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"CAROL DAVILA" BUCHAREST

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PATHOGENIC MODELS OF THE GENESIS OF INTRACRANIAL ANEURYMS. EXPERIMENTAL STUDY IN RATS

PHD THESIS SUMMARY

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INTRODUCTION

This PhD thesis aims to address complex issues in the field of neurosurgery, with a specific focus on cerebral aneurysms, a significant public health problem due to their catastrophic potential and the complexity associated with diagnosis and treatment. In this ever-evolving world of medicine, experience in microsurgical practice and thorough acquisition of theoretical concepts prove to be vital to achieving and maintaining excellence in vascular neurosurgical pathology.

Additionaly, the role of simulation in neurosurgical training is undeniable, even if no existing model can stand for a perfect simulation of reality. However, each simulation model offers unique advantages and disadvantages, and acquiring experience in microsurgical training requires the use of several such models.

Under this framework, the thesis aims to contribute to the existing literature through an approach based on the development of experimental models of aneurysms in rats, aimed at promoting mastery in basic microsurgical techniques. This will be achieved by structuring the research in three diffrent stages: the acquisition of basic microsurgical techniques, complex microsurgical training and the development of microsurgical models of aneurysms, followed by their anatomopathological study.

This approach meets the need for constant improvement of intraoperative skills despite the rapid development of endovascular interventional therapies. However, given certain particular situations that require surgical intervention, the ongoing training of neurosurgeons remains key.

Moreover, we aim to explore the clinical and evolutionary particularities of brain aneurysms according to their location in the brain, an aspect that is particularly relevant but still insufficiently explored in the specialty papers. This multidisciplinary approach will allow us to review cases of Romanian patients in an international context, highlighting any relevant particularities or differences.

Overall, this paper aims to make relevant contributions to the understanding of the complexity of cerebral aneurysms and to the improvement of diagnostic and treatment strategies, by integrating surgical training with the investigation of clinical and evolutionary features of cerebral aneurysms.

SCIENTIFIC PAPERS PUBLISHED

1. Step training in a rat model for complex aneurysmal vascular microsurgery. Dan Martin, Mircea Radu Gorgan. Romanian Neurosurgery (2015) XXIX 4: 493 - 502

2. Ex Vivo Aneurysm models mimicking real cases for the preoperative training of the clipping technique. D. Martin, A. Giovani, Narcisa Bucur, R.M. Gorgan. Romanian Neurosurgery (201) XXX 4: 493 - 502

CHAPTER 1. PATHOGENESIS OF INTRACRANIAL ANEURYSM

1.1. EPIDEMIOLOGY AND RISK FACTORS

Intracranial aneurysms represent acquired vascular lesions that develop mainly in the branches of the cerebral arteries and in the vast majority of cases in the anterior cerebral circulation, near the circle of Willis. The reported prevalence of intracranial aneurysms detected radiologically or in autopsy is approximately 3.2% worldwide, with an average age at diagnosis of 50 years, and an equal gender distribution. [1]. After the age of 50, secondary to hormonal changes, the prevalence in women is higher [2]. Intracranial aneurysms are often found incidentally, their number has increased with the more frequent use of non-invasive imaging investigations. Also, in 20% of cases, patients are diagnosed with multiple cerebral aneurysms and represent an additional risk factor contributing to the increased risk of rupture.

Although rare, aneurysm rupture is a severe complication with a pre-hospital mortality of up to 10%. Rupture of aneurysms can lead to intraparenchymal hemorrhage or, more commonly, subarachnoid hemorrhage (SAH). Among SAH survivors, only one-third have favorable long-term outcomes following treatment [3]. Despite numerous epidemiological studies and risk factors, accurate estimation of the risk of rupture and selecting patients for surgical or endovascular intervention remains a difficult decision.

1.2. LOCATION, SIZE AND MORPHOLOGY

Most saccular aneurysms occur in the anterior cerebral circulation. The distribution varies between different populations and also differs between ruptured and unruptured aneurysms. Ruptured aneurysms are most commonly located in the anterior communicating artery (ACoA), followed by aneurysms in the internal carotid artery (ACI) and middle cerebral artery (MCA). In the posterior circulation, the bifurcation of the basilar trunk is the most common location [4].

1.3. PHYSIOPATHOLOGY OF INTRACRANIAL ANEURYSMS

Cerebral aneurysms are abnormal, acquired dilations of the arterial wall. Most intracranial aneurysms are saccular [13], although fusiform or infectious aneurysms may be identified in certain individuals. They are discovered in approximately 1-2% of patients who undergo brain imaging investigations, however, the anatomopathological studies performed indicate a prevalence among the adult population between 1% and 5%. It represents an extremely rare pathology in children, at this age it is most likely caused by connective tissue diseases [14].

The pathophysiological aspects of intracranial aneurysm formation have led to controversy in their management, given the fact that most aneurysms never bleed during life. The annual risk of rupture is approximately 1%, but may be burdened by massive bleeding and a poor prognosis respectively [15]. Intracranial aneurysms are responsible for the occurrence of SAH in 80-85% of cases [4].

1.4. EVOLUTION TO RUPTURE OF SACULAR ANEURYSM

The evolution of an intracerebral saccular aneurysm is unpredictable and variable. It may remain dimensionally stationary for a good period of time, but episodes of rapid growth may occur, then the risk of rupture increases significantly [1], [24]. Studies suggest that the progression of aneurysms is most likely discontinuous and stochastic rather than linear [25]. Although some aneurysms remain asymptomatic throughout life, there are also situations in which they appear, grow and rupture over a very short period of time, in only a few weeks or months. This was particularly observed in patients with high inhereted risk and in those with a history of SAH caused by the rupture of another aneurysm [26], [27].

CHAPTER 2. DIAGNOSTIC METHODS AND THERAPEUTIC STRATEGIES

2.1. GENERAL CONSIDERATIONS

The primary goal in aneurysm management is to prevent rupture. Until the advent of endovascular treatment options, the preferred method of treatment was surgical clipping. In the early stages, the endovascular approach was reserved only for situations where clipping was not possible due to size or location. Over time, the benefits of endovascular treatment have proven to be superior in certain situations and today it is the preferred option in selected cases [14]. Deciding on one method or the other is influenced by many aspects, aspects that can simplify or complicate the decision, starting from the particularities of the case to the patient's desire and the level of expertise in the medical facilitities available. The option to monitor and not intervene on an intracranial aneurysm is an intensely debated aspect given the fact that, as previously mentioned, a significant percentage will remain asymptomatic throughout life.

2.2. NEUROSURGICAL TREATMENT

The purpose of the decision to treat an unruptured aneurysm is to isolate the aneurysm from the rest of the circulation by clipping the aneurysmal bundle without affecting the patency of the small perforating arterial vessels around the aneurysm. In the case of a ruptured aneurysm, surgery stops the source of bleeding and prevents its recurrence [44]. There are varied techniques which depend not only on the characteristics of the aneurysm but also on the experience level of the medical facility where the neurosurgical intervention will be performed.

New trends in the field of modern surgery aim to achieve "same-day surgeries". This involves discharging the patient on the same day the intervention is performed, to reduce costs and the burden on specialized medical centers, without endangering the patient's life. An observational study, both retrospective and prospective, carried out on a cohort of patients who had undergone microsurgical clipping of an intact aneurysm, showed that for this type of intervention, the short-term hospitalization of selected patients can be taken into account [45]. This trend requires refinement of therapeutic strategies and optimization of patient monitoring outside the hospital.

Surgery of intracranial aneurysms has greatly developed through microsurgical procedures, which today allow access to most locations. From the point of view of the applied surgical techniques, a first classification can be made according to the anatomical location of the aneurysms and the acces method. Craniotomy can be performed in multiple ways, depending on the aneurysm occurance and the experience of the neurosurgeon. For aneurysms located in the anterior cerebral artery, fronto-temporo-sphenoidal craniotomy is the most common and involves a frontotemporal incision and subfascial dissection of the temporalis muscle, followed by the controlled drilling of a small hole in the skull and curvilinear opening of the dura. Other types of craniotomy include: frontal or interhemispheric craniotomy with bicoronal incision [46].

For aneurysms located in the posterior cerebral circulation, things can get significantly more complicated, especially if the aneurysm is located in the P2 segment of the PCA.

This segment is divided into an anterior P2a and a posterior P2p segment by the posterior portion of the cerebral peduncle. Craniotomy can also be performed at the pterional, interhemispheric subtemporal and occipital levels. Although the subtemporal approach allows visualization of the P2a segment, adequate exposure for microsurgery is limited due to its location in the superior cistern. For the P2p segment the preferred approach is the interhemispheric transtentorial where the artery can be easily manipulated.

2.3. ENDOVASCULAR TREATMENT

Endovascular treatment was initially used only in the case of lesions inaccessible from a neurosurgical point of view, especially at the level of the posterior cerebral circulation. Along with the development of techniques, devices and the acquisition of experience, endovascular therapy has expanded its indications, becoming a formidable alternative to surgical treatment [14]. It fosters many advantages, but there are still certain limitations in the choice of this procedure, limitations that are often related to the anatomical location, the size of the aneurysm or the unfavorable geometry, but also the expertise and experience of the interventional radiology team. Although research has shown better results in embolization procedures, they still present the disadvantage of a higher rerooting rate compared to surgical therapy, a rate that also depends on the endovascular technique chosen.

Endovascular techniques are performed under general anesthesia and heparin therapy while the basic principles are similar, regardless of the type of device used. A microcatheter with a metal coil attached is inserted through the guiding catheter, up to the aneurysm location. The metal coil is detached from the catheter with an electric current transmitted through it sealing the opening of the aneurysm. The spiral will remain permanently in this position. There are situations where multiple coils are needed to completely isolate the aneurysm from the rest of the circulation. All procedures are performed under fluoroscopic guidance.

Post-procedural management includes continued heparin therapy for 48h and close monitoring to prevent vasospasm. The patient is discharged with the indication of antiplatelet treatment with low-dose aspirin or clopidogrel for at least 3 months, depending on the patient's characteristics [68].

CHAPTER 3. ANEURISMAL PATHOGENIC MODELS

Training in surgical specialties and especially in cerebrovascular surgery, a subspecialty of neurosurgery, is extremely difficult to achieve due to the growing number of neurosurgical departments and the lack of specific pathologies expertise centers.

To meet the new requirements, special attention is paid to investing in experimental aneurysm models for the training of young specialists. Although there are numerous aneurysm models described in literature to elucidate pathogenesis and optimal therapy, not all are reproducible. Each experimental model presents its advantages and disadvantages in terms of simulating reality, costs, technical possibilities, etc.

STUDY 1: PATHOGENIC MODELS OF THE GENESIS OF INTRACRANIAL ANEURYMS. EXPERIMENTAL STUDY IN RATS.

STUDY METHODOLOGY

AIM OF THE STUDY

Development of a rat microsurgical aneurysm model feasible for neurosurgical training and histopathological study of aneurysms.

STUDY DESIGN

The study was carried out with the help of the biobase microsurgery unit of Floreasca Emergency Clinical Hospital in Bucharest. The experimental animals used were male Brown Norway rats, aged between 10 and 16 weeks (13 weeks in average) and weighing between 250 and 400 grams (mean 320 grams). We performed n=10 rat hindlimb replantations.

The steps of operative surgery and preoperative management are presented in detail. We assessed vascular permeability by clinical assessment - color, temperature, capillary refill time. Rats were inspected daily for signs of infection. Nerve regeneration was assessed by the foot print method.

For anesthesia, the animals were placed in the induction chamber with a flow of anesthetic gas. Rats were anesthetized with Xylazine (0.02 ml) and Ketamine (0.01 ml). Monitoring during anesthesia was performed using the tail pinch reflex, respiratory rate, pulse rate, and tissue color checks. The entire operation was performed under aseptic conditions, and antibiotic prophylaxis was administered using Clavulox 0.1 ml/100 g s.c. at the beginning of the operation. Fluid loss during surgery was compensated with 6-7 ml of 0.9% sodium chloride solution, administered by intraperitoneal injection. No vasodilator or anticoagulant drugs were used, except for limb perfusion.

DISCUSSIONS

Although a few decades ago, the microvascular suturing technique was the domain of neurosurgeons, today almost every surgical specialty uses this technique for its pathology. Many programs have integrated training in microvascular anastomosis techniques into their programs. Surgeons are trained either in thei medical facility, if it has an animal microvascular laboratory, or are referred to centers that run training courses in microsuture.

Materials initially used for learning microsurgical suture and knot techniques are latex and silicone tubing. However, the sensation of handling viable biological tissue is obtained only in small animal laboratories. Models available for training microvascular anastomosis techniques can be classified into three categories: non-biological and non-functional, biological and non-functional, and the vital small animal model, which require investment and maintenance.

Each of these models has advantages and disadvantages, which are well known. Abouod et al. proposed a perfused cadaver head model for training neurosurgical procedures. The success of a microvascular suture, regardless of the technique, can only be proven by the survival of the replanted parts in chronic experiments, for example, tail and limb replantation or organ transplantation in rats.

In conclusion, training in microsurgical techniques is crucial for training surgeons in various specialties. The use of the rat laboratory model is popular in vascular microsurgery and provides a valuable opportunity for developing the skills required in this complicated field.

SUDY 2: EVALUATION OF CLINICAL AND EVOLUTIONARY FEATURES IN PATIENTS WITH CEREBRAL ANEURYSMS IN RELATION OF ANEURYSMS LOCATION

AIM AND OBJECTIVES

The aim of the study was to evaluate the diagnostic and evolutionary features in patients with cerebral aneurysms in relation to thei location.

The specific objectives of this study were:

- Comparison of clinical and imaging characteristics of patients with cerebral aneurysms
- Evaluation of the evolution of cerebral aneurysms in relation to their location
- Investigation of risk factors and prognostic factors that can influence the evolution of cerebral aneurysms according to their location, including the age of patients and associated comorbidities
- Development of a set of recommendations and clinical guidelines for the diagnosis, monitoring and management of cerebral aneurysms according to their location, with the aim of improving clinical decisions and patient prognosis.

STUDY METHODOLOGY

Based on the purpose and objectives of the research, the research design and methodology were defined, its main characteristics being:

- Retrospective - the data were collected between November 1, 2020 and June 1, 2022 for patients hospitalized in a 22-year interval - January 1, 2000 - June 30, 2022
- Unicentric – also included patients admitted to the Bagdasar Arseni Hospital in Bucharest
- Descriptive
- Non-interventional

Eligibility criteria

- Diagnosis of cerebral aneurysm at discharge
- Age over 16
- The presence of all the necessary data

OUTCOMES

Aneurysmal location

Analyzing the data obtained, it can be seen that cerebral aneurysms show a significant variation depending on their location. Among the locations with higher frequencies are the Anterior cerebral artery, internal carotid and middle cerebral artery. The anterior cerebral artery registers the highest frequency, with an impressive number of 1037 cases, followed by the internal carotid with 370 cases and the middle cerebral artery with 399 cases. In contrast, the posterior cerebellum and posterior cerebellum show the lowest numbers of cases, with 25 and 41 cases respectively

DISCUSSIONS

The purpose and objectives of the study to examine the diagnostic characteristics and evolution of cerebral aneurysms according to location, are congruent with the current direction of research in the field of neurosurgery. There are many studies that focus on the clinical and imaging characteristics of cerebral aneurysms, but the approach of this study is unique because it includes a large group of patients – 2840 persons.

Our observations align with existing trends in literature regarding the location of cerebral aneurysms. Similar to previous studies, we found that cerebral aneurysms are common in the region of the anterior cerebral artery, internal carotid, and middle cerebral artery. In particular, the high frequency of aneurysms in the anterior communicating region, evidenced by the 1037 cases recorded in this study, confirms previous findings [102].

The age distribution of patients studied reflects an incidence pattern widely accepted in the existing medical literature. According to previous studies, the average age of patients with brain aneurysms is often around fifty. Our median age of 58 years and average age of 57 is alignment with these findings, suggesting that this study is representative of the broader population of patients with cerebral aneurysms.

Our observations that basilar and internal cerebral aneurysms usually occur in older patients, while posterior cerebellar aneurysms are more common in younger patients [103].

Examination of the data revealed an increased prevalence of cerebral aneurysms in the female population (57.465% of cases) compared to the male population (42.535% of cases), these results are similar to those found in speciality literature [104]. This outcome is consistent for most of the analyzed aneurysm locations, indicating a possible predilection of cerebral aneurysms towards the female sex, regardless of their location.

However, caution is warranted in interpreting these results. Although the data indicate a trend, they do not provide evidence of causation. Factors such as genetic variations, lifestyle behavior and environmental factors may also be involved in influencing the differences observed.

Hypertension is recognized in the medical literature as a major risk factor for the development and rupture of cerebral aneurysms [105]. Regarding the location of aneurysms, studies have indicated that there are some associations between HBP and the location of cerebral aneurysms, but these associations may vary depending on several factors, including ethnicity, sex, family history, and other individual risk factors [106]. In the case of our study, the percentage of patients with a history of arterial hypertension was approximately 19%, with variations in relation to the location of the arterial aneurysm.

Type II diabetes mellitus (DM) is also an important risk factor for cerebral aneurysms. However, some studies have suggested that DM may have a "protective" effect against the development of brain aneurysms, although the exact mechanisms are not fully understood [107]. Analysis of the cases included in the research indicates that DM is present in a lower percentage of cerebral aneurysm cases compared to HBP, which is consistent with the existing medical literature. Also, although there are differences in relation to location, the data do not show a more severe evolution in the case of these patients.

Unfortunately, many brain aneurysms remain asymptomatic until the time of rupture. In literature, it is estimated that approximately 50% to 80% of cerebral aneurysms are asymptomatic, depending on location, size, and the individual patient. They are often discovered accidentally during investigations for other health conditions [108].

Reviewing the collected data, we note that most patients with cerebral aneurysms, regardless of their location, are in a good general condition at the time patients come to the hospital. Specifically, 75.81% of the total of 2840 patients fall into this category. On the other hand, only 9,824% of patients are in a serious condition. These numbers reflect the general trend observed in literature, which suggests that most cerebral aneurysms are asymptomatic until rupture, which is why patients may be in good overall health condition at the time of their diagnosis.

On the other hand, we observe a significant difference depending on the location of the aneurysm. Patients with aneurysms located in the posterior cerebellar artery differ significantly, with 96,000% of them in fair condition and none in severe condition. On the other hand, patients with middle and posterior cerebral aneurysms present the highest percentage of cases in serious condition, respectively 12,030% and 12,195%.

This suggests that the location of the aneurysm can significantly influence the general condition of patients upon presentation, an aspect that must be considered in their case management.

Unfortunately, many brain aneurysms remain asymptomatic until the time of rupture. In the literature, it is estimated that approximately 50% to 80% of cerebral aneurysms are asymptomatic, depending on location, size, and the individual patient. They are often discovered accidentally during investigations for other health conditions [109].

In our study, most aneurysms were diagnosed following the manifestation of symptoms (63.169%), the rest being discovered incidentally. The locations with the highest percentage of diagnoses based on symptoms are the posterior cerebellar artery (72%) and the ophthalmic artery (70.588%). Pericallous aneurysms have the lowest percentage of diagnosis based on symptoms (54.286%) and the highest percentage of incidental diagnosis (45,714%).

It is important to note that the incidental diagnosis of cerebral aneurysms may indicate a lack of obvious symptoms or the fact that patients are not aware of the severity of the symptoms they experience. On the other hand, a higher percentage of diagnoses based on symptoms suggests a higher presence of clinical manifestations that lead patients to seek medical care. The treatment decision may be influenced by the way the aneurysm was discovered, the patient's overall condition, and the potential risk of aneurysm rupture.

When brain aneurysms become symptomatic, they can cause a variety of symptoms, depending on their exact location and size in the brain. Symptoms can range from less specific, such as headaches and dizziness, to specific localized neurological symptoms, such as facial or limb paralysis, visual disturbances, speech difficulties, confusion or even loss of consciousness[110].

Headaches are by far the most commonly reported symptom and are often described as the most severe headaches an individual has ever experienced. These are often accompanied by symptoms such as nausea, vomiting and sensitivity to light. Approximately 50% of patients with ruptured cerebral aneurysms report severe headaches [111]. Headache was the most common symptom, with 51.725% of patients reporting this symptom. Posterior cerebellar aneurysms (64%) and ophthalmic artery aneurysms (61.76%) presented the highest frequency of headache. In the case of internal cerebral aneurysms, 52.67% of patients did not experience headache.

Vertigo or feeling unsteady is less common and is reported by about 10% of patients with brain aneurysms. However, this symptom may be more common with aneurysms affecting certain cerebral arteries that supply blood to brain regions responsible for balance and coordination [112]. Vertigo is a less common symptom, present in only 7.465% of patients. Basilar aneurysms (11.719%) and ophthalmic artery aneurysms (14.706%) recorded higher percentages of patients with vertigo.

Paresis or muscle weakness is another common symptom that occurs when an aneurysm affects the motor areas of the brain or associated neural pathways. Studies show that between 20% and 30% of patients with cerebral aneurysms may have paresis at the time of diagnosis [8]. Paresis was present in 20.317% of patients. Most cases of paresis were recorded in posterior cerebral aneurysms (26.829%), followed by anterior cerebral (22.059%) and basilar (21.094%).

Epileptic seizure and loss of consciousness are considered severe symptoms and are often associated with ruptured or large brain aneurysms. These are uncommon, being reported by less than 10% of patients [8]. Epileptic seizure is not a common complication in patients with cerebral aneurysms, being present in only 1% of cases. No clear conclusions could be drawn according to the location of the aneurysm, given the small number of cases.

Loss of consciousness was reported in only 2% of cases. The highest incidence of this symptom was in pericallosal artery aneurysms (5.71%), while the lowest incidence was in cerebral aneurysms located in the anterior cerebral artery (1.471%). Our study also suggests that vertigo and paresis may be more common in certain aneurysm locations, such as the basilar artery and ophthalmic artery for vertigo and the posterior cerebral artery for paresis.

According to the results of our study, the majority of patients (67%) had a GCS score of 15 at presentation, indicating an unimpaired level of consciousness. The data suggest that patients with posterior communicating artery aneurysms and those with posterior cerebellar artery aneurysms had lower GCS scores, indicating a greater level of neurologic impairment.

Patients with GCS scores of 13–15 were considered to have mild or no impairment, those with GCS scores of 9–12 were considered to have moderate impairment, and those with GCS scores below 9 were considered to have severe impairment. In general, these data are consistent with trends observed in the speciality literature [113].

The results of the analysis performed on the sample of 2,840 patients with cerebral aneurysms indicate a heterogeneous distribution of the duration of hospitalization, with an average value of 10,526 days and a standard deviation of 13,816. This significant variation suggests a wide spread in the data, with admissions ranging from less than a day to a year.

In addition, the location of the aneurysm has been shown to be a determining factor in the length of hospital stay. Patients with aneurysms located in the internal carotid or posterior communicating area had the longest hospital stays, with a maximum duration of 367 days. In contrast, aneurysms located in the posterior cerebellar, anterior cerebellar, midcerebral, and pericalus regions had shorter hospital stays, with average values below 10 days.

Regarding mortality, 15,528% of patients died during hospitalization. The distribution of deaths varied by aneurysm location, with higher rates for basilar, internal carotid, and anterior cerebral aneurysms, while posterior cerebellar, anterior cerebral, and internal cerebral locations had lower rates of death.

GENERAL CONCLUSIONS

1. There is an increased need for training in microvascular anastomosis techniques, with many training programs incorporating such courses. Training can take place either in institutions that have microvascular laboratories, or in specialized centers that organize microsuture courses.
2. Laboratory microsurgical training in rats has become a popular model in microvascular surgery, providing the opportunity to practice and learn from mistakes in a simulated environment before performing surgery on humans.
3. Training in microsurgical techniques is crucial for training surgeons in various specialties, contributing to improved clinical outcomes.
4. The rat hindlimb replantation procedure has been shown to be feasible in a laboratory setting, with an average of operating time of 183 minutes and an ischemia phase of approximately 25 minutes.
5. The procedure had a long-term survival rate of over 90 days for all rats included in the study, indicating considerable clinical success of the microsurgical techniques used.
6. Nerve regeneration progressed steadily over a 6-month period, with all rats demonstrating complete nerve regeneration at 6 months postoperatively.
7. The microsurgical aneurysm model in rats is a valuable tool for neurosurgical training and the histopathological study of aneurysms. Furthermore, it could serve as a model for other future microsurgery studies.
8. In the study on patients diagnosed with cerebral aneurysms, the average age aligns with the literature data, confirming the representativeness of the studied sample. There are significant age differences in the location of aneurysms, with basilar and internal cerebral aneurysms being more common in elderly patients and posterior cerebellar aneurysms in younger patients.
9. Cerebral aneurysms were more common in the female population, indicating a potential female bias.

10. High blood pressure and type II diabetes can be an important risk factor for the development of cerebral aneurysms, but their influence varies depending on the location of the aneurysm and other individual factors.
11. Most patients with cerebral aneurysms are in good general condition at presentation, with a significant difference depending on the location of the aneurysm.
12. Headache is the most common symptom reported by patients with cerebral aneurysms, with variations depending on the location of the aneurysm. Other symptoms, such as vertigo and paresis, are less common but have been seen in higher proportions in basilar and ophthalmic artery aneurysms.
13. In terms of mortality rates, 15.26% of the patients under survey died, most of them being in the group of patients with a serious condition upon presentation (34.62%).
14. The research results reconfirm the vital importance of vascular neurosurgery as a major field in the context of neuroscience. Despite technological advances that have diversified and enriched complementary treatment techniques, rigorous training of young neurosurgeons remains a fundamental pillar in the management of cerebrovascular disorders. Technology can be a plus, but it does not replace the need for solid, in-depth training in vascular neurosurgery, which is key in a hands-on discipline. Young neurosurgeons must be equipped with the skills required to deal with any complication that may arise during the caring of patients with cerebrovascular pathology. The holistic approach, which combines technical knowledge, manual dexterity, and the judicious application of leading technologies, will continue to be a benchmark for excellence in vascular neurosurgery, ensuring that patients receive the highest level of care.

BIBLIOGRAPHY (SELECTED)

[102] A. J. Molyneux *et al.*, “International subarachnoid aneurysm trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised comparison of effects on survival, dependency, seizures, rebleeding, subgroups, and,” *Lancet (London, England)*, vol. 366, no. 9488, pp. 809–817, Sep. 2005, doi: 10.1016/S0140-6736(05)67214-5.

[103] S. Marbacher *et al.*, “Complex bilobular, bisaccular, and broad-neck microsurgical aneurysm formation in the rabbit bifurcation model for the study of upcoming endovascular techniques,” *Am. J. Neuroradiol.*, vol. 32, no. 4, pp. 772–777, 2011, doi: 10.3174/ajnr.A2374.

[104] M. D. Forrest and G. V. O’Reilly, “Production of experimental aneurysms at a surgically created arterial bifurcation,” *Am. J. Neuroradiol.*, vol. 10, no. 2, pp. 400–402, 1989.

[105]Keedy A. An overview of intracranial aneurysms. Mcgill J Med. 2006 Jul;9(2):141-6. PMID: 18523626; PMCID: PMC2323531.

[106]Czyżewski, W.; Hoffman, Z.; Szymoniuk, M.; Korulczyk, P.; Torres, K.; Staśkiewicz, G. The Incidence, Localization and Clinical Relevance of Arterial Fenestrations and Their Association to Brain Aneurysms: A Case–Control Study Based on the STROBE Guidelines. Brain Sci. 2022, 12, 1310.

[107]Md Al Amin Sheikh, Anis Suhaila Shuib, Mohd Hardie Hidayat Mohyi, A review of hemodynamic parameters in cerebral aneurysm, Interdisciplinary Neurosurgery, Volume 22, 2020, 100716

[108]Tada Y, Wada K, Shimada K, Makino H, Liang EI, Murakami S, Kudo M, Kitazato KT, Nagahiro S, Hashimoto T. Roles of hypertension in the rupture of intracranial aneurysms. Stroke. 2014 Feb;45(2):579-86.

[109] Lindgren AE, Kurki MI, Riihinen A, Koivisto T, Ronkainen A, Rinne J, Hernesniemi J, Eriksson JG, Jääskeläinen JE, von und zu Fraunberg M. Type 2 diabetes and risk of rupture of saccular intracranial aneurysm in eastern Finland. Diabetes Care. 2013 Jul;36(7):2020-6. doi: 10.2337/dc12-1048.

[110]Cianfoni A, Pravatà E, De Blasi R, Tschuor CS, Bonaldi G. Clinical presentation of cerebral aneurysms. Eur J Radiol. 2013 Oct;82(10):1618-22. doi: 10.1016/j.ejrad.2012.11.019. Epub 2012 Dec 10. PMID: 23238357.

[111] InformedHealth.org [Internet]. Cologne, Germany: Institute for Quality and Efficiency in Health Care (IQWiG); 2006-. Brain aneurysm: Overview. 2018 Nov 29. Available from: https://www.ncbi.nlm.nih.gov/books/NBK541149/

[112] Date I. Symptomatic unruptured cerebral aneurysms: features and surgical outcome. Neurol Med Chir (Tokyo). 2010;50(9):788-99. doi: 10.2176/nmc.50.788. PMID: 20885113.

[113]Behrouz R, Birnbaum LA, Jones PM, Topel CH, Misra V, Rabinstein AA. Focal Neurological Deficit at Onset of Aneurysmal Subarachnoid Hemorrhage: Frequency and Causes. J Stroke Cerebrovasc Dis. 2016 Nov;25(11):2644-2647.