ÚVOD: Aneurysmata na arteria cerebelli inferior posterior představují poměrně málo častou a heterogenní skupinu se špatnou neurologickou prognózou ve srovnání s jinými intrakraniálními aneurysmaty. První část této práce přináší systematický přehled literatury, která hodnotí bezpečnost a efektivnost léčebných strategií PICA-aneurysmat. V druhé části je představena multicentrická retrospektivní studie, jejímž cílem bylo analyzovat klinický outcome u velké série pacientů léčených současnými technikami mikrochirurgické a endovaskulární léčby.

METODY: Pro metaanalýzu byly systematicky vyhledávány studie publikované do listopadu 2015 pomocí databází Medline, EMBASE, Scopus a Web of Science. Byly zahrnuty studie týkající se léčby PICA-aneurysmat, ve kterých bylo zařazeno ≥ 10 pacientů. Pomocí statistických metod metaanalýzy (random-efekt) byly analyzovány následující parametry: dosažení kompletní okluse, technická úspěšnost, periprocedurální morbidita/mortalita, výskyt iktů, rekurence/hemoragie aneurysmatu, výskyt paralýz kraniálních nervů a dlouhodobá neurologická morbidita/mortalita. Druhou část práce představuje retrospektivní studie zahrnující data 94 pacientů léčených pro PICA-aneurysma od roku 2000 do roku 2015 ve třech neurovaskulárních centrech.

VÝSLEDKY: Do metaanalýzy bylo zahrnuto 29 studií s celkovým počtem 796 PICA-aneurysmat. U prasklých aneurysmat byla dosažena kompletní okluse v 97.1% (95%CI=94.5%-99.0%) u skupiny chirurgicky léčených pacientů a 84.3% (95%CI=73.8%-92.6%) ve skupině endovaskulárně léčených. Rekurence aneurysmatu se vyskytovala v 1.4% (95%CI=0.3%-3.3%) po chirurgickém výkonu a v 8.1% (95%CI=3.6%-10.9%) po endovaskulárním výkonu. Celková neurologická morbidita byla 14.4% (95%CI=8.7%-21.2%) and mortalita 9.8% (95%CI=5.8%-14.8%) po chirurgické léčbě a 15.1% (95%CI=10.5%-20.2%) a 17.1% (95%CI=11.5%-23.7%) po léčbě endovaskulární. U neprasklých PICA-aneurysmat byla kompletní okluse dosažena v 92.9 % (95%CI=79.5%-100%) u skupiny chirurgicky léčených pacientů a 75.7% (95%CI=45.4%-97.1%) ve skupině pacientů absolvujících léčbu endovaskulární. Celkový dobrý dlouhodobý neurologický outcome byl 91.5%

(95%CI=74.4%-100%) u chirurgicky léčených pacientů a 93.3% (95%CI=82.7%-99.5%) u endovaskulárně léčených pacientů.
ZÁVĚR: Prezentovaná metaanalýza i výsledky studie ze tří neurovaskulárních center ukázaly, že obě léčebné modality dosahují vysoké míry úspěšnosti a efektivnosti technického provedení se současně dostatečnou mírou dlouhodobé okluse aneurysmatu. Přesto vyskytující se komplikace nejsou zanedbatelné. Na klinický outcome má určující vliv stav pacienta při příjmu do hospitalizačního zařízení. Naše data potvrdila, že chirurgická léčba PICA-aneurysmat je spojena s vynikajícím angiografickým nálezem. Tyto závěry by měly být zváženy při managementu pacientů s PICA-aneurysmaty. Každopádně volba léčby těchto pacientů by měla být diskutována případ od případu tak, aby získaný benefit byl pro pacienta co nejvyšší a risk výskytu periprocedurálních komplikací byl maximálně limitován. V neposlední řadě záleží také na zvyklostech a zkušenosti daného pracoviště.

Klíčová slova: arteria cerebelli inferior posterior, aneurysma, mikrochirurgie, neurochirurgie, endovaskulární léčba, metaanalýza

ABSTRACT

BACKGROUND: Posterior inferior cerebellar artery (PICA) aneurysms are an uncommon, heterogeneous group of aneurysms with poorer neurological outcomes compared to other intracranial aneurysms. At first, as part A, we conducted a systematic review of the literature to evaluate the safety and efficacy of treatment strategies for PICA-aneurysms.
Subsequently, as part B, we performed a multicenter retrospective study to analyze the outcome in a large series of patients treated with contemporary microsurgical and endovascular techniques.
METHODS: For the meta-analysis, a systematic search of Medline, EMBASE, Scopus and Web of Science was done for studies published through November 2015. We included studies that described treatment of PICA-aneurysms with ≥10 patients. Random-effects meta-analysis was used to pool the following outcomes: complete occlusion, technical success, periprocedural morbidity/mortality, stroke rates, aneurysm recurrence/rebleed, CN-palsies rates, and long-term neurological morbidity/mortality. As the second part, aiming to report the current trends and results in treatment strategies for PICA-aneurysms, records of 94 patients treated for PICA-aneurysms between 2000 and 2015 at 3 large referral neurovascular centers were retrospectively reviewed.
RESULTS: In the meta-analysis, we included 29 studies with 796 PICA-aneurysms. When considering all ruptured PICA-aneurysms, complete occlusion rates were 97.1% (95%CI=94.5%-99.0%) in the surgical group and 84.3% (95%CI=73.8%-92.6%) in the endovascular group. Aneurysm recurrence occurred in 1.4% (95%CI=0.3%-3.3%) after surgery and in 6.9% (95%CI=3.6%-10.9%) after endovascular treatment. Overall neurological morbidity and mortality were 14.4% (95%CI=8.7%-21.2%) and 9.8% (95%CI=5.8%-14.8%) after surgery and 15.1% (95%CI=10.5%-20.2%) and 17.1% (95%CI=11.5%-23.7%) after endovascular treatment, respectively. When considering all unruptured PICA-aneurysms, complete occlusion rates were 92.9% (95%CI=79.5%-100%) in the surgical group and 75.7% (95%CI=45.4%-97.1%) in the endovascular group. Overall long-term good neurological outcome rates were 91.5% (95%CI=74.4%-100%) in the surgical series and 93.3% (95%CI=82.7%-99.5%) in the endovascular group.

Analyzing the current results from 3 referral neurovascular centers, 83 patients met inclusion criteria and of these, 2 died before treatment leaving 81 treated patients (43 underwent endovascular and 38 surgical treatment). Among patients treated endovascularly, procedure-related complications occurred in 4 cases (11.8%). Six patients (19.4%) suffered from complications directly associated with surgery. Recurrences occurred in 3.2% of surgical and in 17.6% of endovascularly treated patients, requiring treatment. Patients with unruptured asymptomatic aneurysms had good outcomes. In the group of 67 ruptured aneurysms, 12 endovascularly (35.3%) and 11 surgically (35.5%) treated patients had Glasgow Outcome Scale (GOS) score 1-3. Of patients in poor neurological condition (Hunt & Hess (H&H) IV-V at admission), 65.2% suffered poor clinical outcomes. Fifty percent of patients with distal and 31.9% patients with proximal ruptured PICA-aneurysms suffered a poor neurological outcome.

CONCLUSION: Our meta-analysis as well as the current results from 3 referral neurovascular high-volume centers demonstrated that both treatment modalities are technically feasible with high rates of technical success and effective with sufficient long-term aneurysm occlusion rates. However, complications are not negligible. Outcomes were mostly impacted by clinical state at admission. Our data confirm that surgical treatment is associated with superior angiographic outcomes. These findings should be considered when deciding the best therapeutic strategy for treatment of PICA-aneurysms. Yet, therapy of PICA-aneurysms should be performed on a selective, case-by-case basis in order to maximize patient benefits and limit the risk of periprocedural complications also depending upon the specific expertise of one's department.

Key words: PICA, aneurysm, microsurgery, endovascular treatment, meta-analysis

1. INTRODUCTION

Aneurysms of the posterior inferior cerebellar artery are rare as these represent between 0.5% and 3% of all intracranial aneurysms.[1-10] The best treatment strategy and technique for PICA-aneurysm continues to be debated.[11, 12] Over the last three decades, several series using both endovascular and open surgical techniques have reported results and complications of treatment for these aneurysms [1, 2, 4, 13-18]. However, most of these series are small[19-23] and it is difficult to have an understanding of the complications and outcomes for treatment of PICA-aneurysms. Furthermore, many prior studies have reported high morbidity and mortality rates of patients having ruptured PICA-aneurysms irrespective of management techniques.[17, 24-26].

To clarify the safety and efficacy of surgical and endovascular treatment of PICA-aneurysms, as part A, we conducted a systematic review of the literature analyzing outcomes by type of treatment, aneurysm rupture status and aneurysm location. In addition, in attempt to describe current results in the treatment of these aneurysms, we report a series of 83 patients with PICA aneurysms from 3 international high-volume referral neurovascular centers.

2. METHODS

2.1 PART A

A comprehensive review of the literature was performed using the keywords “posterior inferior cerebellar artery”, “PICA”, “aneurysm”, “posterior inferior cerebral artery”, “vertebral”, “hemorrhag”, “haemorrhag”, “malform”, “clip”, “coil”, “microsurg”, “embolization”, “flow diversion”, “endovasc”, “catheter”, “stent”, “occlud”, “occlusive”, “revascular” and “percutaneous” in both “AND” and “OR” combinations, to search Pubmed, Ovid Medline, Ovid EMBASE, Scopus and Web of Science. Inclusion criteria were the following: English language, >10 patients, studies published from January 2000 to November 2015, with adequate data on postoperative/postprocedural complications, outcome, and aneurysmal occlusion rate. The exclusion criteria were the following:

studies including only dissecting PICA-aneurysms (due to variable natural histories and different treatment techniques of these aneurysms), case reports, conference abstracts, in vitro, cadaveric or animal studies, review articles, guidelines and technical notes.

The electronic search was supplemented by contacting experts in the field and reviewing the bibliographies of included studies for relevant publications. Abstracts, methods, results, figures and tables of full text for detailed review were searched by three independent reviewers (neurosurgeons O.P. and A.S., and radiologist W.B.) for data on aneurysmal occlusion technique, occlusion rates, procedure-related morbidity and mortality, and treatment-related complications. The reference lists of retrieved articles were also screened for additional studies. Furthermore, in the case of multiple publications from the same institution and or the same authors, only the most recent and updated study was considered to avoid inclusion of overlapping patients.

For each study, the following descriptive clinical and anatomic information was extracted: patient demographics, location, and size of aneurysms, surgical / endovascular indications, the number of parent vessel occlusions and treatment modality. We studied the following outcomes: pre-treatment morbidity, aneurysm rebleeding, aneurysm recurrence, complete occlusion at last follow-up, long-term good neurological outcome, long-term neurological morbidity, long-term neurological mortality, perioperative / periprocedural morbidity, perioperative / periprocedural mortality, intraprocedural aneurysm rupture, parent vessel occlusion, perioperative / periprocedural stroke, acute hydrocephalus, permanent shunting, cranial nerves palsies and technical success.

Proximal PICA-aneurysms were defined either as those located on the anterior medullary and lateral medullary segment of the parent artery according to Lister's classification[27] or as those located on the first 1 cm of PICA according to Drake's classification.[28] Pre-treatment morbidity was defined as a Hunt&Hess classification and/or WFNS classification of SAH of 3 or more. Favorable neurological outcome was defined as a modified Rankin Scale score of 2 or less or as a Glasgow Outcome Scale (GOS) score 4 and 5. In cases where these two scales were not available, favorable neurological outcome was determined if the study used terms such as "no morbidity", "no worsening" or "good recovery". Long-term neurological morbidity

was defined as either an mRS score greater than two, a GOS score less than four, or worsening of pre-treatment status of the patient post-operatively relative to the preoperative baseline score. Aneurysm occlusion was defined as complete occlusion confirmed by imaging examination (DSA, CTA, or MRA) after surgery/endovascular procedure. Perioperative / periprocedural complications were defined as those occurring within 30 days of the surgical procedure.

We performed three subgroup analyses in this study: 1) a subgroup analysis by aneurysm rupture status on presentation to the surgical or endovascular treatment, 2) a subgroup analysis by type of treatment (surgical versus endovascular treatment), and 3) a subgroup analysis by aneurysm location (proximal versus distal location).

2.2 PART B

Following institutional review board approvals, all patients with PICA-aneurysms included in a prospective database of intracranial aneurysms (at Mayo Clinic, Rochester, MN, U.S., at Medical University Innsbruck, Austria as well as at Masaryk Hospital, Ústí nad Labem, Czech Republic) from 2000 to 2015 were included in this study. Information collected in this database included patient demographics and baseline clinical characteristics, aneurysm characteristics, treatment characteristics, and treatment outcomes. Patient demographic data collected included age, sex, baseline symptoms, and baseline neurologic status. Aneurysm characteristics included location and size. Treatment characteristics included type of microsurgery and its surgical approach, in case of endovascular treatment type of device/coils used, number of flow diverters used, and use of stent or balloon assistance.

Treatment outcomes included intraprocedural and periprocedural technical events, clinical events (including aneurysm perforation, thrombosis, neurologic symptoms, medical symptoms, ophthalmologic symptoms, and groin complications), and late technical and clinical events at follow-up. Periprocedural complications were defined as those occurring within 30 days following the procedure, and late events were defined as events occurring after 30 days.

Subarachnoid hemorrhage (SAH) was diagnosed by computed tomography (CT) or lumbar puncture. The location of

hemorrhage in the subarachnoid space, brain parenchyma and in ventricles was evaluated using the Fisher Grading Score. In every patient where multiple aneurysms or other associated vascular anomalies such as AVM or multiple aneurysms were present, the origin of the hemorrhage was identified based on pattern and location of the hemorrhage on CT and/or the irregularity of the aneurysm. If the patient's clinical condition indicated increased intracranial pressure (ICP) and hydrocephalus occurred on the CT scan, placement of an external ventricular drain (EVD) was performed. Pertinent neurological and angiographic findings at all three centers were assessed and discussed by a multidisciplinary team in order to select the best therapeutic strategy with maximizing patient benefits and reducing the periprocedural complications in each case.

Aneurysms were cathegorized according to Drake's classification[29] as proximal and distal. We collected data regarding aneurysm characteristics and morphology.

Depending on the policy of each individual institution further clinical and radiographic follow-up data were obtained at variable periods of follow-up. In detail, clinical follow-up was collected within the first 30 days (Mayo Clinic & Medical University Innsbruck), at the time of radiographic follow-up at 6 and 12 months and 3 years. At Mayo Clinic, clinical follow-up was obtained by a specialized nurse not directly involved with the original procedure, commonly. At the time of follow-up, patients were asked to rate themselves on the basis of the modified Rankin Scale. Patients were also asked to specify the reason for any score higher than zero. A baseline assessment, following the same methodology, was also obtained at the first encounter before aneurysm treatment. Generally, for patients with flow diverters, radiologic follow-up with conventional angiography was recommended at 6, 12, and 36 months, and for patients with coiling or clipping, conventional angiography or MRA was recommended 6 or 12 months after the original procedure, depending on aneurysm characteristics and initial radiographic outcome. Afterward, imaging follow-up for patients with coiling or clipping was individualized according to various patient and aneurysm factors. Aneurysm occlusion on follow-up angiography, MRA, and/or CTA was categorized as "complete" (no filling of the aneurysm sac), "near-complete" (>90% occlusion), and "incomplete" (<90% occlusion).

We studied the following outcomes: 1) the presence of perioperative complications, 2) mid- and long-term complications, 3) target aneurysm rupture, 4) retreatment rates, 5) major recurrence rates, and 6) long-term neurologic outcome. Long-term neurologic outcome was assessed by using standard neurological examinations, the Glasgow Outcome Scale (GOS) or else the modified Rankin Scale and with the methodology detailed above. We also determined whether neurologic disability was secondary to the aneurysm or other symptoms (i.e. back pain, intercurrent nonrelated illness, and so forth). "Neurologic morbidity" was defined as any neurologic deficit that appeared either due to target aneurysms or their surgical or endovascular treatment. "Neurologic mortality" was defined as any death of the patient related to target aneurysms and/or their treatment complications.

3. RESULTS

3.1 PART A

3.1.1 LITERATURE REVIEW

The initial comprehensive literature search yielded 2215 articles. 199 case reports were excluded. On initial abstract and title review, 1980 were excluded as they were deemed not relevant to the current study. 235 studies were reviewed in additional detail. 11 studies were removed as they were conference abstracts. 97 studies were excluded although they dealt with surgical and/or endovascular treatment of PICA-aneurysms, however, did not report any information about study population, treatment technique and/or postoperative/postprocedural outcome of the patients. 98 studies were excluded as they were either dealing with dissecting PICA-aneurysms or had too few patients.

In total, 29 studies with 796 target posterior inferior cerebellar artery aneurysms were included. There were 660 ruptured and 136 unruptured PICA-aneurysms. There were 501 PICA-aneurysms of proximal location and 236 PICA-aneurysms belonged to the distal location (origin). 59 target PICA-aneurysms were not classified due to missing published data. 452 target aneurysms

(56.8%) were treated surgically and endovascular treatment of PICA-aneurysm was performed in 344 target aneurysms (43.2%).

3.1.2 OVERALL OUTCOMES

When considering all patients, complete occlusion rates were 92.2% (95%CI=86.5%-96.6%). Pre-treatment morbidity was 40.8% (95%CI=29.9%-52.2%). Perioperative mortality was 7.2% (95%CI=4.4%-10.6%). Procedure-related morbidity was 8.7% (95%CI=5.7%-12.3%). Procedure-related mortality was 1.4% (95%CI=0.7%-2.4%). Overall long-term neurological morbidity and mortality rates were 13.3% (95%CI=10.1%-16.9%) and 8.0% (95%CI=5.0%-11.6%), respectively. Overall long-term favorable neurological outcome was 80.7% (95%CI=76.5%-84.5%).

3.1.3 OUTCOMES BY TYPE OF TREATMENT AND RUPTURE STATUS

3.1.3.1 OUTCOMES OF SURGICAL TREATMENT FOR RUPTURED PICA ANEURYSMS

When considering surgical treatment of ruptured PICA-aneurysms, complete occlusion rates were 97.1% (95%CI=94.5%-99.0%). Aneurysm recurrence rates were 1.4% (95%CI=0.3%-3.3%) and rebleed rates were 1.9% (95%CI=0.6%-3.9%). Pre-treatment morbidity was 42.3% (95%CI=23.1%-64.5%). Perioperative mortality was 9.3% (95%CI=5.2%-14.5%). Procedure-related morbidity was 10.8% (95%CI=4.7%-19.0%). Procedure-related mortality was 1.7% (95%CI=0.4%-3.7%). Long-term neurological morbidity and mortality rates were 14.4% (95%CI=8.7%-21.2%) and 9.8% (95%CI=5.8%-14.8%), respectively. Long-term favorable neurological outcome rates were 80.9% (95%CI=75.0%-86.2%).

3.1.3.2 OUTCOMES OF ENDOVASCULAR TREATMENT FOR RUPTURED PICA ANEURYSMS

When considering endovascular treatment of ruptured PICA-aneurysms, complete occlusion rates were 84.3% (95%CI=73.8%-

92.6%). Aneurysm recurrence rates were 6.9% (95%CI=3.6%-10.9%) and rebleed rates were 2.7% (95%CI=1.0%-5.1%). Pre-treatment morbidity was 60.1% (95%CI=44.4%-74.9%). Perioperative mortality was 15.1% (95%CI=9.3%-22.0%). Procedure-related morbidity was 14.1% (95%CI=7.4%-22.4%). Procedure-related mortality was 3.5% (95%CI=1.0%-7.3%). Long-term neurological morbidity and mortality rates were 15.1% (95%CI=10.5%-20.2%) and 17.1% (95%CI=11.5%-23.7%), respectively. Long-term favorable neurological outcome rates were 72.4% (95%CI=66.2%-78.2%).

3.1.3.3 OVERALL OUTCOMES FOR RUPTURED PICA ANEURYSMS

When considering all ruptured PICA-aneurysms, complete occlusion rates were 93.4% (95%CI=88.7%-96.9%). Aneurysm recurrence rates were 3.2% (95%CI=1.7%-5.0%) and rebleed rates were 2.3% (95%CI=1.2%-3.8%). Pre-treatment morbidity was 49.6% (95%CI=36.3%-63.0%). Perioperative mortality was 11.7% (95%CI=8.1%-15.8%). Procedure-related morbidity was 11.5% (95%CI=7.0%-16.8%). Procedure-related mortality was 2.0% (95%CI=0.9%-3.4%). Long-term neurological morbidity and mortality rates were 14.7% (95%CI=11.0%-18.7%) and 12.5% (95%CI=9.0%-16.5%), respectively. Long-term favorable neurological outcome rates were 77.0% (95%CI=72.3%-81.3%).

3.1.3.4 OUTCOMES OF SURGICAL TREATMENT FOR UNRUPTURED PICA ANEURYSMS

When considering surgical treatment of unruptured PICA-aneurysms, complete occlusion rates were 92.9% (95%CI=79.5%-100%). Aneurysm recurrence rates were 15.3% (95%CI=2.3%-34.9%) and rebleed rates were 8.5% (95%CI=0.0%-25.6%). Perioperative mortality was 7.1% (95%CI=0.0%-20.5%). Procedure-related morbidity was 31.0% (95%CI=12.3%-53.3%). Procedure-related mortality was 7.1% (95%CI=0.0%-20.5%). Long-term neurological morbidity and mortality rates were 8.5% (95%CI=0.0%-25.6%) and 7.1% (95%CI=0.0%-20.5%), respectively. Long-term favorable neurological outcome was 91.5% (95%CI=74.4%-100%).

3.1.3.5 OUTCOMES OF ENDOVASCULAR TREATMENT FOR UNRUPTURED PICA ANEURYSMS

When considering endovascular treatment of unruptured PICA-aneurysms, complete occlusion rates were 75.7% (95%CI=45.4%-97.1%). Aneurysm recurrence rates were 12.4% (95%CI=1.4%-29.8%) and rebleed rates were 3.7% (95%CI=0.0%-10.6%). Perioperative mortality was 3.7% (95%CI=0.0%-10.6%). Procedure-related morbidity was 5.6% (95%CI=0.3%-15.3%). Procedure-related mortality was 3.7% (95%CI=0.0%-10.6%). Long-term neurological morbidity and mortality rates were 5.1% (95%CI=0.2%-14.4%) and 3.7% (95%CI=0.0%-10.6%), respectively. Long-term favorable neurological outcome was 93.3% (95%CI=82.7%-99.5%).

3.1.3.6 OVERALL OUTCOMES FOR UNRUPTURED PICA ANEURYSMS

When considering all unruptured PICA-aneurysms, complete occlusion rates were 86.7% (95%CI=74.6%-95.5%). Aneurysm recurrence rates were 9.0% (95%CI=2.9%-17.6%) and rebleed rates were 3.5% (95%CI=0.3%-9.0%). Perioperative mortality was 7.2% (95%CI=4.4%-10.6%). Procedure-related morbidity was 15.3% (95%CI=7.3%-25.4%). Procedure-related mortality was 3.5% (95%CI=0.3%-9.0%). Long-term neurological morbidity and mortality rates were 5.5% (95%CI=1.3%-11.9%) and 6.4% (95%CI=1.8%-13.1%), respectively. Long-term favorable neurological outcome was 90.2% (95%CI=82.4%-96.0%).

3.1.3.7 OVERALL OUTCOMES BY TYPE OF TREATMENT

Complete occlusion rates were higher in patients undergoing surgical treatment (98.0%, 95%CI=96.3%-99.1%) when compared to those undergoing endovascular treatment (79.7%, 95%CI=70.2%-87.9%) (P<0.0001). Patients undergoing surgical treatment had significantly lower rates of aneurysm recurrence (1.1%,

95%CI=0.3%-2.3%) when compared to those undergoing endovascular treatment (8.1%, 95%CI=5.2%-11.7%) (P<0.0001). There was no statistically significant difference in pre-treatment morbidity between groups (34.8% in the surgical group versus 42.5% in the endovascular group, P=0.468). However, patients undergoing surgical treatment had lower rates of perioperative mortality (3.6%; 95%CI=1.7%-6.2%) when compared to those undergoing the endovascular treatment (10.2%; 95%CI=5.8%-15.5%) (P=0.017). Procedure-related morbidity rates were 8.9% (95%CI=4.9%-14.0%) in the surgical group and 11.7% in the endovascular group (95%CI=6.3%-18.6%) (P=0.467). Patients undergoing surgical treatment had similar rates of procedure-related mortality (1.2%; 95%CI=0.3%-2.5%) when compared to those undergoing the endovascular treatment (2.6%; 95%CI=1.0%-4.9%) (P=0.208). Neurological morbidity rates were similar between groups (14.7% in the surgical group versus 12.8% in the endovascular group; P=0.591). Patients undergoing surgical treatment had significantly lower rates of neurological mortality rates (4.6%; 95%CI=2.0%-8.1%) when compared to those undergoing endovascular treatment (11.9%; 95%CI=7.2%-17.5%) (P=0.017). The rate of overall favorable neurological outcome in patients undergoing surgical treatment was83.2% (95%CI=79.4%-86.7%) compared to 77% (95%CI=68.5%-84.6%) for patients receiving endovascular treatment.

3.1.4 OUTCOMES BY ANEURYSM LOCATION

3.1.4.1 SURGICAL TREATMENT

When considering surgical treatment of both proximal and distal PICA-aneurysms, there were no statistically significant differences in any of the safety and efficacy outcomes by aneurysm location. Complete aneurysm occlusion rates were similar in both groups (98.0% in the proximal location group versus 95.5% in the distal location group) (P=0.270). There were no statistical differences in terms of aneurysm recurrence rates (2.8% in the proximal location group versus 1.1% in the distal location group, P=0.313). Pre-treatment morbidity was 42.6% in the proximal location group and 51.8% in the distal location group (P=0.463). Perioperative mortality rates were similar in both groups (8.3% in the proximal location group

versus 8.9% in the distal location group, P=0.900). There was a trend towards higher rates of procedure-related morbidity in patients harboring proximal PICA-aneurysms (11.2%, 95%CI=5.9%-17.7%) when compared to patients with distal PICA-aneurysms (5.5%, 95%CI=2.0%-10.5%) (P=0.127). Procedure-related mortality rates were similar in both groups (1.2% versus 1.3%; P=0.938). There were no statistically significant differences in terms of neurological morbidity (16.9% versus 11.4%; P=0.353), neurological mortality (7.1% versus 11.6%; 0.255) and favorable neurological outcome (80.9% versus 86.5%; P=0.261) between groups.

3.1.4.2 ENDOVASCULAR TREATMENT

When considering endovascular treatment of both proximal and distal PICA-aneurysms, there were no statistically significant differences in any of the safety and efficacy outcomes by aneurysm location. Proximal PICA-aneurysms had slightly lower rates of complete occlusion (82.6%, 95%CI=70.6%-92.0%) when compared to those in the distal location (92.5%, 95%CI=75.6%-100%) (P=0.230). Aneurysm recurrence rates were 5.7% in the proximal location group and 8.9% in the distal location group (P=0.490). Patients with proximal PICA-aneurysm had slightly lower rates of pre-treatment morbidity (48.7%, 95%CI=26.3%-71.4%) when compared to those with distal PICA-aneurysm (56.8%, 95%CI=29.9%-81.9%) (P=0.645). There was a trend towards higher rates of perioperative mortality in patients harboring proximal PICA-aneurysm (12.7%, 95%CI=6.4%-20.7%) when compared to patients with distal PICA-aneurysm (4.1%, 95%CI=0.0%-11.8%) (P=0.071). Procedure-related morbidity rates were 12.7% in the proximal location group and 7.3% in the distal location group (P=0.391). Procedure-related mortality rates were similar between groups (3.4% in the proximal location group and 2.9% in the distal location group; P=0.875). Neurological morbidity rates were 10.3% in the proximal location group and 17.1% in the distal location group (P=0.367). Patients harboring proximal PICA-aneurysm had higher rates of neurological mortality (13.7%, 95%CI=7.0%-22.0%) when compared to those with distal PICA-aneurysm (4.1%, 95%CI=0.0%-11.8%) (P=0.050). Lastly, there was a trend towards higher rates of long-term favorable neurological

outcome favoring the proximal location group (78.8% versus 62.4%; P=0.117).

3.2 PART B

From 2000 to 2015, 94 consecutive patients harboring PICA-aneurysms were referred to three institutions: Medical University Innsbruck, Austria; Mayo Clinic, Rochester, MN, USA; Masaryk Hospital, Ústí nad Labem, Czech Republic. Amidst these 94 patients, 70 presented with SAH and/or intracerebellar hemorrhage, 5 patients developed neurological symptoms of brainstem and lower cranial nerve compression, 12 patients were asymptomatic with incidental PICA-aneurysm and 7 patients had dissecting PICA-aneurysms. Four patients were excluded due to missing informed consent. In addition, 7 patients with dissecting aneurysms were also excluded because of completely different nature as well as treatment approaches in these aneurysms. Finally, 83 patietns were included in the study. PICA-aneurysms were classified into two groups: ruptured (n=67) and unruptured PICA-aneurysms (n=16). Of note, fourteen patients included in this study were already reported as part of a single center experience.[30]

3.2.1 RUPTURED PICA ANEURYSMS

3.2.1.1 PATIENTS

There were 67 patients harboring ruptured PICA-aneurysm. One patient with an AVM presented with multiple distal feeding pedicle PICA-aneurysms. The clinical condition of patients with ruptured aneurysms was assessed using the H&H score, 26 patients were classified as H&H IV-V (38.8%) and 41 patients (61.2%) as H&H I-III. Pre-treatment PICA-aneurysm rerupture occurred in 7 cases (10.4%) resulting in a rapid decline of neurological state in 6 patients (9.0%). Of note, two patients (3.0%) admitted in deep coma (H&H V) with massive cerebral edema on initial CT scan, did not improve after intensive systemic and neurological reanimation and died without any further treatment of the aneurysm.

3.2.1.2 INITIAL RADIOGRAPHIC FINDINGS

As mentioned above, two patients (3.0%) with H&H V did not improve despite all required intensive measures and died without any further treatment. Additionally, radiologic data were not available for two patients (3.0%).

A total of 67 patients with ruptured PICA-aneurysms presented with a SAH. Of these, Fisher grade 4 was noted in 53 cases (76.1%). Three patients (4.5%) had an intraparenchymal hematoma. Acute hydrocephalus occurred in 51 cases (76.1%) leading to an initial placement of EVD in 43 patients (64.2%). As a consequence, 18 patients (26.9%) developed shunt-dependent hydrocephalus.

A total of 27 patients (40.3%) were diagnosed with other intracerebral vascular malformations such as coexisting aneurysms, cavernomas, dural arteriovenous fistulas or AVMs. Multiple aneurysms were found in 12 patients (17.9%). Six patients (9.0%) presented with associated AVMs; four of them were localized in the posterior fossa.

Of note, at Mayo Clinic, it is preferred to use DSA as a diagnostic tool in order to identify the intracerebral anomaly and discover the source of hemorrhage as the endovascular approach is here a first-line treatment for intracranial aneurysms. This was the case of 25 patients (96.1%) from 26 treated patients with symptomatic aneurysms. In Innsbruck and Ústí nad Labem CTA is the standard aneurysm-diagnostic tool. We perform DSA if endovascular treatment is considered, if CTA is negative, or if a suspicion arises of a small aneurysm, or in case of a need to analyze flow dynamics. In these cases, DSA is the next step in the diagnostic process.

3.2.1.3 THERAPY

Overall, 34 patients (52.3%) underwent endovascular procedures and microsurgery was initially performed in 29 patients (47.7%) with two additional patients after failed primary intented endovascular treatment.

Surgical approach was planned and tailored based on size, shape, rupture status, and clinical condition of the patient. While planning the surgical trajectory, the location of the aneurysm based upon the segmental anatomy of PICA, its relationship to the

anatomical midline (10 mm or less being considered significant), brainstem and cerebellum, and the variability in the vessel's origin was carefully assessed.

The far lateral approach and variations of suboccipital craniotomy in the sitting or lateral position were predominantly used due to aneurysm proximal location in most cases. Direct aneurysm clipping was utilized in 30 patients (96.8%), while in one case (3.2%) it was necessary to excise the aneurysm and reconstruct the parent artery with an end-to-end bypass. In two patients (6.5%), due to malignant edema, it was indispensable to perform partial parenchymal resection to access the aneurysm.

3.2.1.3.1 INITIAL ANGIOGRAPHIC RESULTS OF ENDOVASCULAR TREATMENT

Of 34 endovascularly treated patients, parent artery occlusion was performed in five patients (14.7%). Postoperative follow-up immaging revealed patent PICAs in the remaining 29 cases (85.3%) and aneurysm neck remnants (near-complete occusion) in 9 cases (26.5%). In two patients (5.9%), the former intention of endovascular treatment failed and the patients subsequently underwent surgery.

3.2.1.3.2 INITIAL ANGIOGRAPHIC RESULTS OF SURGICAL TREATMENT

Amongst the 31 surgically treated patients, postoperative angiography showed that the PICA was occluded in two cases (6.5%). In one patient (3.2%) the parent artery occlusion occurred inadvertently after direct clipping of the aneurysm while in the other patient (3.2%) both the right and left distal PICA branches were sacrificed during AVM resection. Aneurysm neck remnants (near-complete occlusion) were present in 6 cases (19.4%).

Among the six patients with AVM (9.5%), two had ruptured aneurysms involving the distal PICA segment which was also feeding the AVM. One of these distal aneurysms was resected along with the AVM (and both right and left distal PICA branches were sacrificed), the other distal PICA-aneurysm associated with AVM was coiled and the patient underwent surgery for AVM resection. One of the six

patients with AVM was treated for proximal PICA-aneurysm and the distal cerebellar AVM in the same session.

3.2.1.4 COMPLICATIONS

3.2.1.4.1 COILING-RELATED COMPLICATIONS

Of 34 patients treated endovascularly, 4 patients (11.8%) experienced procedure-related complications. Of these, as the most adverse event with lethal consequences, intraprocedural aneurysm rupture occurred in two patients (5.9%) resulting in rapid neurological decline, hemodynamic failure and death in both cases. One patient (2.9%) suffered hemiparesis and ophthalmoparesis from a pontine infarction. One other patient (2.9%) developed a pseudoaneurysm of the femoral artery which was treated with thrombin injection. In addition to the periprocedural complications, nine patients in the endovascular group (26.5%) also experienced swallowing problems during the hospital stay, however these were felt to be related to the direct effects of the initial hemorrhage. PEG placement was mandatory in seven patients (20.6%) and eight patients (23.5%) required a tracheotomy. In addition, one patient (2.9%) developed bilateral asymmetric fourth cranial nerve palsy with diplopia and the consequent corrective surgery at follow-up afterwards.

3.2.1.4.2 SURGERY-RELATED COMPLICATIONS

Among the 31 operated patients, 6 patients (19.4%) experienced surgery-related complications. Accidental PICA occlusion occurred in one patient (3.2%) resulting in symptomatic cerebellar stroke. 6 patients (19.4%) experienced postoperative lower cranial nerve palsies. Of these, the lower cranial nerve dysfunction resulted in aspiration pneumonia in two patients (6.5%). All six patients (19.4%) required PEG insertion after surgery. Tracheotomy was mandatory in three patients (9.7%). Not surprisingly, with the exception of one distal PICA-aneurysm, all were localized on the proximal segment of PICA in these patients.

3.2.1.5 CLINICAL AND RADIOGRAPHIC FOLLOW-UP

Clinical outcome and follow-up. Among the 67 patients with ruptured PICA-aneurysms, 32 patients (47.8%) were discharged from the hospital in an excellent clinical condition (GOS 5), 10 patients (14.9%) showed a GOS of 4, 8 patients (11.9%) had a GOS of 3, 10 patients (14.9%) presented with severe deficits and a GOS of 2 and 7 patients (10.4%) died. When considering the neurological outcome at discharge by aneurysm location, 50% patients with ruptured distal PICA-aneurysm presentend with poor clinical outcome at the time of discharge (GOS 1-3) compared to 31.9% of patients with ruptured proximal PICA-aneurysm.

When comparing the clinical outcome at discharge by treatment strategy, neurological morbidity rates were similar between both endovascular and surgical group. 12 patients (35.3%) in the endovascular group showed a poor outcome at discharge (GOS 1-3) when compared to 11 patients (35.5%) in the surgical group. Of note, 15 patients (44%) of patients in the endovascular group and 9 patients (29%) in the microsurgical group had presented with very poor clinical condition at admission having H&H score of IV or V (P=0.009).

Clinical and radiographic follow-up examinations were available for 48 of living patients, ranging from 1 month to 10 years. Among the 21 patients (32.3%) who experienced lower cranial nerve palsy after treatment, follow-up information was available in 14 (66.7%). Complete remission was observed in 10 patients (71.4%). In the remaining 4 patients (28.6%), one patient (7.1%) suffered persistent mild dysphagia and vocal cord paralysis with subsequent corrective surgery. One patient (7.1%) showed permanent tenth and twelfth cranial nerve palsy, one patient (7.1%) died due to aspiration pneumonia most likely caused by significant lower cranial nerve palsy and one patient (7.1%) presented with persistent vocal cord paralysis resulting in a hoarse voice. Of 2 patients who developed postoperative motor deficits, the hemiparesis recovered completely only in one patient, while the other remained. Persistent oculomotor impairment with the following exposure keratopathy occurring in one patient (7.1%) led to corrective surgery. Two additional patients (3.0%) suffered from short memory impairment.

Of 6 (19.4%) initially diagnosed aneurysm neck remnants with near-complete occlusion rates after surgery, one remnant (3.2%) remained stable and in three patients (9.7%) the originally diagnosed remnant was not visible on the non-invasive imaging study at one year

follow-up. A new fusiform dilatation of the PICA developed in the remaining case (3.2%).

Among patients undergoing endovascular treatment, five patients (14.7%) required retreatment due to growing aneurysm remnants / major recurrences during follow-up. These were treated with flow diverting technique in one patient (2.9%), microsurgery in one patient (2.9%), and additional coil embolization in the remaining 3 patients (8.8%). An asymptomatic progressive occlusion of the PICA was diagnosed in one patient (2.9%) at follow-up after endovascular treatment.

3.2.2 UNRUPTURED PICA ANEURYSMS

3.2.2.1 PATIENTS

Twelve patients with incidental asymptomatic PICA-aneurysms and four patients with presenting with mass effect due to unruptured PICA-aneurysms were included in this series.

3.2.2.2 INITIAL RADIOGRAPHIC FINDINGS

Multiple intracranial aneurysms were present in 4 patients (25.0%). Four aneurysms (25.0%) caused brainstem compression with subsequent neurological deficits and in one patient (6.3%) brainstem edema was also present.

3.2.2.3 THERAPY

Microsurgery was performed in 7 patients (43.8%). In particular, two giant (28.6%) and one large PICA-aneurysm (14.3%) required a complex surgical strategy including trapping and PICA bypass or VA-PICA anastomosis. 9 patients (56.2%) underwent endovascular treatment.

3.2.2.3.1 ANGIOGRAPHIC RESULTS OF ENDOVASCULAR TREATMENT

Aneurysmal remnants were present in three patients (33.3%) after coil embolization. Two of these remnants (22.2%) were managed conservatively, while the third patient with a developed major recurrence of a giant PICA-aneurysm requiring further treatment. Consequently, an additional endovascular procedure consisting of pipeline embolization was considered. Finally, the patient endovascular PICA occlusion since good collateral flow was present.

3.2.2.3.2 ANGIOGRAPHIC RESULTS OF SURGICAL TREATMENT

Postoperative radiographic studies showed patency of the PICA in all but one patient (14.3%) after surgery.

3.2.2.4 COMPLICATIONS

One patient (14.3%) developed acute transient ophthalmoplegia with resultant diplopia after endovascular treatment. There were no surgery-related complications in the unruptured group.

3.2.2.5 CLINICAL AND RADIOGRAPHIC FOLLOW-UP

All patients with unruptured PICA-aneurysms were discharged in good neurological condition. Fifteen patients (93.8%) were available for follow-up. The above-mentioned acute ophthalmoplegia after coiling resolved completety.

4. DISCUSSION

This systematic review and meta-analysis of 796 posterior inferior cerebellar aneurysms receiving either surgical or endovascular treatment, as part A, demonstrated that in general, both treatment modalities are technically feasible with high rates of technical success of over 95%, and safe with good long-term neurological outcomes of approximately 80%. When considering treatment strategies for ruptured PICA-aneurysms, both treatment approaches have similar long-term neurological morbidity rates of approximately 15%. Not surprisingly, surgical treatment has higher long-term complete aneurysm occlusion rates. Similarly, when considering treatment of unruptured PICA-aneurysms, surgery shows higher long-term

complete aneurysm occlusion rates. Notably, surgical treatment is associated with higher rates of procedure-related morbidity in these aneurysms. However, overall favorable neurological outcome rates are similar between both treatment modalities.

In our subgroup analysis by type of treatment, we found that surgical treatment also had higher overall complete occlusion rates and significantly lower rates of aneurysm recurrence. Meanwhile, endovascular treatment was associated with higher rates of overall neurological mortality and intraprocedural aneurysm rupture. Nevertheless, there were no differences in terms of procedure-related morbidity, mortality, or long-term favorable neurological outcomes suggesting that both treatment strategies of PICA-aneurysms are safe and effective. However, complications are not negligible with the procedure-related morbidity of approximately one tenth of treated patients in both groups. Both treatment strategies were associated with relatively high rates of acute hydrocephalus and cranial nerves palsies.

Of note, management and treatment strategies of ruptured or unruptured PICA-aneurysms have been developing based on local experience and treatment policy. Our multicenter study of 83 treated PICA-aneurysms, as part B, demonstrates that in general, neurological outcome at discharge after microsurgical or endovascular treatment for ruptured PICA-aneurysms does not differ. However, the overall results closely correlate with the patient's clinical condition at admission. In patients having poor neurological condition (H&H score IV-V at admission, rupture of a PICA-aneurysm resulted in 65.2% probability of poor neurological outcome (GOS 1-3). Not surprisingly, the most substantial differences between microsurgery and endovascular treatment were the rates of aneurysms remnants / major recurrences requiring retreatment favoring the surgical group.

These findings are important as they confirm that both surgical and endovascular techniques are safe with appropriate favorable neurological outcomes. Our data suggest that surgical treatment is associated with superior angiographic outcomes. Furthermore, endovascular treatment of PICA-aneurysms is associated with higher rates of neurological mortality and intraprocedural aneurysm rupture. It is important to note that these differences could be a reflection of the patient populations as patients who have more morbidity or poorer neurological function on presentation may be more likely to undergo coiling. These findings

should be considered when deciding the best therapeutic strategy for treatment of PICA-aneurysms. Yet, therapy of posterior inferior cerebellar artery aneurysms should be performed on a selective, case-by-case basis in order to maximize patient benefits and limit the risk of periprocedural complications.

Results of treatment are affected by the size, morphology, and localizations of PICA-aneurysms. Surgical treatment offers the possibility to decompress surrounding anatomical structures and preserve the PICA or its perforators.[26] Endovascular treatment may be demanding often due to the broad neck of these aneurysms, the fusiform shape as well as the highly variable origin and tortuosity of the PICA. Notwithstanding, numerous recent studies reported successful endovascular treatment of PICA-aneurysms.[13, 31-39]

Comparisons of overall neurological outcomes between surgical and endovascular treatments of PICA-aneurysms in the literature are limited largely due to the small sizes and non-comparative character of most case series.[17, 40, 41] The overall neurological outcome of endovascularly treated PICA-aneurysms is reported to be between 66% and 82%.[2, 14, 42] Some recently published surgical series demonstrated higher rates of good neurological outcomes ranging from 80% to 89%.[8, 17, 43-46] The largest surgical series of 91 distal posterior inferior cerebellar artery aneurysms to date by Lehto et al[1] reported, that 91% of patients surviving beyond one year, recovered to their former or an independent state of life. Our findings are similar to those in these prior reports, with the rates of good neurological outcomes of 77% of patients in the endovascular group and 83.2% of patients in the surgical group.

Regardless of methods, many studies reported high rates of technical success in treating PICA-aneurysms.[1, 2, 26] Chalouhi et al[2] reported 76 PICA aneurysms treated preferentially using endovascular approaches. The technical success rate was 96.3%. Complete aneurysm occlusion was achieved in 63.4% of patients. In comparison, Lehto et al[1] demonstrated high rates of technical success and especially of complete occlusion in 94% of the saccular and in 88% of the fusiform aneurysms. Likewise, Sejkorova et al[26] reported high rates of technical success and complete aneurysm occlusion rate in 100% of patients treated surgically. In our analysis, the high rates of technical success of over 96% in both groups are in line with those in their prior reports.

Aneurysm recurrence following endovascular coiling is a common problem occurring in roughly up to one fifth of cases depending on the series. The incidence of endovascularly treated PICA-aneurysms has been reported to be between 0% and 18.8%.[2, 17, 47] Our combined analysis of almost 800 PICA-aneurysms found that patients undergoing endovascular treatment had a recurrence rate of 8.1%. In the surgical group the rate of the aneurysm recurrence was 1.1%.

Irrespective of rapidly developing therapeutic advancements, PICA-aneurysms, especially in cases presenting with intraparenchymal hemorrhage, continue to be associated with high rates of morbidity and mortality often associated with the neurological consequences of the acute hemorrhage upon adjacent neural structures. This is especially true in patients with poor neurological condition at admission. In our study, of 26 patients presenting with initial H&H score of IV-V at admission, 18 patients (69.2%) showed a poor clinical outcome or died (GOS 1-3).

It is essential to note that complications occurring due to the original hemorrhage or related to treatment have at times are of temporary character but require additional aggressive treatment. In our study, a total of 17 patients undergoing endovascular treatment (39.5%) and 14 patients treated surgically (36.8%) required extra interventions to treat periprocedural complications such PEG tube placement, VP shunt insertion, corrective surgery of eyes or vocal cord paralysis or retreatment of major recurrences. Likely, in the Barrow Ruptured Aneurysm Trial (BRAT),[48] patients with PICA-aneurysms showed a high incidence of lower cranial nerve palsies resulting in the need for tracheostomy and/or PEG in 50% of patients. Lower cranial nerve dysfunction may have long-term consequences for patients, but the recovery rates within 6 months are as high as 76%.[1, 49] In our study, lower cranial nerve deficits requiring PEG tube placement occurred in 19.4% of surgically and in 23.5% of endovascularly treated ruptured PICA-aneurysms and of these, 73% of patients with adequate follow-up recovered within 6 months. Of note, in defiance of the high rates of in-hospital complications (many related to the original clinical presentation), overall outcomes at discharge showed no significant difference between the two treatment modalities (favorable neurological outcomes rates of patients with a ruptured aneurysm at discharge were 64.7% in the endovascular group versus 64.5% in the

surgical group. Importantly, among patients with ruptured aneurysms a higher percentage of patients presenting with H&H grades IV and V underwent endovascular therapy. These results emphasize the importance of a selective case-by-case approach in the treatment of these aneurysms in order to maximize patient benefits and limit the risk of periprocedural complications.

Ultimately, given not only the aforementioned results, the decision regarding whether to treat the PICA-aneurysm either with endovascular or surgical therapy should be taken on a case-by-case basis considering many factors such as aneurysm location and its shape, feasibility of coiling and local neurosurgical and endovascular expertise.

In conclusion, regardless of both treatment strategies, urgent therapy of ruptured PICA-aneurysms is crucial due to minimizing the subsequent risk of re-rupture[2, 50-52] as rebleeding rates of ruptured PICA-aneurysms may be as high as 78%.[53] Our study revealed that surgical treatment is associated with superior angiographic outcomes. Additionally, surgery was related to higher rates of cranial nerves palsies especially in patients harboring proximal PICA-aneurysms. Besides, endovascular treatment was associated with significantly higher rates of parent vessel occlusion resulting in higher rates of perioperative stroke in patients with distal PICA-aneurysms. Accordingly, our data suggest that while endovascular therapy could be a reasonable first-line treatment option for proximal PICA-aneurysms due its minimally invasive nature, surgery remains high effective first-line choice for distal PICA-aneurysms.

5. CONCLUSIONS

The combined meta-analysis of almost 800 PICA-aneurysms treated with both surgical and endovascular techniques (part A) as well as our results of 83 treated PICA-aneurysms treated at three large international referral neurovascular centers (part B) demonstrated that in general, that both the endovascular and the surgical treatment modalities are technically feasible with high rates of technical success, and safe with similar neurological morbidity and mortality rates. Not surprisingly, our data suggest that overall neurological outcome is associated with the patient neurological condition at admission.

Complications of the original hemorrhage and of treatment are not negligible and related to cranial nerve morbidity and hydrocephalus. Surgical treatment of both ruptured and unruptured PICA-aneurysms is associated with overall superior angiographic outcomes but also with higher rates of cranial nerves palsies in patients harboring proximal PICA-aneurysms. Besides, endovascular treatment was associated with significantly higher rates of parent vessel occlusion resulting in higher rates of perioperative stroke in patients with distal PICA-aneurysms. While endovascular therapy could be a reasonable first-line treatment option for proximal PICA-aneurysms due its minimally invasive nature, surgery remains highly effective first-line choice for distal PICA-aneurysms.

These findings should be considered when deciding the best therapeutic strategy for treatment of PICA-aneurysms.

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A) First author / contributed equally authorship:

1) **Petr O**, Sejkorová A, Bradáč O, Brinjikji W, et Lanzino G. Safety and Efficacy of Treatment Strategies for Posterior Inferior Cerebellar Artery Aneurysms: A Systematic Review and Meta-analysis. Acta Neurochirurgica 2016. (**IF 1.766**)
2) Sejkorová A, **Petr O**, Mulino M, Hejčl A, Thomé A, Sameš M, et Lanzino G. Management of Posterior Inferior Cerebellar Artery Aneurysms: What factors play the most important role in outcome? Acta Neurochirurgica (under review, minor revisions only). Anticipated date of acceptance Winter 2016. (**IF 1.766**)

3) **Petr O**, Lanzino G. Brainstem cavernous malformations. J Neurosurg Sci. 2015 Sep; 59(3):271-82. Epub 2015 May 6. Review. PubMed PMID: 25943871. (**IF 1.651**)
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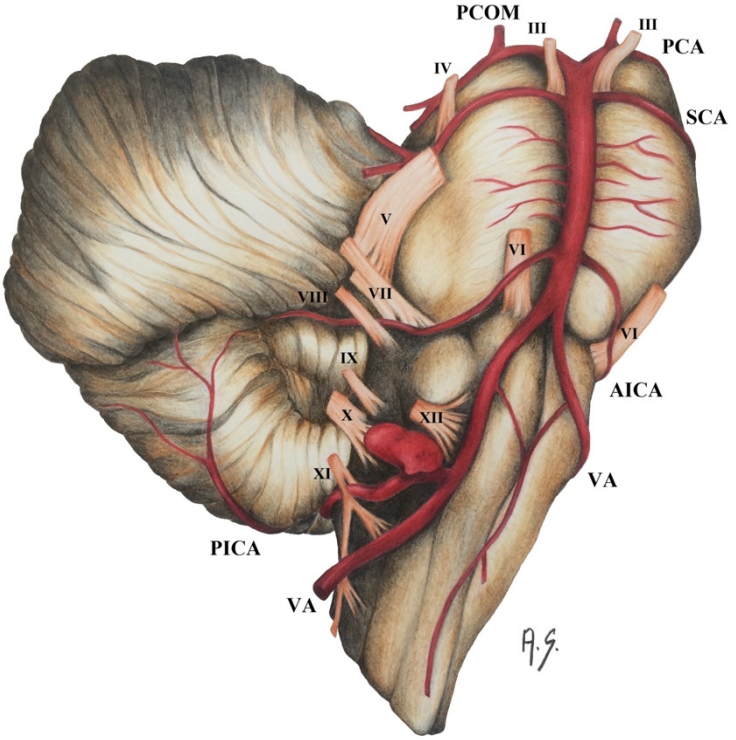

Artist rendering of the vetrolateral surface of the brainstem and cerebellum.
[A. Sejkorová]