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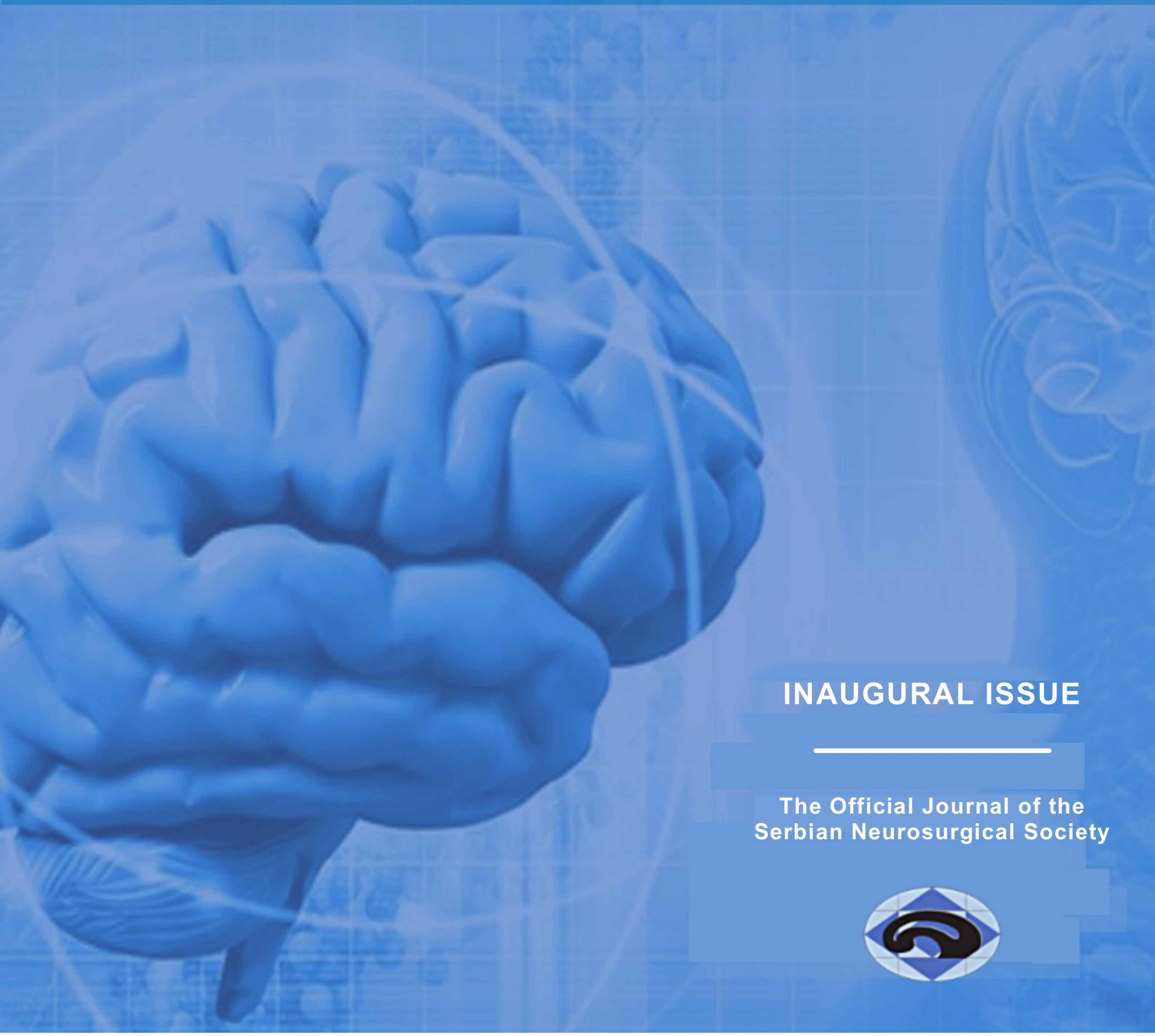

INAUGURAL ISSUE

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Contents

INAUGURAL EDITORIAL

A warm Serbian welcome!

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Welcome to the inaugural issue of Neurohirurgija – The Serbian Journal of Neurosurgery. Launched in 2021 as the official journal of the Serbian Neurosurgical Society, this new serial publication brings an important recognition of the professional efforts of the Serbian Neurosurgical Society and marks a major milestone in its further development. It is indeed a great honour and privilege for me as President of the Serbian Neurosurgical Society to be entrusted with the editorship of this new forum of international academic exchange, aimed at promoting neurosurgery without borders.

In line with the current trends in neurosurgery and neuroscience, The Serbian Journal of Neurosurgery will foster a comprehensive intradisciplinary, interdisciplinary and multidisciplinary approach, covering all neurosurgical sub-specializations and related disciplines. Encompassing different specialties that collaborate to improve outcomes for patients with neurosurgical and related diseases, it will include all aspects of case assessment and surgical practice and all types of research, emphasizing clinical rather than experimental material.

The Journal will publish high-quality original research articles, as well as relevant comments and correspondences on all neurosurgical and related interdisciplinary topics. The envisaged publication dynamics is two issues per year, plus two supplements per year, with free access to scientific articles for individuals and maximally efficient time-to-publication process.

All papers submitted for publication are subject to rigorous and independent double-blind peer-review, in order to ensure the quality of the Journal, comprehensive citation in the major abstracting and indexing databases, and the resulting impact factor.

The inaugural issue comprises six articles (four by Serbian authors and two by international authors), covering several important fields of neurosurgery, including trauma, vascular, and tumors neurosurgery.

Group of Siberian neurosurgeons presented their amazing experience in the surgical treatment of complex middle cerebral artery aneurysms, while the Turkish group from Koc University reported a case of patient with an unusual bilateral germinoma.

Associate Editor, Prof. Pavlićević contributed to the issue with an original research paper on the risk-factors for infection in patients with war traumatic brain injuries in a series of more than 200 survived patients.

To complement the Inaugural issue, Prof. Samardžić wrote an excellent review of nerve transfers used for functional priorities restoration in patients with brachial plexus injury, while colleagues neuroradiologists from Belgrade described the endovascular treatment of traffic accidents associated traumatic intracranial aneurysms, as an interdisciplinary topic, proving our will to accommodate such contributions in our journal in the future as well.

Last but not least, the Inaugural Issue also introduces a Special Topic on the use of ultrasound in neurosurgery tentatively titled "NEUROSONOLOGY X NEUROSURGERY" with the first paper on the basics of intraoperative ultrasound use in cranial neurosurgery, completing the lucky 7 with this Editorial.

I am sincerely grateful to all the colleagues who contributed to the first issue of The Serbian Journal of Neurosurgery: the authors, the reviewers, the editorial team, and the members of the International Editorial and Advisory Board, who generously shared their outstanding reputation and contribution in the field providing continuous support to the activities of the Serbian Neurosurgical Society.

With a view to the reputable international and interdisciplinary editorial structure, it is with firm belief and commitment that I express the hope that Neurohirurgija – The Serbian Journal of Neurosurgery will grow into a significant, recognizable and long-lasting platform for promoting neurosurgery without borders.

Lukas Rasulić

Prof. Dr. Lukas Rasulić, Editor-in-chief

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WITH INTERNATIONAL PARTICIPATION

CURRENT CONCEPT IN MILITARY NEUROSURGERY
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ORIGINAL RESEARCH

Risk factors for postoperative infection and its impact on overall outcome after combat related head injuries

Goran Pavlićević, MD, PhD[1]

1. Clinic for Neurosurgery, Military Medical Academy, Belgrade, Serbia

Abstract

Introduction: The prevalence of penetrating head injuries (PBI) has increased during the latest wars, comprising up to 37,4% of all injuries. The microbiology of modern war wounds depends on the climatic and geographical features of the theater of combat.

Material and methods: A total of 286 patients were operated on after penetrating cranial combat injury in our institution between 1991-1999, of which 202 were included in this study based on inclusion criteria of combat-related cranial injury, absence of severe abdominal or chest combat injuries, and ability to report for a follow-up exam. Initial surgical treatment included removal of devitalized soft tissue and bone fragments with craniectomy and removal of devitalized brain tissue, easily accessible intracerebral bone and metal fragments, and intracranial hematoma. All patients received standardized postoperative care with triple antibiotics.

Results: Infection occurred in 36 patients (17,82%), most commonly in the form of brain abscess (31, 86.11%), in addition to meningitis (4, 11.1%) and osteomyelitis and epidural infection (1, 2.78%). Retained metal and bone fragments and postoperative CSF leak had significant influences on the occurrence of postoperative infection.

Conclusion: Postoperative infection considerably worsens long-term functional outcome, and it was favored in patients with retained metal and bone fragments and postoperative CSF leak. Autograft appears as preferable option for dural reconstruction in penetrating combat-related cranial injuries, although our study failed to find statistically significant correlation between the postoperative infection and the material used for the reconstruction.

Keywords: combat injury; head; brain; traumatic brain injury; infection; outcome

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Introduction

The prevalence of penetrating head injuries (PBI) has increased in the latest wars in south-east of Ukraine, Iraq, Afghanistan, and Syrian Arab Republic, comprising up to 37,4% of all injuries [1,2].

The microbiology of modern war wounds is unique to each military conflict depending on the climatic and geographical features of the theater of combat [3,4]. The mechanism of high velocity weapons injury predisposes to development of intracranial infection, mostly due to the cavitation effect, causing initial expansion in brain tissue (often 10 to 20 times the size of the projectile), which collapses under negative pressure that may draw in external debris [27]. Patients with severe head injuries are also prone to infection as they have prolonged intubation, decreased respiratory function, prolonged immobilization, and posttraumatic immunosuppression.

On the other hand, different types of invasive monitoring, including intracranial pressure monitoring, increase the risk for wound infection.Cranial infection after war injury can develop in the form of epicranial infection, osteomyelitis, epidural abscess, subdural empyema, meningitis, brain abscess, or ventriculitis. All forms of posttraumatic infection considerably increase mortality and morbidity.

The current concept of surgical treatment is controversial given uncertainty regarding the infective potential of retained intracranial foreign object and the different surgical strategies are used [5,6,7,8,10,12,13,14,15,19,20,21,25,26]. We present our experience of postoperative infection in patients with combat-related penetrating cranial injuries and the long-term functional outcome of these events.

Materials and methods

Patient selection

A total of 286 patients were operatively treated after penetrating cranial combat injury in our institution between 1991-1999. For this study, the data of 202 patients were retrospectively reviewed, and Glasgow outcome score (GOS) was determined on examination. The inclusion criteria were as follows: combat-related cranial injury, absence of severe abdominal or chest combat injuries, and ability to report follow-up examination. Forty-one patients died during initial treatment because of the severity of injury (92% of them had GCS≤8), and they were excluded from the study. Forty-three patients were also excluded from the study as they were lost to follow-up (due to the address change, death etc.).

Initial surgical treatment

Initial surgical treatment after craniocerebral injury included removal of devitalized soft tissue and bone fragments with craniectomy and removal of devitalized brain tissue, easily accessible intracerebral bone and metal fragments, and intracranial hematoma. The dura was closed and rendered watertight, which in almost all cases required a dural autograft (periosteum, temporalis fascia, fascia lata) or allograft. In cases with opened air cavities, obliteration of these cavities was performed with fat graft followed by suturing of the graft (periosteum, fascia, muscle) to dura and the epicranial aponeurosis (***Figure 1***). Soft tissues were closed without suture tension.

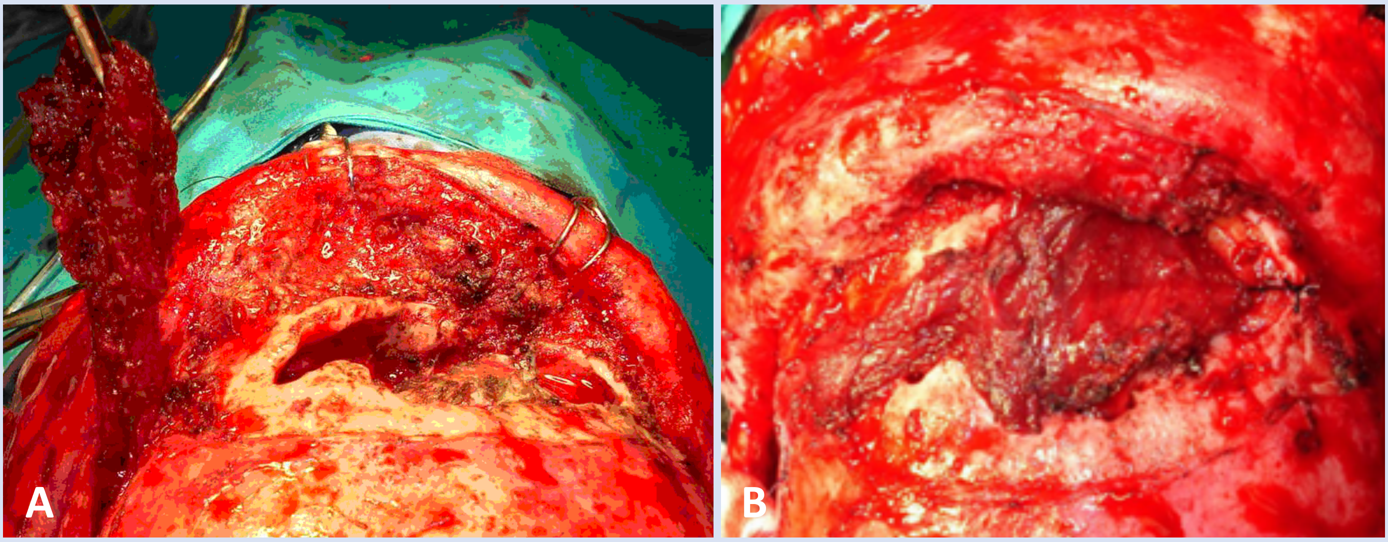

Figure 1. Surgical air cavities obliteration. A. Preparation of the graft. B. Graft in place secured with sutures.

Postoperative care

Drains were removed when the daily drainage volume was less then 50 ml, at least 24-48 hours after the operation. Subsequent epicranial collections were removed by puncture under sterile conditions and treated with compressive dressings until coalescence between the skin flap and the graft occurred. Third generation cephalosporine, aminoglycoside and metronidazole were used for prophylaxis over a ten-day period. Postoperative cerebrospinal fluid (CSF) leak was treated with lumbar drainage for 7 days. In the cases with persistent CSF leak, wound revision was performed.

Assessment of outcome

The mean postoperative follow-up period was 12.3 years (10-15 years). A follow-up CT was done to locate any retained metal or bone fragments and to assess the dominant localization of brain damage before control examination. GOS was determined on control examination.

Statistical analysis and Factors Influencing the Outcome

We evaluated the influence of the following 7 factors: age, mechanism of injury (bullet or explosive injury), localization of injury, dura (autograft or allograft), communication with paranasal cavities, retained metal or bone fragments (larger than 10mm) and postoperative CSF leak, on the development of postoperative intracranial infection. We have also analyzed the influence of postoperative infection on the Glasgow outcome score.

Data processing was performed using SPSS 11.5 (SPSS Inc., Chicago, Illinois, United States of America) for Windows. Average values were presented as mean ± standard deviation. P values less than 0.05 (two-tailed) were considered to be statistically significant. Groups were compared using an unpaired Student t test for parametric data and the Mann-Whitney U test for nonparametric data. Data for 3 or more groups were compared using 1-way analysis of variance, the Kruskal-Wallis H test.

Results

Characteristics of the series

All patients were males, aged from 18 to 61 years of age (average of 30,61±9,5years). Only five patients were older than 50 years.

Considering the mechanism of injury, 136 (67.4%) patients had explosive injuries, and 66 (32.6%) had injuries caused by bullets. The most severe brain damage was localized most often in frontal region 89 (44,1%), then parietal (84, 41,1%), occipital (16, 7,9%) and the temporal 13 (13, 6,4%) regions. Opened air cavities were noted during operation in 11 patients (5,4%), and 17 (8,4%) patients had retained bone or metal fragments larger then 10mm in brain tissue. For dural repair, autograft (fascia lata or periosteum) was used in 47 (23,3%), and allograft in 155 patients (76,7%).

CSF leak was noted in 10 patients (4,9%). According to the Glasgow Outcome Score, 116 patients (57.4%) had a good recovery, 55 (27.2%) were left with moderate disability, and 31 (15.3%) of the patients were severely disabled.

Risk factors for infection and influence on functional outcome

Infection occurred in 36 patients (17,82%), most commonly in the form of brain abscess (31, 86.11%), in addition to meningitis (4, 11.1%) and osteomyelitis and epidural infection (1, 2.78%). Infection developed from 3 to 18 days after debridement and was caused by gram positive bacteria in 60% of the cases.

Postoperative infection occurred almost equally among the patients of different age (29,2 vs 31,1 years) and among patients with different mechanisms of injury (17,65% after explosive and 18,18% after bullet injury).

Infection most commonly occurred in in the dominant occipital region of brain injury (37,5%), then in parietal region (19,04%), temporal region (15,38%) and most rarely frontal localization (10,5%) The distribution of infection was the same across different localizations (Kruskal Wallis test, $p>0,05$).

Infection occurred in 1/11 (9.1%) patients with open cavities and in 35/191 (18.3%) without open paranasal cavities (Mann-Whitney U test $p>0,05$).

Type of the dural graft was not associated with developing an infection (10,6% in autograft group, 20% in allograft group, Mann Whitney U test $p>0,05$).

Postoperative infection was twice as frequent in patients with retained fragments in brain tissue (6/17, 35.3%) as it was in those without retained fragments (30/185, 16.2%), (Mann Whitney U test $p<0,05$).

Postoperative infection occurred in 40% of patients with CSF leak and in 16,7% without CSF leak (Mann Whitney U test, $p<0,05$. There were a small number of patients (10) with CSF leak in study.

According to GOS, good recovery was noted in only 16.7% of patients with infection and in 66,27% of the patients without infection. Moderate disability occurred 50% of cases with infection and 22,29% without infection, and severe disability occurred in 33,4 % of patients with infection and 11,4% without infection (Kruskal Wallis Test $p<0,001$).

Discussion

In patients with combat-related penetrating brain injury, the incidence of wound contamination ranges from 39-80% [3,4,26]. The high incidence of wound contamination results from contaminated foreign objects, skin, hair, and bone fragments driven into the brain tissue along the projectile tract [12]. High velocity projectiles, dominantly used in wars, create temporary cavitation during brain penetration as a result of the transmission of the kinetic energy of the projectile into surrounding tissue. Formation of a temporary cavitation produces an enormous increase in intracranial pressure. The temporary cavitation then collapses, resulting in negative intracranial pressure. Due to brain elasticity, the cavitation forms and then collapses several times. When negative intracranial pressure occurs during the temporary cavitation collapse, aspiration of the foreign contents into the wound occurs, causing additional contamination of the intracranial space [11]. Bone fragments have higher potential for infection than metal fragments as high kinetic energy and temperature from metal fragments during brain penetration sterilizes surrounding brain tissue. Necrotic and devitalized brain tissue around the projectile trajectory also increases risk for the development of infection.

The main goals of surgical treatment of casualties with penetrating brain injuries are to normalize intracranial pressure and to prevent infection. Operative techniques have been changed to reduce risk factors for postoperative infection over time.

The principles of penetrating head trauma management, radical debridement of the scalp and skull and aggressive irrigation of the projectile trajectory to remove foreign bodies with water-tight closure. were established by Harvey Cushing during the World War One. T Using this approach Cushing significantly decreased infection rates, which reportedly mitigated the major cause of mortality due to penetrating head injuries [7].

Experiences gained during the Korean War and Vietnam War have changed surgical approaches such that that only easily accessible fragments should be removed, as evacuating the foreign bodies that are distant from the projectile trajectory may result in additional neurologic deficit or a lesser degree of recovery of functions due to brain damage [7,15]. Fragments distant from the projectile trajectory are left in the brain tissue [7,15]. This strategy was used in the majority of operative treatments during recent wars, including wars in the former Yugoslavia in the 1990s [21].

Many studies conducted in last decades of the 20th century suggested that retained metal and bone fragments in the brain did not increase the incidence of immediate or late complications such as infection or epilepsy [20,21,19]. As a result, conservative management of retained shrapnel is recommended in view of low long-term infection rates and worsened neurological outcome with shrapnel retrieval [12,13,14,15,5].

Surgical strategy has shifted further toward the conservative approach based on studies in which minimal debridement or even simple wound closure was successfully used as the only surgical treatment in war victims [8,20]. Some authors have even found out that conservative approach promoted superior outcomes to standard surgery, as no mortality in was noted in conservatively treated patients in comparison to 48,5% of mortality rate in surgically treated cases [10].

With the adoption of a less aggressive approach of treatment, it is likely that large percent of the patients will have retained intracranial fragments.

in contrast, other studies have suggested that retained bone and metal fragments are the risk factor for development of postoperative infection [22,24] and that the presence of intracranial retained foreign bodies promotes worse outcome in comparison with their absence [25]. Some studies found out that foreign bodies have the potential to initiate infection decades after the injury: brain abscess has been noted in patients 30 and 52 years after the injury around the retained shrapnel [6,23]. Long-term follow-up also revealed potential complications such as migration of the foreign bodies or development of the hydrocephalus [23]. Foreign bodies in the eloquent cortex may also increase the risk of posttraumatic epilepsy [16,24]. Those findings rendered it acceptable to remove all bony and metallic fragments that are accessible without additional trauma to non-damaged brain regions [24].

Careful preoperative planning for secondary removal of retained missile fragments, the use of neuronavigation system, and choosing a less invasive approach for the exact intraoperative localization of the fragment can result in extraction without additional neurologic deficit, infections, or seizures [24].

In our series, bone and metal fragments that were distant from the projectile trajectory were left intact. Postoperative infection was twice as frequent in patients with retained fragments in brain tissue than those without retained fragments. These finding support the view that additional effort should be used to remove retained brain fragments using contemporary devices such as neuronavigation, open multi-slice computed tomography, and minimal invasive surgical approaches.

CSF leaks after penetrating brain injury are highly predictive of infectious complications [17]. Infection rates in patients with CSF leak are 49,5-68% compared to 1,5-4,6% in those without leak (17,18,19,). In our study, the infection rate was 40% in patients with leak relative to 16,7% in without leak. Our results suggest that early revision surgery is better option than lumbar drainage as CSF leak carries a high risk for postoperative infection.

Anterior cranial fossa injury is an important subgroup of craniocerebral missile injuries, as the projectile trajectory traverses the facio-orbital plane before penetrating the cranium. CSF spaces communicate with air-filled mucosa-lined spaces, and patients may later develop CSF rhinorrhea or orbitorrhea [9]. Such patients are prone to infection. The infection rate in some studies is higher in patients with anterior cranial fossa injury [11].

In our study, the presence of open air cavities was not a risk factor for postoperative infection, as the incidence of CSF leak in this location was similar to other locations. We can conclude that appropriate surgical technique, including using fat graft for obliterating paranasal cavities and pericrania-fascia lata flap for covering anterior base, can prevent CSF leak and diminish the risk for infection in this location.

In combat penetrating craniocerebral injury, dura is usually lost, necessitating the use of dural substitutes. Some authors suggest that autologous tissues are preferred because a synthetic dural substitute, as a foreign body, may become a potential source of infection, particularly in grossly contaminated wounds (9,11). Using of auto or allograft in our study was not a statistical risk factor for postoperative infection, but patients receiving allograft had postoperative infection twice as frequently as patients with autograft.

Increasing age is correlated with a worse prognosis in penetrating brain injury, especially in patients older than 50 years (11,12). In our study, infection was almost equal in different age groups, but we have only five patients older than 50 years, and the soldiers were in good physical condition and without comorbidities.

Comparing groups with different GOS in our study revealed that postoperative intracranial infection had strong influence on functional recovery, as the chance for good recovery based on GOS was four times higher in patients without infection.

Conclusion

Postoperative infection considerably worsens long-term functional outcome. Retained metal and bone fragments and postoperative CSF leak have significant influences on occurrence of postoperative infection. Although our study failed to find statistically significant correlation between the postoperative infection and the material used for dural reconstruction, autograft appears as preferable option in penetrating combat-related cranial injuries

Disclosures

Conflict of Interest: The author certify that he have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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Informed consent: Informed consent was obtained from the reported individual.

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LITERATURE REVIEW

Motor nerve transfers for restoration of upper arm function in adult brachial plexus injuries- basics, advantages, problems and strategies

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Abstract

Introduction: Nerve transfers are the only surgical option for reconstruction of directly irreparable injuries of the brachial plexus. In the recent years, there has been a trend toward the increased use of nerve transfers, with the introduction of new methods and novel indications. Patients with total brachial plexus palsy generally have poor outcomes due to the limited number of donor nerves. On the contrary, patients with partial injuries involving the C5, C6, and sometimes C7 spinal nerves have favorable outcomes in a large majority of cases. In both situations, restoration of elbow flexion and shoulder functions are the main priorities. The purpose of this review article to characterize the advantages, problems and controversies of nerve transfers.

Methods: PubMed/Medline database was searched for English-language original research and series of adult patients who received nerve transfers for functional restoration of the upper arm, performed within one year after injury and with minimum follow-up of one year. Literature search for outcome analysis was limited to articles published after 1990, amounting to 45 systematic reviews / meta-analyses of the most common nerve transfers (intercostal, spinal accessory, fascicular, and collateral branches of the brachial plexus). Analysis of clinical outcomes was based on Medical Research Council (MRC) grading system for muscle strength, and grades M3 or more were considered as useful functional recovery.

Results: A total of 70 articles were included. Generally, intraplexal nerve transfers resulted in a higher rate and better quality of recovery compared to extraspinal transfers. Grades M3 or higher were obtained in 72% of the intercostal and 73% of the spinal accessory nerve transfers for restoration of elbow flexion, and in 56% vs. 98% of transfers for restoration of shoulder function. Among intraplexal nerve transfers, elbow flexion was restored in 84% to 91% of the medial pectoral, 100% of the thoracodorsal, and 94% to 100% of the single or double fascicular nerve transfers. Shoulder function was restored in 81,8% of the medial pectoral, 86% to 93% of the thoracodorsal, and 100% of the triceps branch nerve transfers. Dual nerve transfer (simultaneous reinnervation of the suprascapular and axillary nerves), resulted in 100% rate of recovery.

Conclusion: Double fascicular transfer for restoration of elbow flexion and dual nerve transfer for restoration of shoulder function resulted in the most favorable results relative to other transfers, especially regarding quality of recovery. Medial pectoral and thoracodorsal nerve transfers were reasonable alternatives for restoration of both functions.

Keywords: brachial plexus; closed injury; donor nerve; functional priority; nerve transfer; recipient nerve.

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Introduction

Nerve transfer or neurotization involve reinnervation of the distal denervated, functionally important arm nerves using intact expendable nerves as donors. A variety of donor nerves, extraplexal or intraplexal, have been used with varying efficacy.

The history of nerve transfers dates back over 100 years. The first report, published by Tuttle in 1913, involved use of the spinal accessory nerve and elements of the cervical plexus as donors. Thereafter, there were only few reports concerning mainly intraplexal procedures in neurotization of the axillary and/or musculocutaneous nerve. In 1920, Vulpius and Stoffel published on the use of the brachial plexus branches to the pectoral muscles as donors. In 1929, Foerster reported nerve transfer using the branches to the latissimus dorsi and subscapular muscles. Finally, in 1948, Lurja reported the use of the pectoral and thoracodorsal nerves in repair of the upper trunk injuries[1,2]. Seddon, in 1963, reanimated nerve transfer procedures, publishing the use of the third and fourth intercostal nerves in reinnervation of the musculocutaneous nerve[3]. Pioneers in modern reconstructive surgery of the brachial plexus injuries – Aligmantas Narakas, Hanno Millesi and Yves Alnot – generated significant enthusiasm in 1970s and 1980s. They introduced, along with several other authors, numerous innovative techniques. The main goal was reinnervation of the upper arm nerves and restoration of their functions, including elbow flexion, shoulder abduction and external rotation.

Extraplexal transfers included the spinal accessory nerve[4,5,6,7], anterior branches of the cervical plexus[8], phrenic nerve[9], contralateral C7 spinal nerve[10] and upper intercostal nerves[11,12,13] as donors. These transfers were predominantly performed in patients with total brachial plexus palsy. Most intraplexal transfers was introduced during the last two decades of the 20th century. The advent of this modern era of nerve transfers occurred as series of studies explored new possibilities in this field. These nerve transfers included the use of the medial pectoral[15,16,17,18,19], thoracodorsal[15,17,19,20,21], fascicles of the ulnar and median nerves[22,23,24,25,26] and triceps branches of the radial nerve[17,28] as donors. These nerves are available for transfer in cases with upper brachial plexus palsy involving the C5 and C6 spinal nerves, with or without involvement of the C7. A complete or near complete recovery is expected.

Indications for motor nerve transfers and the patient population who may benefit from such operations continue to expand. The first indications were directly irreparable traction injuries of the brachial plexus with cervical spinal root avulsion or high intraforaminal spinal nerve injuries[29]. Thereafter, indications were significantly extended including[30,31,32]:

1 Extensive longitudinal nerve defects
2 Extensive neuroma in continuity
3 Injury to several nerve elements at different levels
4 Partial nerve injuries with clearly defined neurological deficit in one part of the plexus
5 Injuries to one nerve element at several levels
6 Associated vascular and significant bone injuries
7 Significant scarring at the site of injury
8 Surgery delayed for more than 12 months

In elderly patients and those with unsuccessful previous direct nerve repair, nerve transfers may be used as well.

Novel indications for nerve transfers with initial success and expected validation in the future:

1 Spinal cord injuries since these patients have intact lower motor neurons below the level of injury with preserved connection to the target muscles[33,34,35]
2 Radiation-induced brachial plexopathy[36]
3 Parsonage-Turner syndrome[37,38]
4 Contralateral C7 spinal nerve transfer in patients with chronic stroke for motor improvement and reduction of spasticity[39]

An ideal timing for nerve transfer has not been yet established. However, it is widely accepted that surgery should be done in a period between 3 and 5 months after injury if there are neither clinical nor electromyographic signs of recovery[29,30,31]. Target muscle should be reinnervated between 12 and 18 months in order to prevent muscle atrophy and loss of the motor end plates. The presence of fibrillation potentials after this period is an indication that denervated muscle is still viable. Regardless, some authors do not recommend surgery after postinjury period of 9 months. The recommended timing is different for special cases. The proposed timing of surgery for radiation-induced brachial plexitis and Parsonage-Turner syndrome is between 6 and 9 months, if there is no signs of recovery[37]. In patients with spinal cord injury or chronic stroke there is no time limit because of preserved lower motor neurons[34]. Contraindications for nerve transfer are rare and include presence of a superior reconstructive option, excessive surgical delay (>18 months), and muscle strength in the donor innervation zone of less than Medical Research Council (MRC) grade 4.

The purpose of this review article is to characterize the advantages, problems and controversies of nerve transfers and derive some guiding recommendations on their use in brachial plexus reconstructive surgery, for restoration of upper arm motor functions.

Methods

This is a literature review with comparative analysis of the upper arm functions recovery following the most common extraplexal (spinal accessory and intercostal nerves) and intraplexal (single or double fascicular, thoracodorsal, medial pectoral and triceps branches of the radial nerve) nerve transfers.

The PubMed/Medline database was searched for English-language articles containing the MeSH terms "brachial plexus" in conjuction with words "injury" or "trauma” and "nerve transfer" in the title.

Inclusion criteria

1 closed brachial plexus injury
2 upper, extended upper or total brachial plexus palsy
3 timing of surgery less than 12 months after injury
4 follow-up period at least 12 months
5 ≥ 6 cases

Exclusion criteria

1 obstetric brachial plexus palsy

2 peripheral nerve injuries to the axillary and/or musculocutaneous nerve

3 patients older than 65 years

4 combined nerve transfer with nerve grafting

5 combined nerve and tendon transfers

The query returned 680 articles, 70 of which fulfilled the inclusion and exclusion criteria, and were included in this review. In addition to the original research papers, 45 systematic reviews / meta-analyses published after 1990 were selected for statistical analysis. *p* value of 0.05 or less with the use of Pearson's Chi square, Fisher, ANOVA and Mann-Whitney test was considered as significant.

Analyses used recipient nerves (musculocutaneous, axillary and suprascapular) as dependent variables and donor nerves as independent variables. The significance of the other independent variables such as patient's age and timing of surgery was not extracted.

Grades of M3 or higher on the MRC Manual Muscle Testing Scale were considered useful functional recovery and grades M4 or M5 as a higher quality of recovery for elbow flexion and shoulder abduction.

Review

Advantages of nerve transfers

Motor nerve transfers have several advantages over nerve repair[29,30,31]:

1 Possibility for direct nerve anastomosis in the majority of intraplexal nerve transfers, avoiding interposition of nonvascularized nerve graft with an average of 30% of additional axonal loss across the second suture line.

2 Anastomosis closer to the target muscle where the number of nerve fibers in a recipient

3 nerve is lower and a distal dissection enables separation of the sensory nerve fibers.

4 Shorter distance and time span for regeneration, with an earlier reinnervation

5 Surgery outside the zone of injury and scarred bed

6 Faster recovery with its higher quality

7 Surgical procedure is more technically straightforward and can be performed with significant gain in operative time.

Compared to the musculo-tendinous transfer, there are also several advantages[16,39]:

1 Preservation of the original tendinous attachment

2 Preservation of the tension and orientation of the original muscle fiber

3 Minimal dissection of the target muscle and formation of adhesions

4 Possible reinnervation of several muscles

5 Possible simultaneous motor and sensory reinnervation

6 Simpler procedure with significant gain in operative time

7 Shorter time needed for immobilization

8 Obtained results rarely exceed grade M3, but the outcome is more predictable.

Factors favoring musculo-tendinous transfers are longer delays of surgery and absence of an active target muscle.

Functional priorities

The functional priorities for motor nerve transfers in patients with upper or total brachial plexus palsy are (1) strong and full range elbow flexion, (2) shoulder stabilization, (3) shoulder abduction and (4) shoulder external rotation. Lower priorities are elbow extension and preservation of brachio-thoracic pinch[28,31,41].

The recovery of all functions is equally important since this enables the movements, especially elbow flexion, to translate to functionality[41]. Elbow flexion could be restored by nerve transfers to the musculocutaneous nerve or its fascicles to the biceps and brachialis muscles. The musculocutaneous nerve contains from 3.069 to 7.911 myelinated fibers[42,43]. The average numbers in motor branches is 1.840 for the biceps and 1.826 for the brachialis muscles[44]. These muscles are responsible for elbow flexion and forearm supination.

Shoulder functions could be restored by nerve transfers to the axillary and/or suprascapular nerve, and the preferred option is a nerve transfer to both nerves. The axillary nerve contains between 4.967 and 8.437 myelinated fibers[42,43], with an average of 7.877, and 80% are motor fibers[45]. The number of motor fibers in the anterior branch of the axillary nerve ranges from 2.700 to 4.052[27,45]. The axillary nerve innervates the deltoid muscle, which acts as arm abductor. Its posterior part acts as an external arm rotator together with the teres minor muscle[19]. Finally, the suprascapular nerve contains approximately 3.500 myelinated fibers[42,43]. This nerve innervates the supraspinatus muscle that is responsible for initiation of arm abduction and the infraspinatus muscle responsible for arm external rotation.

Restoration of elbow extension is especially important in spinal cord injuries given the arm is especially important for support[33,34,35]. Nerve transfer could be performed using different donors to the long or medial branch of the radial nerve.

Donor nerves

Generally, there is no ideal motor donor nerve. Regardless, there are several important criteria for the choice of donor nerve[30,31,32]:

1 Expendable nerve or nerve with duplicated function

2 Close proximity to the recipient nerve, facilitating a direct anastomosis. This is the case in a large majority of infraclavicular intraplexal nerve transfers. On the contrary, nerve grafts are necessary in nerve transfers of the ipsilateral or contralateral C7 spinal nerve and in all extraplexal nerve transfers, except in spinal accessory to suprascapular nerve transfer.

3 Close proximity to the target muscle and its endplates to decrease the regeneration distance.

4 Pure motor fiber composition, possibly with a few sensory fibers

5 Large number of motor nerve fibers

6 Donor-recipient motor nerve fibers ratio 0,7 or greater promotes improved outcomes[44]. However, mismatch in the number of the motor nerve fibers should not always be a problem because only 20% to 30% of motor fibers are sufficient for reinnervation of muscles with a simple function, such as the biceps muscle. Moreover, collateral axonal sprouting may produce an excess of approximately 30% of axons.

7 Maximal nerve diameter matching enables more precise coaptation. The existing problem could be solved using several techniques such as epi-perineural anastomosis, fishmounting of the donor nerve epineurium, bundling of several donor nerve branches, and combined use of the donor nerves.

8 MRC grade at least M4 in donor innervation zone

9 Synergistic function with the recipient nerve offers more effective and faster cortical reintegration owing to efficient cerebral plasticity based on pre-existing cerebral and medullary interconnections[17,29,41].

The number of the myelinated nerve fibers in individual donor nerves vary widely:

1 Number of myelinated nerve fibers with mixed fiber composition averages 16.472 in C5, 27.421 in C6, and 23.781 in the C7 spinal nerve[43].

2 Anterior branches of the cervical plexus contains an average of 4.090 motor fibers.

3 The spinal accessory nerve contains an average of 1.700 motor fibers at its distal end.

4 3rd through 6th upper intercostal nerves contain between 1.200 and 1.700 myelinated fibers, with an average of 500 to 700 motor fibers at the midaxillary line. In the succeeding upper intercostal nerves, the number of fibers gradually diminshes for 10% at every 10 cm[46].

5 Thoracodorsal nerve contains 1.530 to 2.480 or up to 3.496 motor fibers, as well as approximately 1.453 in its lateral branch[46,47].

6 The medial pectoral nerve contains between 1.170 and 2.140 motor fibers, with an additional 400 to 600 in its branches[46].

7 The branch of the radial nerve to the long triceps head contains an average of 2.303 motor fibers, while the branch to the medial head includes 2.198 motor fibers[45].

8 The ulnar nerve branch to the flexor carpi ulnaris muscle contains an average of 1.318 motor fibers, while the median nerve branch to the flexor digitorum sperficialis muscle has 1.860[44].

Problems in the upper arm motor nerve transfers

There are several potential problems in nerve transfers for restoration of the upper arm motor functions, including (a) donor nerve morbidity, (b) possible co-contractions, (c) need for cortical re-education, (d) muscle loss for musculo-tendinous transfer, and (e) pre-existing donor nerve injury that may be a contraindication for nerve transfer.

Donor nerve morbidity is an important drawback, especially in cases with suboptimal grade M3 or M4 function of the synergistic muscles.

Potential functional loss after donor nerve section could be diminished in several ways depending on the type of nerve transfer:

1 In transfers of the ipsilateral or contralateral C7 spinal nerve, potential motor weakness and sensory loss recover spontaneously due to functional overlapping with neighboring spinal nerves[10, 39].

2 In spinal accessory nerve transfer, functional loss of the trapezius muscle could be diminshed using a distal section of the donor nerve with preservation of the upper and middle muscle parts, especially in cases with independent innervation from the C3 and C4 spinal nerves[5,6]. Paralysis of the serratus muscle and regained powerful external arm rotation may contribute to scapular winging[40].

3 In medial pectoral nerve transfer, important factors for diminishing functional loss of arm adduction are multiple innervation patterns of the nerve and preservation of some branches to the pectoral major muscle[18].

4 In thoracodorsal nerve transfer, some function could be retained using one of two branches to the latissimus dorsi muscle owing to a large number of motor fibers. Additiona; ly, partially preserved function of the synergistic teres major muscle in cases of predominant innervation from the C7 spinal nerve may be a contributig factor to arm adduction[21,47].

5 Preservation of one triceps branch (medial or lateral) of the radial nerve is sufficient for elbow extension[27,28].

6 In fascicular nerve transfers, significant motor deficit is exceptional[25,26].

Possible co-contractions could be useful in cases with synergistic function of the donor and recipient nerves, such as in spinal accessory nerve to the suprascapular nerve transfer. This also occurs in fascicular transfers with finger flexion when attempting elbow flexion or in medial pectoral nerve to musculocutaneous nerve transfer with arm adduction in the same situation[22,40]. Some authors favor this transfer in relation to the single or double fascicular transfers[40]. On the contrary, in spinal nerve transfers, there is a massive cross-innervation of the synergistic and antagonistic muscles with disabling co-contractions[14,29].

Function after nerve transfer is dependent on the donor nerve to some extent, and there is a need for cortical re-education. Some antagonistic functions, such as that of the deltoid muscle following the thoracodorsal or medial pectoral nerve transfer, could be successfully retrained in a relatively short period due to a closer functional relationship and cerebral cortical representation.

Muscle from the donor innervation zone is lost in musculo-tendinous transfer. Therefore, a balance of potential risks and benefits should be carefully estimated in individual cases.

A potential problem in nerve transfers is the degree of pre-existing donor nerve injury, which may result in variations in obtained results. There is always some damage to the nerves that are functional but located on the "edge" of lesion. Notably, muscle weakness becomes apparent when 50% of the motor fibers are lost. Fibrillation potentials detected on electromyography indicate potential injury to the donor nerve and may guide the selection of the type of nerve transfer[40].

Outcomes in the literature

Results of the most common nerve transfers in restoration of upper arm function were obtained from published systematic reviews / meta-analyses, demonstrating variable outcomes depending on the donor nerve choice for upper and total brachial plexus palsies. The comparisons below are nerve transfers versus nerve grafts.

Extraplexal nerve transfers included the spinal accessory and intercostal nerve transfers to the musculocutaneous and axillary or suprascapular nerves.

Generally, in transfers to the musculocutaneous nerve, grades M3 or more were obtained in an average 71% of cases (range: 64% to 88%) and grades M4 or M5 in an average 37% of cases[31,48]. Intercostal to musculocutaneous nerve transfer without nerve grafts resulted in grades M3 or greater in 72% of cases and in grades M4 or M5 in 41% of cases. In transfer with the use of nerve grafts, corresponding rates of recovery were 47% and 32%, respectively[48]. Spinal accessory nerve transfer to the musculocutaneous nerve resulted in grades M3 or more in an average 77% of cases[31,48,49]. Grades M4 or M5 were obtained in 29% of cases[48].

For nerve transfers in restoration of shoulder abduction, grades M3 or more were obtained in an average 73% of cases and grades M4 or M5 in an average 27%[48]. Spinal accessory to the suprascapular nerve transfer resulted in grades M3 or more in 79% to 95% of cases[49,50,51,52,53], with an average range for shoulder abduction of 50 degrees and for shoulder external rotation of 45 degrees[54]. Spinal accessory to the axillary nerve transfer yielded grade M3 or greater in 60% to 75% of cases[17,55]. Intercostal nerve transfer to this nerve resulted with grades M3 or higher in 33% to 67% of cases[17,48,55]. Available data for grades M4 or M5 in this transfer were limited.

Intraplexal nerve transfers included the medial pectoral nerve, thoracodorsal nerve, fascicles of the ulnar and median nerves, and triceps branches of the radial nerve, and demonstrated results superior to the extraplexal[51,54,56].

In restoration of elbow flexion, total rate of recovery, grades M3 or higher ranged between 96% and 98% of cases and grades M4 or M5 between 83% and 88% of cases[54]. Grades M3 or higher, and M4/ M5 for individual types of nerve transfer occurred in 100% and 91,6% of cases for the thoracodorsal nerve[19,21], 84% to 91% of cases and 64% for the medial pectoral nerve[18,19], 94% to 100% of cases and 70% to 100% of cases for Oberlin's single ulnar nerve fascicle[57,58,59,60], and 95% to 100% of cases and 80% to 95% of cases for single median nerve fascicle transfers, respectively[24,61].

In restoration of shoulder abduction, grades M3 or higher occurred in 86% to 93% of cases for thoracodorsal nerve[19,21,55], 81,8% of cases for the medial pectoral nerve[18,21], and 100% of cases for Somsak's triceps branch of the radial nerve transfers[27,62]. Grades M4 or M5 were present in 70,4%, 63,6% and 91,3% of cases, respectively. Average ranges of motion were 92 degrees (range: 65 to 120 degrees) for shoulder abduction and 93 degrees (range: 80 to 120 degrees) for shoulder external rotation[57].

Double fascicular transfer in restoration of elbow flexion yielded grades M3 or higher in 97% to 100% of cases and M4 or M5 in 85% to 100%[25,26,64]. However, some authors did not find any significant difference in outcomes for single fascicular transfers, except for the strength of elbow flexion[65,66]. Other studies have provided supportive evidence. Grades M3 or more were registered in 92,9% to 98,2% of cases for single and 95% to 100% of cases for double fascicular transfers. Corresponding rates of recovery grades M4 and M5 were 83% and 95% of cases with greater elbow flexion strength[60].

Dual nerve transfer for restoration of shoulder abduction and external rotation presents a simultaneous reinnervation of the suprascapular nerve using the spinal accessory nerve and the anterior division of the axillary nerve using one triceps branch of the radial nerve or intercostal nerves as donors[50]. M3 or greater grades of recovery for shoulder abduction were obtained in 100% of cases and grades M4 or M5 in 87% to 100% of cases with an average range of motion 122 degrees (range: 45 to 170 degrees). Corresponding rates of recovery for shoulder external rotation were 86% to 100% for grades M3 or higher and 87% for grades M4 and M5with an average range of motion 108 degrees (range: 97 to 121 degrees), significantly higher than in single nerve transfers[58,60,63].

Comparative statistical analysis

Statististically significant differences in teh efficacy of nerve transfers for restoration of elbow flexion were documented between:

1. Double fascicular vs. single fascicular, thoracodorsal or medial pectoral nerve transfer in achieving M4 or M5[54,67]
2. Single fascicular, thoracodorsal or medial pectoral vs. spinal accessory or intercostal nerve transfer[17,68]
3. Intercostal nerve transfer without and with an interpositional nerve graft[48]
4. Intercostal nerve transfer without an interpositional graft vs. spinal accessory nerve transfer[48]

Statistically significant difference in nerve transfers for shoulder function, predominantly shoulder abduction was documented between:

1. Dual nerve transfer vs. single transfer to the axillary or suprascapular nerve[58,60]
2. Thoracodorsal or medial pectoral nerve transfer to axillary nerve vs. spinal accessory to suprascapular nerve transfer[54]
3. Spinal accessory to suprascapular nerve transfer vs. Transfer to the axillary nerve[48]
4. Spinal accessory vs. intercostal nerve transfer to the axillary nerve[48]

In the other situations, on the basis of recovery percentages, there was a trend toward superior results between intraplexal and extraplexal nerve transfers[17,54].

Generally, the available data demonstrated strong evidence in favor of double fascicular transfer in restoration of elbow flexion and dual nerve transfer in restoration of shoulder function[54,58,60,67].

Surgical strategies

Restoration of upper arm function – elbow flexion, shoulder abduction, and shoulder external rotation – is the main priority in nerve transfers for brachial plexus injuries, independent of the extent of injury.

In upper brachial plexus palsy, the result of motor nerve transfers may be complete functional recovery. In these cases, the surgical strategy is determined by integrity of the C7 spinal nerve given is importance in innervation of the thoracodorsal nerve and the motor branch to the long head of the triceps muscle.

In cases with avulsion of the C5 and C6 spinal nerve roots and an intact C7 spinal nerve, intraplexal nerve graft repair may be considered[31]. In recent reports, a combination of nerve transfers has been recommended, including dual nerve transfer for restoration of shoulder function and fascicular nerve transfers for restoration of elbow flexion[31,58]. Transfer of the medial pectoral and thoracodorsal nerves could be a valuable option for both functions[17,19,40]. The strategy in cases of the injuries with involvement of the C7 spinal nerve is similar. However, Somsak's procedure cannot be used in majority of cases and could be subsituted with transfers of the medial pectoral or intercostal nerves to the axillary nerve[69].

On the basis of our results, we favor transfer of the thoracodorsal and medial pectoral nerves in restoration of both functions. In restoration of shoulder function, we reinnervate only the axillary nerve. There are two reasons for this strategy: (a) supraspinatus muscle has important role in initiation of arm abduction and attracts the majority of axonal sprout in relation to the infraspinatus muscle, and (b) some external rotation may be established by reinnervation of the theres minor muscle and posterior part of the deltoid muscle, with contribution of long head of the biceps muscle[17,19].

In cases with total brachial plexus palsy, extraplexal nerve transfers are the only possibility. Our proposed combination includes spinal accessory to the suprascapular and upper intercostals to the axillary and musculocutaneous nerves. Another possible option is the contralateral C7 spinal nerve transfer to the lateral and posterior cords[69].

Restoration of elbow extension in C5 to C7 or total brachial plexus palsy is less critical but should be considered whenever possible, as it provides better elbow control via antagonistic feedback to the elbow flexors[63]. Transfers to the radial nerve or its branches to the triceps muscle have been attempted using different donors depending on the extent of injury[70].

Conclusions

On the basis of this review and the results in the literature, we make several conclusions with practical implications.

1. Patient selection is crucial, especially in terms of age, time elapsed from injury, and readiness of the patient to wait 6 to 9 months for reinnervation in contrast to the 4 and 8 weeks needed for activation following musculo-tendinous transfer.
2. Primary exploration of the brachial plexus is still advisable in a large number of cases because evaluation of the extent of brachial plexus injury and identification of viable proximal nerve stumps can inform the operative approach. Exceptions are the presence of scarred bed or associated major vascular injury.
3. Nerve transfer should be performed preferably between 3 and 5 months.
4. Reinnervation of the recipient nerve should be done as close as possible to the target muscle in order to reduce reinnervation time.

   Therefore, neurotization of the recipient nerve at its periphery is more effective than in at its central part. Additionally, it is crucial to ensure an adequate length of nerve stumps for tensionless direct anastomosis.
5. Synergistic muscle function between the donor and recipient nerves requires less postoperative re-education based on pre-existing cerebral cortical and medullary interconnections.
6. Results of ipsilateral nerve transfers are superior to these of contralateral ones.
7. Results of intraplexal transfers are significantly better than extraplexal transfers.
8. Double fascicular transfer for recovery of elbow flexion offers better quality of recovery compared to single nerve transfers.
9. Dual nerve transfer for restoration of shoulder function is more effective method than single nerve transfers. Recovery rates for shoulder external rotation are lower than for shoulder abduction.
10. Nerve transfers using single spinal accessory nerve transfer have not proven to be superior because of importance of the scapular motion associated with this nerve. This nerve should not be considered as particularly expendable.
11. Intraplexal nerve transfers performed earlier than 6 months following injury in patients under 40 years of age offer excellent results.

Disclosures

Conflict of Interest: The author certify that he have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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LITERATURE REVIEW AND A SERIES OF CASES

Microsurgical management of complex middle cerebral artery aneurysms

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Abstract

Introduction: Management of complex aneurysms of the middle cerebral artery (MCA) is challenging and requires individualized treatment strategies. Our review aimed to analyze experience with the treatment of complex MCA aneurysms using revascularization and artery sacrifice techniques.

Methods: We have reviewed 9 original articles on patients' treatment with complex MCA aneurysms. Depending on the localization of the complex aneurysms of MCA, various methods of parent artery sacrifice, revascularization strategies, surgical results, outcomes, and complications were reviewed.

Results: We have analyzed the treatment of 244 patients with 246 complex MCA aneurysms in 9 different groups. From 67 to 100% of cases, the aneurysms were occluded successfully. Bypass patency resulting from the performed revascularization methods was from 83.3 to 100%. The main complications included ischemic disorders related to occlusion of the bypass graft or perforators injury. Morbidity in some reviews varied from 2.4 to 6.9%. The majority of patients in late follow-up showed good outcomes 0-2 on the modified Rankin scale and 4-5 on Glasgow Outcome Scale. Illustrative clinical cases of the patients with complex MCA aneurysms treated at the Federal Neurosurgical Center were presented.

Conclusion: Complex aneurysms of the MCA are very challenging lesions. The surgical strategy for treating complex MCA aneurysm should take into account vascular anatomy, complex morphology, its localization, and rupture status of each case.

Keywords: giant aneurysm; complex aneurysm; middle cerebral artery; bypass surgery

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Introduction

Regardless of their localization, treatment of complex intracranial aneurysms (CIAs), especially for complex middle cerebral artery (MCA) aneurysms, requires special skills and knowledge in vascular neurosurgery and presents a great challenge even for an experienced surgeon. The pathology includes aneurysms larger than 2.5 cm; aneurysms involving perforating vessels (lenticulostriate arteries or LSA) or efferent arteries; previously endovascularly or surgically treated aneurysms; aneurysms of complex shape (fusiform, serpentine or dolichoectatic); mycotic or infected aneurysms; dissected aneurysms; aneurysms with a wide or absent well-defined neck; thrombosed aneurysms; aneurysms with atherosclerotic or calcified walls and neck lesions. The angioanatomical features of the MCA are additional challenge for complex aneurysms surgery. Complex MCA aneurysm surgery is often not limited to simple clipping or clip reconstruction of the aneurysm's neck but may demand a more complex procedure to occlude the aneurysm.

The variety of approaches for surgical treatment of complex MCA aneurysms and a large number of different revascularization techniques is dictated not only by the aneurysms' anatomical features but also by their localization that explains the lack of unified treatment strategies.

Materials and methods

To analyze the features of surgical treatment and the results of surgery in patients with complex MCA aneurysms, 9 original papers were reviewed (Table 1). The papers concerning CIAs of other localizations, as well as those describing single cases, were excluded. In total, the surgical treatment of 244 patients with 246 complex MCA aneurysms was analyzed. Such treatment features as surgical treatment algorithms, methods of blood flow shutdown; revascularization techniques; vascular graft types; and patient outcomes and complications were considered.

Table 1. Treatment of patients with complex MCA aneurysms of different localizations.

Authors, Year	Patients	Aneurysm localization			Aneurysm occlusion technique						Bypass type			Graft type	Periop. control	Postop. control
		M1	Bif.	Distal	DC	RC	PO	DO	Tr/Res	ICA sacrifice	Coiling	EC-IC	IC-IC	Comb.			
Zhu et al., 2013	58	7	28	24	8	25			25	1		17	5		RAG	ICG-VA, Doppler, SEP/ MEP	CTA, MRI, DSA
Wessels et al., 2019	50	5	30	15			19	10	21			31		18	RAG, SVG	ICG-VA, Doppler	MRI, CTA, DSA
Natarajan et al., 2019	42	12[1]	20	11	5	20	4	1	16			28	24		RAG, SVG	ICG-VA, Doppler	DSA
Meybodi et al., 2017	30	8	5	17			8	1	21			12	13	5	RAG, SVG	SEP, MEP - monitoring	Angiography
Kivipelto et al., 2014	24	7	8	9	4		6[2]	8	6			21	4		SVG	ICG-VA, DSA, ultrasonic flow probe	CTA, DSA
Kalani at al., 2012	16	5	2	9			8[3]	4	1			16			RAG, SVG	Catheter angiography, ICG-VA	Angiography
Wang et al., 2018	12	5	6	1			8		4			12			RAG	ICG-VA, Doppler	CTA
Lee et al., 2018	6		1	5	2				3		1	6			not applied	ICG-VA, Doppler	DSA
Ravina et al., 2019	6		4	2	1	3[4]			2				6		not applied	ICG-VA	Angiography, CTA

M1 - M1 segment; **Bif**. –M1-M2 bifurcation; **Dist** - distal segment; **DC** – direct clipping; **RC** – reconstructive clipping; **PO** – proximal occlusion; **DO** – distal occlusion; **Tr/Res** – trapping/resection; **EC-IC** - extra-intracranial bypass; **IC-IC** - intra-intracranial bypass; **Comb.** – combined revascularization.

Footnotes:

1. including 3 anterior temporal artery bifurcation;
2. 1 endovascular proximal occlusion;
3. aneurysm occlusion include 2 spontaneous thrombosis and 1 aneurysm wrapping/proximal endovascular occlusion;
4. microsurgical strategy include 2 proximal clip occlusion and 1 aneurysm trapping.

Classification of complex MCA aneurysms

The pathology includes aneurysms larger than 2.5 cm; aneurysms involving perforating vessels (lenticulostriate arteries or LSA) or efferent arteries; previously endovascularly or surgically treated aneurysms; aneurysms of complex shape (fusiform, serpentine or dolichoectatic); mycotic or infected aneurysms; dissected aneurysms; aneurysms with a wide or absent well-defined neck; thrombosed aneurysms; aneurysms with atherosclerotic or calcified walls and neck lesions [1,2,3,4]. The angioanatomical features of the middle cerebral artery (MCA) are an additional complication for complex MCA aneurysms surgery. For example, limited accessibility of the M1 and M2 branches often hidden behind the mass of a giant aneurysm, and LSA or efferent arteries involvement with the aneurysm's wall or bottom create high risks of ischemic complications [4,5,6,7,8]. Also, the MCA supplies the largest and most important areas of the cerebral hemispheres and, at the same time, does not have communicating vessels similar to those of the anterior and posterior cerebral arteries providing compensatory blood flow in case of main vascular trunk occlusion. Hence, blood flow disturbance in the MCA territory can lead to severe complications and gross neurological deficits [2]. Moreover, complex MCA aneurysm surgery is not often limited to simple clipping or clip reconstruction of the aneurysm's neck but requires more complex approaches to occlude the aneurysm using various revascularizing techniques. Depending on their localization, the complex MCA aneurysms were classified into those affecting the M1 segment (pre-bifurcation aneurysms); aneurysms of M1 bifurcation (bifurcation aneurysms); and more distal (M2-M4) aneurysms (post-bifurcation aneurysms) [2,9]. Zhu et al., 2013 identified three types of complex MCA aneurysms: M1 aneurysms (type A); bifurcation or M2 segment (type B); M3 and more distal segments (type C) [4]. Wessels et al., 2017 proposed a more complex classification of the pathology, including 6 subtypes such as fusiform/dysplastic M1 aneurysms without signs of parietal thrombosis (type 1a) [8]; those with parietal thrombosis (type 1b); bifurcation aneurysms domed upward (type 2a); those laterally domed (type 2b); those domed downward (type 2c); M2-M3 aneurysms with no bifurcation involved (type 3) [8]. The authors advocated various methods and algorithms for surgical treatment of the pathology based on the affected MCA segment summarized in Table 1.

Surgery of complex MCA aneurysms

M1 segment

The papers reviewed mark this segment as the hardest one. Complex M1 aneurysms accounted for about 20% of the pathologies treated (see Table 1). Different complex aneurysms might develop in this segment, with fusiform ones being the most frequent [9]. The absence of a neck, often detached and fragile walls, and presence of intraluminal thrombosis made both direct clipping and reconstructive clipping difficult, provoking many recanalizations, complications, and mortalities. Endovascular options in such cases were also limited [9].

The M1 aneurysms in the considered series might involve the LSA or efferent vessels that further complicated their surgical treatment due to the high risk of circulatory disorders in the subcortical structures [7,10]. Approximately in 25% of the cases, the LSA originated from an aneurism [2], which had to be taken into account when selecting a treatment strategy as well as the presence or absence of a rupture [2].

LSA involvement (type Ia according to Wessels 2017 [8]), made it impossible to perform direct clipping, clip reconstruction, or trapping due to the high risk of stroke in the subcortical structures. In such a situation, the optimal solution was either proximal or distal occlusion of blood vessels [2,11,12] followed by a bypass to maintain blood flow in the MCA territory [6,]7. In case of non-functioning LSA involvement due to either intimal dissection or the presence of parietal blood thrombus in aneurysm cavity (type Ib according to Wessels 2017 [8]), one could perform trapping under electrophysiological monitoring to reduce the risk of subcortical stroke. Another option for both Ia and Ib types was performing a high-flow extra-intracranial anastomosis (EICA) to revascularize one of the M2 branches, perfuse the M1-M2 bifurcation and arrange retrograde flow to go through the aneurysm to the LSA [8,10]. The bypass technique included internal carotid artery/external carotid artery/common carotid artery (ICA / ECA / CCA) – MCA [2,10], ICA / ECA / CCA –MCA [2,10], maxillary artery (IMA)– MCA [13] with high-flow grafts from the radial artery (RA) or saphenous vein (SV).

As for low-flow anastomoses, according to Natarajan 2019, a superficial temporal artery (STA)-MCA bypass had low efficiency for revascularization of the M1 segment 10. Nevertheless, it was previously shown that this anastomosis created blood flow up to 100 ml/min in the M1 segment, which is sufficient for supplying the entire MCA territory that requires no more than 50 ml/min [9]. An alternative option could be an STA-MCA bypass with radial artery graft (RAG) followed by aneurysm trapping [4].

Direct or reconstructive clipping (clip reconstruction) was preferred as the simplest option when perforating vessels of the M1 segment were not involved with the aneurysm's wall, or bottom, direct or reconstructive clipping (clip reconstruction) was preferred as the simplest option. Also, coagulation could reduce the aneurysm in size and make it suitable for clipping [4]. These techniques minimized the risk of stroke [4]. More complex approaches were used if clip reconstruction was not applicable due to LSA absence. So, in the presence of a short area of pathology with the afferent and efferent vessels of sufficient tortuosity and length, trapping and resection could be performed, followed by end-to-end re-bypass formation [2]. If a more extended area was resected and there was a tension in the connected artery ends or a pathologically altered aneurysmal wall was retained, it was permissible to perform graft interposition. As for the grafting strategy, preference was given to RA grafts since they were an excellent match to the M1 segment in diameter.

Another alternative to re-bypass or interposition was EICA (low-flow or more often high-flow one) [2], or IMA -MCA bypass with RAG [3]. It should be noted that STA-RAG-MCA bypass required a short interposition graft and no additional neck incision [4].

Bifurcation segment

Complex aneurysms of MCA bifurcation in the considered patient series required more complex revascularization techniques. Unlike the M1 aneurysms, they were often thrombosed, had a saccular structure [14] could reach larger sizes (if compared to the M1 aneurysms), and often had an impact/mass-effect on the surrounding structures [9].

The bifurcation aneurysms were distinguished by the number of M2 branches involved (usually one or two) that could originate either from the wall or the bottom of the aneurysm. In the series analyzed, they accounted for up to 41% of all the complex MCA aneurysms considered.

To treat a bifurcation aneurysm, one could perform the traditional multi-clip reconstruction [9], but this technique was not applicable in all the cases, and sometimes one had to resort to more complex surgical treatment options, which usually included direct clipping of the aneurysm and one M2 branch, revascularization and occlusion of the second M2 branch using various bypasses (either low – and high-flow EICA or intra-intracranial (IC-IC) bypass) [4,10,15]. If both M2 branches were involved, a side-to-side IC-IC bypass, in-situ bypass (M2-M2, M3-M3) with further proximal or distal occlusion [7,9] or trapping of the entire bifurcations with aneurysms (if no LSA involvement) could be performed [4,15]. Proximal occlusion was preferable in case of aneurysm rupture, distal occlusion - if the M1 segment was difficult to access for clipping or if it carried the LSA [9]. To avoid serious ischemic complications, all branches of the MCA bifurcation were revascularized [10]. The advantage of the IC-IC bypass over EICA was a relatively straightforward performance and good donor-recipient matching. The technique required creating only one bypass and needed no graft harvesting, avoiding harvesting-related complications. Besides, if compared to EICA, IC-IC bypass had higher postoperative patency [15]. If it was impossible to create an IC-IC bypass for revascularization of both M2 branches, high-flow EICA with a Y-grafting (RA or SV) [10], or STA-RA-MCA, STA-MCA bypasses could be performed [4].

Distal segments

In the considered patient series, the aneurysms of distal localization accounted for about 39% of the complex MCA aneurysms. They were smaller in size and after their resection, small excisional spaces usually remained [2]. Distal MCA aneurysms were easier to revascularize [10], which led to more tremendous surgical success if compared to the M1 aneurysms. The proximal and distal MCA segments were easily accessible by performing wide Sylvian fissure dissection. It is also important that perforating arteries were usually not found at this level 8. If direct clipping of such an aneurysm was impossible, proximal or distal (in the absence of rupture), occlusion could be performed. Their relative accessibility also made trapping or resection possible 8. The creation of a single or double-barrel STA-MCA bypass was the simplest method to revascularize the distal branches of the segment [8]. Since the M2-M3 segments were quite redundant and tortuous and had a sufficient length, their aneurysms could be easily resected using an end-to-end bypass (re-bypass), or by performing RAG or SVG interposition followed a side-to-side bypass, or by reimplantation to preserve blood flow in the distal MCA [10]. Equally, one could perform an in-situ IC-IC bypass (e.g., M3-M3) [4,15].

Analysis of the various strategies for surgical treatment of MCA aneurysms in the considered patient series has demonstrated that high-flow EICA and proximal occlusion, as well as trapping and resection of the aneurysm, are the most common surgery of M1 MCA aneurysms as well as STA-MCA EICA with RAG is the most common bypass. Direct clipping or clip reconstruction followed by IC-IC or STA-MCA bypass are the optimal strategies for the treatment of MCA bifurcation aneurysms.

The method of choice in the surgery of distal MCA aneurysms is proximal occlusion and trapping/resection. STA-MCA bypass and IC-IC re-bypass are the most common revascularization options, unlike high-flow EICA that is not so commonly used. Interestingly, the most common occlusion techniques have been proximal occlusion, resection/trapping, and clip reconstruction. As for revascularization methods, STA-MCA bypass (including that with RAG) and high-flow EICA have been the most common.

The choice of occlusion and revascularization method has been determined by the surgeon's preference and CIA localization and angioanatomy, e.g. while Zhu et al., 2013 preferred clip reconstruction, trapping, or resection followed STA-MCA bypass with RAG for all the three MCA segments [4], Wang et al., 2019 preferred to perform IMA bypass with RAG [3], Kivipelto et al., 2014, Kalani et al., 2012 and Lee et al., 2018 relied on STA-MCA bypass to treat bifurcation, distal complex MCA aneurysms [6,7,16] and Ravina et al., 2019 mainly performed IC- IC bypasses [15]. High-flow EICA was used for revascularization, followed by proximal (more often) or distal occlusion or trapping of the complex aneurysms [8].

Revascularization and bypass patency

According to the authors, the main objective of revascularization in complex MCA aneurysms treatment was to provide blood flow in the distal segments of the MCA and maintain retrograde blood flow in the proximal segments without perfusion deficit in case it was impossible to clip the aneurism or there was a high risk of ischemic disorders due to aneurism occlusion [1,7,9,17,18]. The need for revascularization in the considered patient series varied between 1 [7,9] and 2.1% [2].

In the patient series reviewed, a total of 216 revascularization bypasses were performed. Among them, low-flow STA-MCA bypasses prevailed (35.5%), while high-flow ECA-MCA and intracranial bypasses were performed less frequently (24 and 24 %, respectively). Anastomoses with the maxillary artery comprised 5,5% of the total, and combined revascularization was performed in 6 % of the cases.

As a graft, RAs and SVs were used with the choice to be determined by blood supply requirements in the area to be occluded [19], RAGs were chosen more often (see Table 1). To monitor bypass patency, intraoperative indocyanine green videoangiography (ICG-VA) /contact Dopplersonography and postoperative angiography were used (see Table 1). In general, in the late postoperative period, the bypasses had good patency (95% of patients had 83.3-100% patency rate, Table 2).

According to the authors, bypass surgery was a non-standard procedure and required careful preoperative planning for each patient [9,20]. The most important issues in the planning are determining the strategy of how to handle the aneurysm and choose the kind of revascularization [21].

To date, despite numerous variants of revascularizing techniques have been proposed [2,6,7,22], there is no general strategy for their application to treat complex MCA aneurysms. In general, high-flow anastomoses were chosen to revascularize large-diameter proximal arteries or multiple distal branches in the case of pre-bifurcation and bifurcation aneurysms, and low-flow anastomoses - for revascularization of small-diameter distal arteries [2,20] (***Table 3***).

Table 2. Complex MCA aneurysm treatment results: bypass patency, the efficiency of occlusion, and treatment outcomes.

Authors, Year	Patients, n	Patients with ruptured aneurysms, n	Aneurysms, n	Bypasses, n	Bypass occlusion, long-term period, n	Residual aneurysm, long-term period, n	Follow up, months (mean)	mRS			GOS		
								0-2	3-5	6	4-5	2-3	1
Zhu et al., 2013	58	27	59	22	1	11	38				52	3	4
Wessels et al., 2019	50	2	50	49	2	11	6	42	5	3			
Natarajan et al., 2019	42	13	43	52	1	0	39	36	5	1			
Meybodi et al., 2017	30	8	30	30	3	1	28	24	6	0			
Kivipelto et al., 2014	24	2	24	25	2	0	27	20	3	1			
Kalani et al., 2012	16	2	16	16	1	3	2	13	3	0			
Wang et al., 2018	12	3	12	12	2	0	53	12	0	0			
Lee et al., 2018	6	3	6	6	0	0	52	6	0	0			
Ravina et al., 2019	6	0	6	6	0	2	12	6	0	0			

Table 3. Different types of bypasses which are used in CIA treatment.

Type of bypass	Donor	Recipient	Flow type	Flow	Graft
Low-flow 1 barrel bypass	Superficial temporal artery, Occipital artery	M2, M3, M4, P2, PICA, AICA	Low-flow	Till 50 ml/min	-
Low-flow 2 barrel bypass	Superficial temporal artery, Occipital artery	M2, M3, M4, P2, PICA, AICA	Low-flow	Till 100 ml/min	-
Middle-flow bypass	Internal maxillary artery	M2, M3, P2	Middle-flow	Till 130 ml/min	Radial artery, saphenous vein
High-flow bypass	External carotid artery, Common carotid artery	M2, M3, P2	High-flow	Till 150 ml/min (RAG)	Radial artery, saphenous vein
	Vertebral artery (V3)			Till 250 ml/min (SVG)	
Intra-intracranial bypass	Intracranial arteries	M2, M3, A3, A4, PICA	Low-flow/Middle-flow/High-flow		+/-

A3, A4 - anterior cerebral artery segments; **M2, M3, M4** –middle cerebral artery segments; **P2** – posterior cerebral artery segment; **AICA** - anterior inferior cerebellar artery; **PICA -** posterior inferior cerebellar artery.

The choice of bypass depended on a revascularized area and the decision was based on intraoperative Doppler flow measurements and angiographic images [6,7,23] as well as on preoperative tests for assessing compensatory collateral blood flow [9]. Intraoperative volumetric flow ultrasound fluorimetry was another important tool for determining the type of bypass in any given situation.

The efficiency of CIA occlusion

As shown in Table 1, in the considered patient series, various occlusion techniques were used depending on complex MCA aneurysm localization: proximal occlusion (23%), trapping (19%), distal occlusion (10%), direct clipping (in 8%), clipping with reconstruction (19%), aneurysm resection (21%) and coiling (0.4%). The efficiency of aneurysm occlusion varied from 68 to 100% among different authors (see Table 2) . In 5 of the 9 studies, residual aneurysm cavities were observed in the postoperative period. Zhu et al., 2013 had 11 residual aneurysms out of the 59 complex MCA aneurysms treated (19%), none of them requiring further surgical treatment, so only one patient underwent a reoperation during a two-year follow-up period [4]. According to Wessels et al., 2019, postoperative angiography at 3 - month follow-up revealed partial occlusion in 11 (22%) patients who also did not require reoperation [8]. In one patient, a residual aneurysm was a deliberate solution to allow for subsequent coiling [2].

In the series by Kalani et al., 2012, 12 out of 16 (75%) aneurysms were completely occluded in the postoperative period. However, residual aneurysms were observed in 3 cases (two of them were subsequently clipped, and one – coiled) [6].

In the series by Ravina et al., 2019, two residual aneurysms were observed. In one patient, the aneurysm was filled retrogradely through an anastomosis to maintain perfusion of the perforating arteries. In the second - the residual aneurysm had a small calcified neck that was not compressed by the clip's jaws [15]. Radiographically a residual aneurysm is an aneurysm with a portion filled with contrast after clipping [5]. However, despite such intraoperative controls as ICG-VA and Doppler, the percentage of postoperative residual aneurysms varied from 4 to 19% in the series reported by Dellaretti et al., 2017 [5]. Atherosclerotic lesion/calcification of the aneurysmal walls and intraaneurysmal thrombotic masses created an obstacle for aneurysm complete occlusion after clipping [24]. In addition, complete and timely thrombosis in the aneurysm cavity did not always occur after proximal or distal complex MCA aneurysm occlusion. It was shown that the frequency of residual aneurysms increased with their size and the patient's age, the prevalence of atherosclerotic processes in the aneurysmal wall, as well as with the number of clips applied to the aneurysm, all of them causing an increased risk of incomplete occlusion [5].

Complications, mortality, and treatment outcomes

All the complications in the considered patient series can be divided into ischemic, infectious, hemorrhagic, and others (Table 4). Despite constantly improving surgical techniques and a variety of intra- and postoperative control methods, various complications occurred during complex MCA aneurism treatment, most of them associated with the development of vascular thrombosis and ischemia [23,25,26].

The most common cause of the complications was a stroke that developed either in the MCA territory or in the subcortical structures due to bypass occlusion or its inadequate functioning or impaired blood flow in the LSA.

Table 4. Complications of complex MCA aneurism treatment.

Complications	Zhu et al., 2013	Wessels et al., 2019	Natarajan et al., 2019	Meybodi et al., 2017	Kivipelto et al., 2014	Kalani et al., 2012	Wang et al., 2018	Ravina et al., 2019
Stroke, n	5	2	6	2	6	3	2	
Epidural hematoma, n			1	1				
Subdural hematoma, n			1		2			
Intracerebral hematoma, n	2		1		4			
Hemorrhage from cervical anastomosis, n		1						
Hydrocephalus, n					1	2		
Meningitis, n	3				5			
Pneumonia, n			1		6			
Epidural infection, n			1					
Seizures, n	2							
Deep venous thrombosis, n					1			
Suture sinus, n								1
Skin necrosis, n					1			

Ischemic disorders were observed almost in all groups by various authors (7 out of the 9). In 11 out of 26 cases (42.3%), ischemic disorders in the postoperative period were associated with bypass occlusion, (Table 5). Other reasons for ischemic disorders were SVG stenosis; bleeding from the anastomotic zone [8]; irreversible cerebral ischemia due to prolonged temporary clamping [24]; lack of revascularization of the second M2 branch of the MCA; perforators damage or vasospasm [4,10,24].

According to Kalani et al., 2012 a stroke could also develop in a functioning bypass due to thrombotic masses from aneurysm cavity; temporary clamping; and inadequate blood flow through the bypass [6]. In addition to symptomatic anastomosis occlusions, there were asymptomatic cases that produced no ischemic disorders [2,10] (Table 5).

Table 5. The number of performed bypasses/ bypass occlusions vs. the number of strokes caused by bypass occlusion.

Authors, Year	Bypasses, n	Bypass occlusions, n	Strokes (all reasons), n	Strokes due occlusion, n	Asymptomatic bypass occlusion, n
Zhu et al., 2013	22	1	5	1	
Wessels et al., 2019	49	2	2	2	
Natarajan et al., 2019	52	1	6		1
Meybodi et al., 2017	30	3	2	2	1
Kivipelto et al., 2014	25	2	6	2	
Kalani 2012 et al.,	16	1	3	1	
Wang et al., 2018	12	2	2	2	

Infections were the second most common complications in the complex MCA aneurysms treated (see Table 4). Postoperative meningitis, pneumonia, and epidural infection requiring bone flap removal prevailed in this group. In most cases, these complications were cured with antibiotic therapy.

Hemorrhagic complications were also widespread in the patient series (5 out of the 9 cohorts). The most frequent manifestations were the formation of intracerebral, subdural, and epidural hematomas and bleeding from the anastomotic area (Table 4). In several cases, a reoperation was required to remove a hematoma.

In the series by Zhu et al., 2013, 2 patients developed seizures [4] another two - skin necrosis around the edges of the surgical wound, and one of them required skin transplantation [7]. In another series, two patients developed hydrocephalus, which was an indication for shunt system implantation [6,7]. In one case, a patient developed deep venous thrombosis of the lower extremities and pulmonary embolism [7] and another one – the wound separation followed by suture sinus formation treated conservatively in a course of 2 weeks [15]. In the considered patient series, the average mortality was 2.9% ranging from 2.4 to 6.9 % in different cohorts (Table 6).

Table 6. Patient mortality after complex MCA aneurysm treatment.

Authors, Year	Stroke, n	Due to rupture of an aneurysm, n	Pulmonary embolism, n	Sepsis, n	Nonsurgical-related diseases, n
Zhu et al 2013		2			2
Wessels et al 2019	1		1		
Natarajan et al 2019				1	
Kivipelto et al 2014		1			

The most common reasons for patient mortality while complex MCA aneurysm treatments were aneurysm rapture and severe SAH (3 patients) [4,7]. In the late postoperative period, such reasons were pulmonary embolism and sepsis (2 patients) [8,10]. Ischemic strokes due to bypass occlusion occurred only in 1 patient in 7 [8] (Table 6).

Even though a quarter of the patients in the series had ruptured aneurysms before surgery, the overall outcomes of surgical treatment were good, and in 211 patients (86.5%), they were assessed as 0-2 and 4 -5 points on the mRS and GOS scales, respectively (see Table 2). It is noteworthy that in the patients with unraptured aneurysms, the outcomes were better than in those with the SAH caused by a rapture. At the same time, the outcomes in patients with unruptured aneurysms were better than in those with SAH due to the ruptured aneurysm.

Illustrative cases

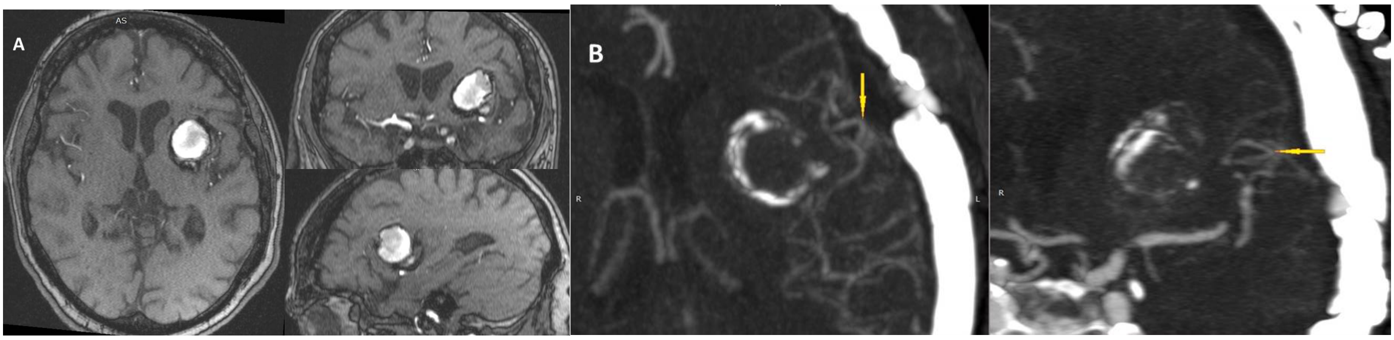

Figure 1. A 71-year-old woman with a giant thrombosed aneurysm in the M3 segment of the left middle cerebral artery (MCA). A-before treatment. B-after treatment: the arrow shows a functioning intra-to-intracranial microanastomosis.

Case 1

A 71-year-old woman presented with a history of headaches and seizures she had had since 2013. She was diagnosed to have a giant thrombosed aneurysm in the M3 segment of the left middle cerebral artery (MCA). The aneurysm of 26-26 mm in size had calcinated wall and compressed the neighboring regions of the brain, causing edema and a moderate mass effect. The patient underwent left osteoplastic pterional craniotomy with intra-to-intracranial microanastomosis between the M3 segments of MCA, aneurysm trapping and thrombectomy from the aneurysm sac. The postoperative period was uneventful (**Figure 1).**

Case 2

A 7-year-old boy presented with a partially thrombosed pseudotumor saccular aneurysm of 24x17 mm in axial size and 23 мм in vertical size of the temporal M2 branch of the right MCA. The patient underwent right osteoplastic pterional craniotomy with extra-to-intracranial microanastomosis between the frontal branch of the right superficial temporal artery (STA) and the M4 segment of the left MCA and microsurgical removal of the aneurysm. In the postoperative period, the patient developed a liquor cushion under the flap to regress later and a slight left hemiparesis. Postoperative brain MSCT showed the lumen of the MCA-STA bypass had not narrowed, and the aneurysm had obliterated (**Figure 2).**

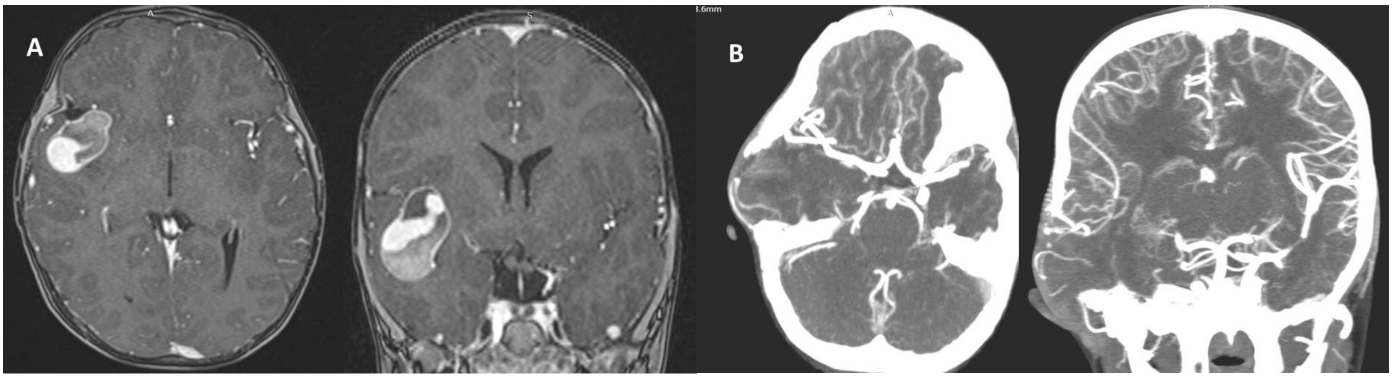

Figure 2. A 7-year-old boy with a partially thrombosed pseudotumor saccular aneurysm of the temporal M2 branch of the right MCA. A-before treatment. B-after treatment.

Case 3

A 12-year-old boy presented with a history of headaches he had had since June 2019. Angiographic MRI and MSCT imaging of the patient's extra-and intracranial arteries detected a fusiform aneurysm of the M2 segment of the left MCA. Its maximum diameter was 17 mm, and the length – 36 mm. The patient underwent left osteoplastic pterional craniotomy with double-barrel extra-to-intracranial microanastomosis between the frontal and parietal branches of the left STA and the cortical segments of the left MCA. The aneurysm was clipped. In the postoperative period, the patient's neurological status improved to match the preoperative level. Postoperative control imaging showed the aneurysm had completely obliterated while the bypasses had remained functional and patent (**Figure 3**).

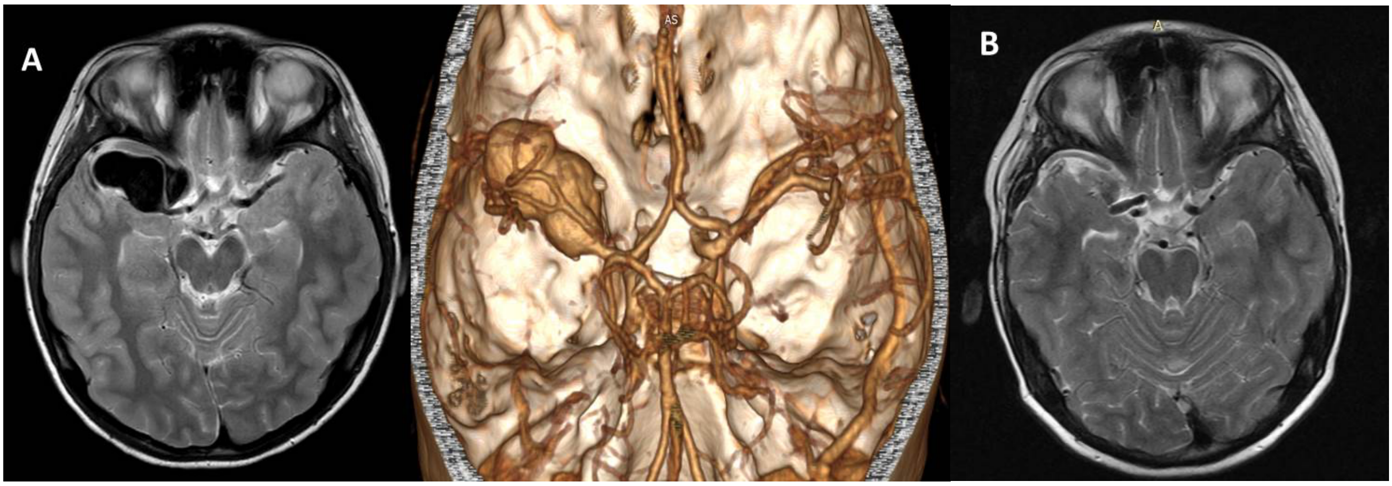

Figure 3. A 12-year-old boy with a fusiform aneurysm of the M2 segment of the left MCA. A-before treatment. B-after treatment

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Conclusion

For the time being, microsurgical treatment of complex MCA aneurysms remains a method of choice if compared to the endovascular techniques [12,27], so many centers still prefer surgical clipping to endovascular treatment [12] due to its low mortality and higher success rate in experienced hands and specialized centers [27,28].

Nevertheless, recently we have seen a tendency to apply the multidisciplinary approach combining surgical and endovascular techniques for the treatment of complex MCA aneurysms [29,30]. Hybrid techniques make it possible to expand an intervention range due to a skillful combination of revascularization and endovascular occlusion techniques during one surgical session.

Treatment of CIAs and complex MCA aneurysms, in particular, is a difficult process requiring combining different surgical approaches in every individual case to achieve the main goal that is a good outcome, especially in the presence of ruptured aneurysms. Complicating the surgery significantly increases the risks of hemorrhagic and ischemic complications. In our opinion, in the presence of so many available techniques, the main purpose of a surgeon is to obtain the necessary results applying the simplest approaches. Following this paradigm in the treatment of complex MCA aneurysms allows one to avoid complications and reduce mortality.

Complex intracranial aneurysms are surgically demanding lesions. It is obvious that surgical planning and treatment of complex MCA aneurysms depends on their morphology, localization (M1 segment, bifurcation, or distal MCA segments), anatomical and angioarchitectonical features, and requires an individual approach to every patient. Careful preoperative planning, intraoperative hemodynamic (ICG-VA, contact Doppler) and electrophysiological assessment, adequate revascularization, and postoperative examinations (MSCT, MRI, angiography) will help to reduce the risk of complications and mortality in the patients.

Disclosures

Conflict of Interest: All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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LITERATURE REVIEW AND A SERIES OF CASES

Traumatic intracranial aneurysms associated with traffic accidents and endovascular management options

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Abstract

Traumatic intracranial pseudoaneurysms are a rare form of aneurysm, comprising 1% of all aneurysms. Traumatic intracranial pseudoaneurysms are a complication of head injuries following traffic accidents, most often associated with skull fractures. Traumatic intracranial pseudoaneurysms are composed of a blood clot and small amount of fibrous tissue, occuring when the arterial wall breaks due to trauma and bleeding is confined only by the adventitia or surrounding tissues. Rupture of traumatic pseudoaneurysms, which occurs in up to 50% of all cases, is typically delayed following the initiating trauma. The delayed presentation, challenging diagnosis, and inadequate treatment options contribute to an overall poor prognosis for these lesions.

A review of the relevant literature and discussion of management options is presented with the cases of two patients who developed traumatic intracranial pseudoaneurysms following road traffic accidents who were treated with endovascular embolization in our institution.

The case studies confirm that conservative management is rarely appropriate. Instead, endovascular embolization represents an appropriate treatment option for these pseudoaneurysms due to their fragility and tendency to rupture. Most importantly, early, precise diagnosis with cerebral angiography and prompt treatment are essential to minimize mortality and morbidity.

Keywords: intracranial aneurysm; traffic accidents; polytrauma; intracranial pseudoaneurysm; endovascular treatment.

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Introduction

Almost one-third of all reported traumatic head and neck injuries are the result of road traffic accidents [1]. Significant vascular injuries occur in 1% to 3% of these patients [2]. Traumatic intracranial pseudoaneurysms (TIPA) are rare complications of traumatic brain injuries (TBI), most often associated with skull fractures [3]. TIPAs are rare among aneurysms, comprising 1% of all aneurysms [3]. The rupture of these pseudoaneurysms, which is typically delayed from days to weeks following the initiating trauma, 21 days on average, is associated with mortality as high as 50% and significant morbidity [4,5,6]. TIPAs are often described as a pulsating hematoma, which forms when the arterial wall is ruptured by trauma, and bleeding is confined only by the adventitia or surrounding tissues [7]. Unlike the structure of a true aneurysm, which contains all standard anatomical layers, the walls of TIPAs are com¬posed mainly of a blood clot and a small amount of fibrous tissue [3,5,7].

These pseudoaneurysms may be missed on initial investigation and may present as a delayed hemorrhage in a patient otherwise recovering well from a traumatic brain injury (TBI) 8. The most common presentation of these pseudoaneurysms is hemorrhage, with acute deterioration and new neurological deficit, although patients may present with ischemic events or remain asymptomatic until the pseudoaneurysm is diagnosed on follow-up imaging 8. Given their rarity and often indolent nature, TIPAs present both diagnostic and management challenges, especially in cases of polytrauma.

Although cerebral angiography represents the prefered modality for diagnosis and endovascular embolization represents the favored management strategy [8], the rarity of these aneurysms necessitates further examination. In this study, we investigate the outcomes of patients with TIPAs developed after traffic accidents who were treated with endovascular embolization in our institution and review the relevant literature.

Review

Formation

Histologically, traumatic aneurysms can be categorized as true, false, or mixed, with false aneurysms, also known as pseudoaneurysms, being the most common 4,9. In pseudoaneurysms, the wall of the aneurysm is formed only by the surrounding structures, particularly a hematoma [4]. The possible mechanisms for the development of TIPA involve either direct vascular injury secondary to skull fracture or stretching of the vessels by adjacent forces [3,6,9].

Location

In a closed head injury, the ICA is the most common location for the development of TIPAs [4,10]. However, although traumatic intracranial dissections at this level have been reported after road traffic accidents, TIPAs more often occur at the various levels of the vertebral arteries, followed by the extracranial parts of the ICA and common carotid artery [14,15].

The anatomical locations of TIPAs reflect the underlying mechanism of injury. Infraclinoid ICA aneurysms are commonly associated with skull base fractures [4,9,11]. At its supraclinoid segment, the ICA shifts from a relatively fixed structure in the skull base and cavernous sinus to a relatively mobile structure as it ascends into the cisternal spaces 6. It is possible that either movement of the supraclinoid segment against the anterior clinoid process or stretching of the ICA at this transition zone leads to the formation of these pseudoaneurysms [6,12,13]. This mechanism appears to apply to our first case.

Detection

The clinical course of a pseudoaneurysm is unpredictable since all three layers of the artery are disrupted, and bleeding and rebleeding easily occur [5]. Delayed growth and late detection of pseudoaneurysms are common [3]. TIPAs are commonly asymptomatic, but the most common symptomatic presentation is delayed intracranial hemorrhage with subsequent neurological deterioration. Imaging follow-up for patients with head trauma assists in diagnosis of asymptomatic cases. The primary goal in the management of these patients is early identification and intervention to prevent bleeding.

Although CTA has improved significantly over the past few years as a non-invasive screening method to detect intracranial aneurysms, it is not as sensitive as DSA [5]. DSA thus remains the gold standard in the diagnostic work-up of intracranial aneurysms and should be obtained in the setting of all severe head injuries, particularly in patients with penetrating head injuries or intracranial hemorrhage [3]. Angiographic features, including a poorly defined neck, irregular aneurysm wall, unusual location such as at a peripheral vessel rather than at a major proximal branching point, and delayed filling and emptying of the contrast from the aneurysm, differentiate TIPAs from congenital aneurysms [4,16,17].

The timing of angiography remains controversial. Angiography performed within hours of injury may be normal because these aneurysms develop over time [4]. Delaying angiography to optimize the visualization of an aneurysm after brain injury has been suggested [4]. However, when the du Trevou et al. [18] compared the outcomes of trauma patients undergoing early and delayed angiography, they concluded that postponing angiography in patients with a high risk of traumatic intracranial aneurysm was unsafe [4]. Therefore, early angiography should be considered in the setting of severe head injuries, and follow-up angiography should be obtained if the initial study is negative [4].

Management

Since TIPAs rarely regress and have a high incidence of rupture, early and effective treatment is an imperative. Improved survival rates have been reported in treated patients relative to untreated patients [4,9,19]. Techniques for the treatment of TIPAs, includ¬ing clipping, excision with or without arterial bypass, trapping, or neurointerventional ra¬diological approaches have been performed successfully [4,6,20]. The development of novel endovascular tools and techniques has shifted treatment to endovascular rather than open techniques. Surgery with direct neck clipping is difficult due to the fragility and broad neck of the pseudoaneurysm. However, directly embolizing the pseudoaneurysm is also risky because the false sac may result in bleeding during the intervention [6,20,21].

Case series

We retrospectively reviewed our institutional database at the Interventional Neuroradiology Department at the Clinic for Neurosurgery of the University Clinical Center of Serbia for cases in which a TIPA developed after traffic accidents and was treated with endovascular embolization between 2011 and 2021.

Overview

We found two cases of TIPA associated with traffic accidents and treated with endovascular embolization in our department within the last ten years. In both cases, traumatic pseudoaneurysms were formed after skull base fractures in young adults following traffic accidents. Skull base fractures were diagnosed on initial computed tomography (CT) imaging immediately after presentation to the Emergency Department, while pseudoaneurysms were diagnosed on follow-up CT angiography imaging (CTA) during the hospitalization. The patients did not experience new symptoms or neurological deficits that could be associated with the development of the pseudoaneurysms. CTA was performed solely according to the protocol in practice at our institution for treating patients with skull base fractures.

Case 1

In the first case, the pseudoaneurysm formed at the posterior wall of the clinoid segment of right internal carotid artery (ICA) (***Figure 1A***) We decided to treat this pseudoaneurysm with endovascular placement of platinum coils. The pseudoaneurysm was excluded from circulation with minor residual contrast filling (***Figure 1B***). Residual filling of the pseudoaneurysm fundus was increased on follow-up digital subtraction angiography imaging (DSA) three months after the procedure, so we decided to perform an additional intervention to enable complete occlusion of this pseudoaneurysm (***Figure 1C***). An intracranial braided stent (Leo+, Balt, Montmorency, France) was placed into the clinoid segment of the ICA over the aneurysm neck, and the pseudoaneurysm was filled with additional coils, completely excluding it from circulation (***Figure 1D***).

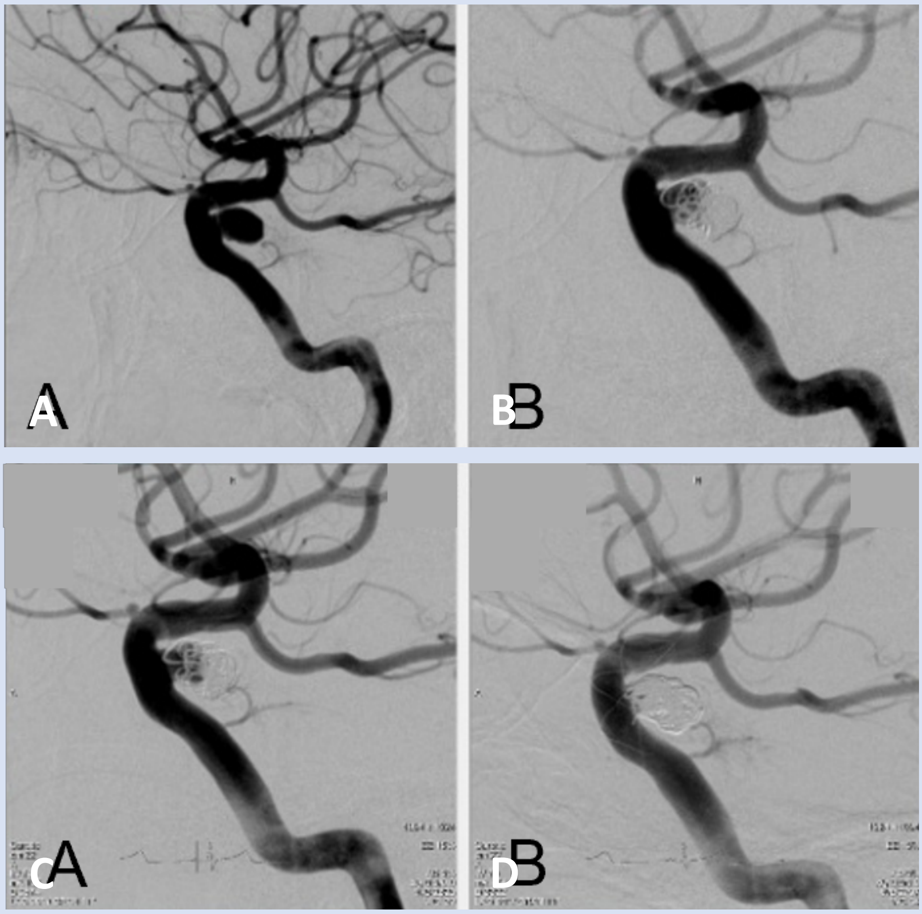

Figure 1. Traumatic pseudoaneurysm formed at the posterior wall of the clinoid segment of the right internal carotid artery. A. Initial DSA confirmation of aneurysm formation. B. Endovascular treatment of this pseudoaneurysm with the placement of platinum coils into the pseudoaneurysm fundus. C. Increased residual filling of the pseudoaneurysm fundus on follow-up DSA three months after the initial procedure. D. Reintervention with the placement of intracranial braided stent into the clinoid segment of the ICA over the pseudoaneurysm neck. The aneurysm filled with additional coils, such it was completely excluded from circulation.

This pseudoaneurysm remained completely occluded at follow-up DSA one-year later. The patient has not experienced any symptoms from this pseudoaneurysm before, in between, or after the treatments.

Case 2

In the second case, the pseudoaneurysm formed at the anterior wall of the cavernous segment of right ICA. (***Figure 2A***) After treatment with endovascular placement of platinum coils, the pseudoaneurysm was excluded from circulation with minor residual fundus filling. (***Figure 2B***) Residual filling was increased on follow-up DSA three months after the procedure, so we decided to perform additional intervention as described in the first case. (***Figure 2C***) A stent was placed over the aneurysm neck to stabilize the coil package, and the pseudoaneurysm was filled with additional coils, such that it was excluded from circulation. (***Figure 2D***) Follow-up DSA six months after the reintervention showed that this pseudoaneurysm has remained completely occluded**.**

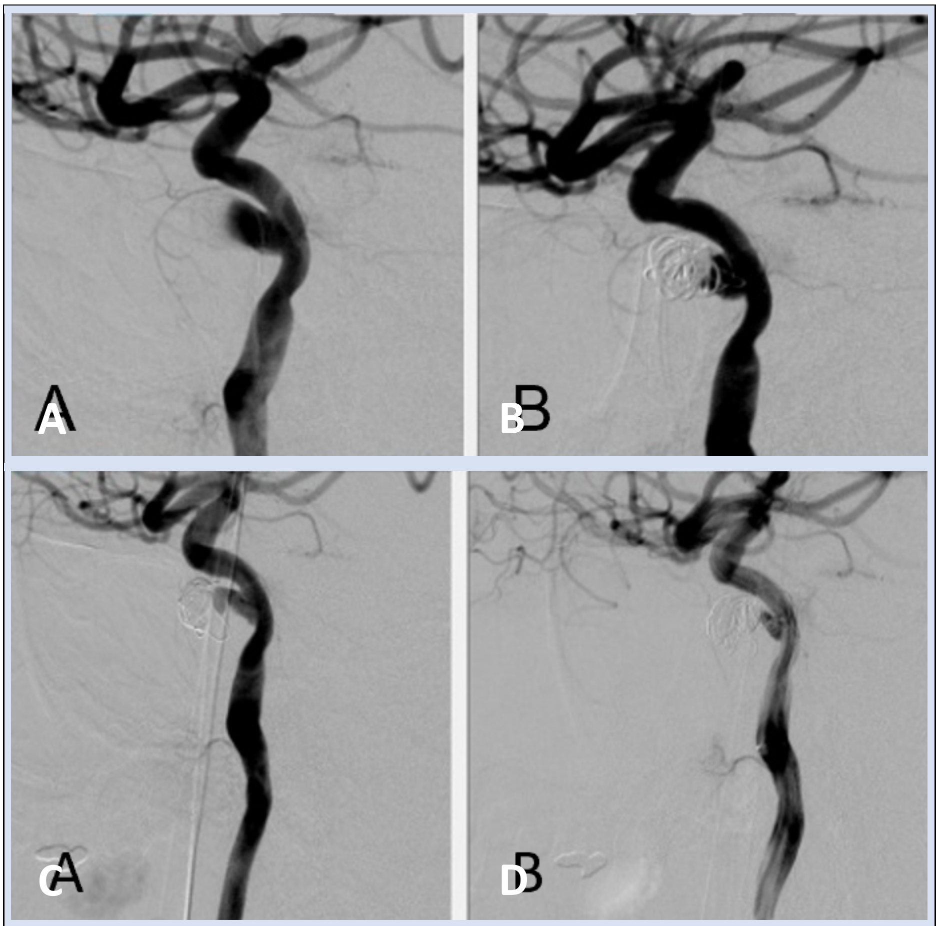

Figure 2. Traumatic pseudoaneurysm formed at the anterior wall of the cavernous segment of the right ICA. A. Initial DSA confirmation of aneurysm formation. B. Endovascular treatment of this pseudoaneurysm with the placement of platinum coils into the pseudoaneurysm fundus. C. Residual filling of the pseudoaneurysm fundus was increased on follow-up DSA three months after the initial procedure. D. A stent was placed over the pseudoaneurysm neck to stabilize the coil package, and more coils were added. The pseudoaneurysm was excluded from circulation.

Discussion

Our cases are remarkably similar. Both patients were young adults with multiple traumatic injuries after traffic accidents. Although both pseudoaneurysms had a wide neck, stent placement was avoided during the initial treatment encounter because stent placement requires antiplatelet therapy, which should often be avoided in patients with recent polytrauma. Complete aneurysm occlusion was attempted with coils alone. Unfortunately, on follow-up angiograms, the pseudoaneurysms were not completely excluded from circulation. Stents were placed in both cases to protect the vessels with thicker packing of coils to prevent migration into cerebral vessels. Stents were placed a few months following the initial trauma, thus avoiding the risk of side effects associated with antiplatelet therapy. Our cases demonstrated that the enlargement of the pseudoaneurysm fundus is common in TIPAs, likely due to the pseudoaneurysmal nature of these lesions.

Conclusion

Suspicion for TIPAs should be maintained for all patients with severe head injuries following road traffic accidents, especially if they present with delayed neurological deterioration. Given traumatic intracranial pseudoaneurysms may present both diagnostic and management challenges, especially after polytrauma cases, conservative management is rarely appropriate. Instead, endovascular embolization represents an appropriate treatment option for these pseudoaneurysms due to their fragility and tendency to rupture. Most importantly, early and precise diagnosis with cerebral angiography and prompt treatment are essential to minimize morbidity and mortality.

Disclosures

Conflict of Interest: The author certify that he have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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CASE REPORT

A state of art management of a bilateral basal ganglia germinoma: case report

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Abstract

Central nervous system germinomas are the most frequent germ cell tumors, predominantly affecting adolescents and young adults. They are generally midline tumors primarily located in the pineal gland and suprasellar regions. Basal ganglia germinomas (BGGs) are rare and generally unilateral, with only 16 histopathologically-confirmed bilateral BGGs reported to date. In this paper, we are presenting a rare case of bilateral BGG in a 14-year-old boy. The neuroradiological findings of bilateral BGGs are presented, and the strategy for their management is discussed while considering previously reported cases. A 14-year-old suffering from involuntary jerking movements of the right shoulder and arm was referred to our department. An MRI scan revealed diffuse T2/FLAIR hyperintensity in the bilateral basal ganglia, and MR spectroscopy suggested a malignant disease. A stereotactic biopsy was performed, and the histologic examination revealed germinoma. Neoadjuvant chemotherapy followed by whole ventricular radiation therapy with a boost to the tumor was initiated. Although BGGs are mostly unilateral, bilateral entities are rarely seen. Despite excellent survival rates, symptomatic outcomes may be unfavorable. Therefore, it is crucial to recognize the initial MRI findings and diagnose these tumors early to maximize symptomatic relief while minimizing complications.

Keywords: basal ganglia; germinoma; intracranial; stereotactic biopsy.

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Introduction

Central nervous system germinomas are the most frequent germ cell tumors (GCTs), predominantly affecting adolescents and young adults, with the overwhelming majority diagnosed under 20 years of age[1]. A strong male predominance is observed. GCTs are generally midline tumors primarily located in the pineal gland and suprasellar regions and spreading along the ventricular surfaces. However, basal ganglia germinomas (BGGs) are rare and generally unilateral, comprising approximately 5-10% of intracranial germinomas[2].

In this case report, we describe the clinical characteristics, imaging examinations, pathological characteristics, management, and outcome of an unusual case of bilateral BGG, as well as provide a literature review.

Case report

A previously healthy 14-year-old boy presented with involuntary jerking movements of his hand and right shoulder with progression over eight months. He also experienced headache, right eye twitching, loss of balance, forgetfulness, and word-finding difficulty.

An outpatient neurological evaluation was performed, and head magnetic resonance imaging (MRI) findings were unremarkable. One year later, he underwent a repeat cranial MRI due to progressive symptoms, and a bilateral cystic mass was visualized at the bilateral basal ganglia. He was then referred to our clinic for a stereotactic biopsy.

On admission, neurological examination revealed grade 3/5 right hand flexion, myoclonus of the right fingers, and right-sided eye twitching. No cognitive deterioration was noted. There was no family history of neurologic disorders in terms of neurodegenerative or metabolic diseases. Laboratory data, including serum AFP and β-hCG levels, were unremarkable.

A presurgical MRI revealed bilateral basal ganglia lesions along the 3rd ventricle associated with the anterior commissure. The lesion involved bilateral septa formations with multiple compartments. Post-contrast images showed intense peripheral enhancement. Perfusion-weighted images revealed increased perfusion parameters, most prominent in the peripheral and septal parts of the lesions.

Based on the negative tumor markers and imaging parameters, germinoma of the basal ganglia was suspected. Stereotactic biopsy of the lesion at the level of the right basal ganglia was performed (***Figure 1***).

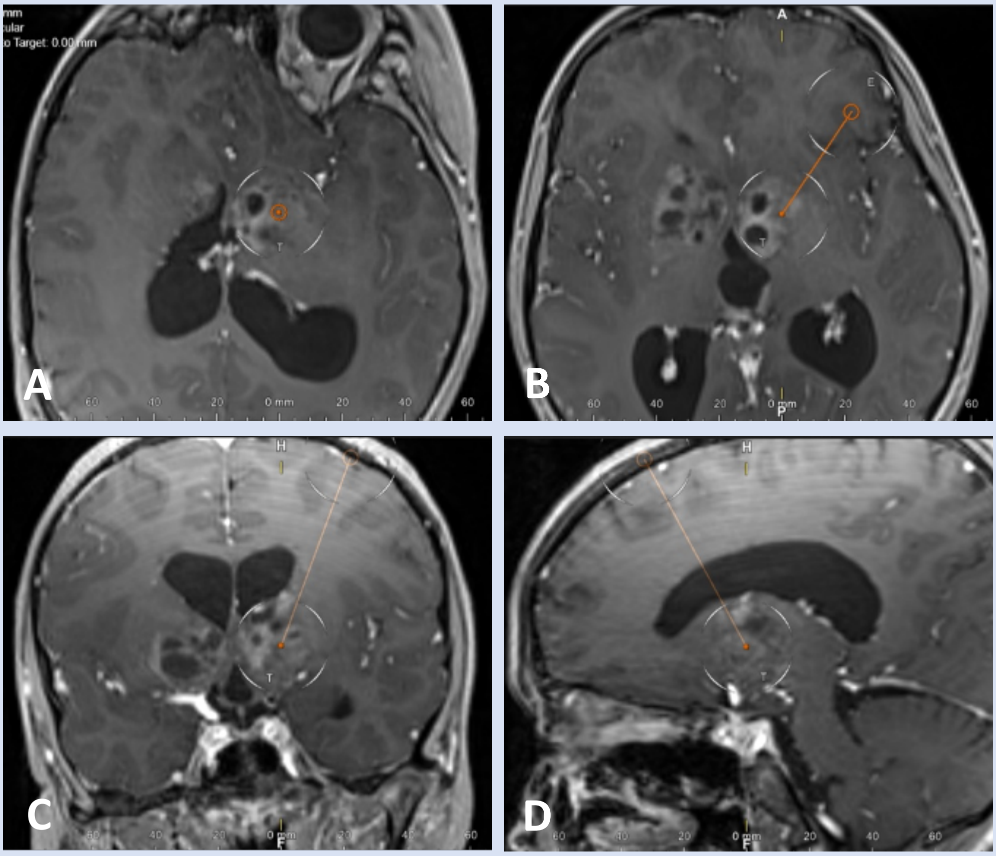

Figure 1. Stereotactic biopsy planning of the lesion located in the right basal ganglia. A. Oblique. B. Axial. C. Coronal. D. Sagital.

Histopathological investigation was consistent with germinoma. Immunohistochemical studies showed expression of SALL4, CD117, and OCT4 in tumor cells (***Figure 2***).

After the definitive pathological diagnosis, neoadjuvant chemotherapy (CTx) with carboplatin and etoposide, followed by whole ventricular radiotherapy (RT) with a boost to the tumor, was initiated. The patient remained alive at the time of writing this article with unchanged symptoms.

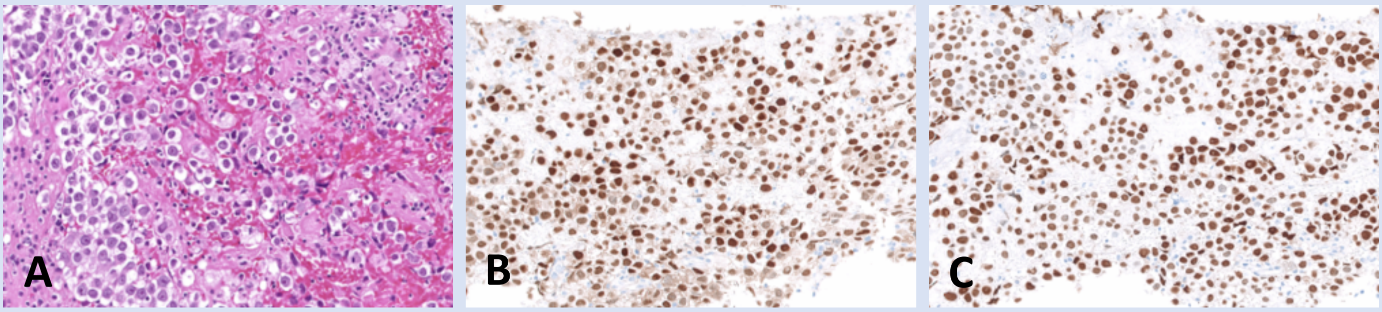

Figure 2. Hematoxylin & eosin-stained section prepared from the stereotactic biopsy specimen demonstrates a high-grade tumor composed of polygonal cells with pale/clear cytoplasm and large nuclei with prominent nucleoli A. Immunohistochemical studies revealed positivity with B. OCT4 and C. SALL4 antibodies. (Scale bar = 50 µm).

Discussion

Germinomas are the most common GCTs. Entrapment of the migrating totipotent cells during neural tube growth is considered the underlying etiology of germinomas[3]. According to the literature, the incidence of germinoma is higher in Japan and far East Asia than in western countries, with a male predominance (male-to-female ratio 20:1)[4,5]. Most of the patients are adolescents or young adults at the time of the diagnosis[1]. The most frequent locations for germinomas are pineal and suprasellar regions. BGGs are very rare, and bilateral BGGs are even more rare.

A literature review using PubMed with search terms "bilateral," "basal ganglia," "germinoma," and "germ cell tumor" revealed only 11 papers reporting 22 cases of bilateral BGGs (only 16 histopathologically-confirmed) in the English literature to date (***Table 1***)[5-15]. Kobayashi et al.[6] reported the first cases of bilateral BGGs in two boys aged 14 and 13 years in 1989. Both cases were managed with whole skull irradiation without definitive tissue diagnosis. Recently, Huang et al. [15] reported a similar case in a 8-year-old boy who presented with mild cognitive impairment, involuntary movement of his right arm, increased muscle tone of bilateral extremities without muscle weakness, and signs of precocious puberty.

Table 1. General characteristics of previously reported histopathologically-confirmed bilateral basal ganglia germinoma[5-15]

Reference	Age	Gender	Tumor location	Duration of symptoms (months)	Symptoms/Signs
Kobayashi et al., 1989	14	M	Bilateral basal ganglia	11	Slowly-progressing left hemiparesis, followed by personality and mental changes, bilateral dystonic-athetoid movements, hydrocephalus
Wong et al., 2008	13	M	Bilateral basal ganglia, thalamus	20	Left hemiparesis, drooling, speech disturbances, dysphagia, lethargy
Sonoda et al., 2008	8	M	Bilateral basal ganglia	7	Precocious puberty
Rossi et al., 2008	14	M	Bilateral basal ganglia	NA	Right hemiparesis, speech disturbance, hypertonia, hyperreflexia, mental deterioration
Ji Hoon Phi et al., 2010	13	M	Bilateral basal ganglia	30	Hemiparesis, bulbar sign, abnormal behavior, hiccup, and vomiting
	15	M	Bilateral basal ganglia	13	Hemiparesis, hiccup, and vomiting
	19	M	Bilateral basal ganglia	8	Hemiparesis, bulbar sign
	13	F	Bilateral basal ganglia, subependymal seeding	3	Hemiparesis, bulbar sign, abnormal behavior, memory disturbance, poor school performance
Tso et al., 2014	14	M	Bilateral basal ganglia, thalamus, periventricular region	12	Cognitive disturbance
Wataya et al., 2015	15	M	Bilateral basal ganglia	8	Tetraparesis, cognitive disturbance, mask-like face, speech disturbance, urinary/bowel incontinence
Konovalov et al., 2016	14	M	Bilateral basal ganglia	6	Tetraparesis, hypertonia, fatigue, drowsiness, speech disturbance
Nodomi et al., 2017	14	M	Bilateral basal ganglia	12	Left hemiparesis
Kang et al., 2020	10	M	Bilateral basal ganglia	N/A	N/A
	12	M	Bilateral basal ganglia	N/A	N/A
	19	M	Bilateral basal ganglia	N/A	N/A
Huang et al., 2020	8	M	Bilateral basal ganglia	24	Walking and writing disorders, cognitive decline, speech disturbance, nocturnal enuresis, polydipsia, polyuria, precocious puberty, and thermoregulatory problems
Present study	14	M	Bilateral basal ganglia	8	Involuntary movements of right shoulder and hand, right eye twitching, loss of balance, forgetfulness, speech disturbance, headache

The clinical presentation depends on the tumor's location and includes hemiparesis, raised intracranial pressure; hydrocephalus; Parinaud's syndrome; diabetes insipidus; visual disturbance; pituitary failure; precocious puberty; and speech, behavioral or psychiatric disturbances[1,11]. According to the literature, the duration of the symptoms in patients with bilateral BGG varies between 3 to 24 months, with a mean duration of 14 months. This indicates that the clinical course of this tumor group is generally slow, and that early diagnosis is mostly challenging.

Neuroimaging has a vital role in the diagnosis of germinomas. Although conventional imaging is rarely sufficient for diagnosis, germinomas are well-delineated and isointense to hypointense to gray matter on T1-weighted images, and isointense or hyperintense on T2-weighted images. Germinomas usually show strong and uniform contrast enhancement. As germinomas are highly cellular, most demonstrate significantly restricted diffusion[16]. The CT and MRI findings of BGGs are somewhat distinct from those of the pineal and suprasellar regions in terms of tumor size, cystic changes, and intratumoral hemorrhage.

Table 2. Management of previously reported histopathologically-confirmed bilateral basal ganglia germinoma[2,6-15]

Reference	Surgery	Chemotherapy	Radiation therapy	Outcome	Recurrence	Follow-up (months)
Kobayashi et al., 1989	Open biopsy + cyst evacuation	N/A	WBRT: 40.2 Gy	Mild left hemiparesis and involuntary movements, unchanged mental state, improved level of consciousness	None	24
Wong et al., 2007	STR	N/A	LBRT: 49.9 Gy; WBRT: 27.9 Gy	Tumor free, hemiplegia, slurring speech	None	153
Sonoda et al., 2008	STX biopsy	ICEx3	WBRT: 24 Gy	Cured	None	46
Rossi et al., 2008	STX biopsy	ICEx4	CSI: 24 Gy, WBRT: 16 Gy	Neurological deficits unchanged	None	16
Ji Hoon Phi et al., 2010	STX biopsy	CCG 9931	LBRT (BG): 54 Gy, WVRT: 54 Gy	Deteriorated motor functions	N/A	35†
	STX biopsy	KSPNO	LBRT (BG): 27 Gy, CSI: 23.4 Gy	Motor deficits unchanged	None	43
	STX biopsy	BEP	LBRT (BG): 50.4 Gy, WVRT: 36 Gy	Motor deficits unchanged	None	13
	STX biopsy	BEP	BG: 54 Gy, WB: 36 Gy, CSI: 21 Gy	Deteriorated motor functions	None	42
Tso et al., 2013	STX biopsy	N/A	N/A	Mild mental retardation, dystonia, and bradykinesia	None	N/A
Wataya et al., 2015	Open biopsy + ETV	CAREx3	WBRT: 24 Gy	Increased speech and activity, improved urinary incontinence	None	N/A
Konovalov et al., 2016	GTR	N/A	N/A	Improved activity level, regressed retardation, motor deficits unchanged	None	84
Nodomi et al., 2017	STX biopsy	ICE	WBRT: 24 Gy	Cured	None	10
Kang et al., 2020	STX biopsy	No	WVRT: 30 Gy + PB: 24 Gy	Cured	None	22
	STX biopsy	Yes, not known	CSI: 23.4 Gy + PB: 24 Gy	Cured	None	74
	STX biopsy	Yes, not known	CSI: 19.8 Gy + PB: 24 Gy	Cured	None	71
Huang et al., 2020	STX biopsy	N/A	N/A	Symptoms unchanged	N/A	N/A
Present study	STX biopsy	CARE	WVRT: 30 Gy + PB: 24 Gy	Symptoms unchanged	None	6

STR: subtotal resection, **GTR**: gross-total resection, **STX**: stereotactic, **ETV**: endoscopic third ventriculostomy, **ICE**: ifosfamide+cisplatin+etoposide, **BEP**: bleomycin+etoposide+cisplatin, **CARE**: carboplatin+etoposide, **CYCE**: cyclophosphamide+etoposide, **CCG**: Children's Cancer Group, **KSPNO**: Korean Society for Pediatric Neurooncology, **CSI**: craniospinal irradiation, **PB**: primary boost, **WBRT**: whole brain radiation therapy, **WVRT**: whole ventricle radiation therapy, **BG**: basal ganglia, **LB**: local brain, **SS**: suprasellar, **P**: pineal, **N/A**: not available, †: patient died

The initial appearance of BGGs on CT scan is that of an irregularly defined, isodense or slightly hyperdense lesion with no mass effect[17,18]. A single calcified spot may occur first, appearing several years prior to diagnosis. MRI findings of BGGs vary. Early MR images demonstrate lesions that are mostly ill-defined, homogenous with subtle or no contrast enhancement, similar to cerebral infarctions or gliomas. However, as the disease progresses, greater contrast enhancement, internal capsule invasion, mass effect, peritumoral edema, and cystic and necrotic changes can be seen[2,9,10,17,18]. Furthermore, CT and MRI findings of ipsilateral cerebral, basal ganglia, and brainstem atrophy are common features of BGGs[19,20]. Ipsilateral cerebral hemiatrophy is due to Wallerian degeneration of thalamus and basal ganglia afferent fibers and retrograde degeneration of efferent fibers due to the damage and loss of ganglia cells and nerve fibers caused by tumor invasion and infiltration[1,19]. Cystic structural changes are thought to originate from previous hemorrhages as well as tumor enlargement and disease progression[2,20]. BBGs, however, also represent a diagnostic problem to many clinicians without these apparent imaging features. For instance, in the study by Tso et al.[10], two of the five cases were initially misdiagnosed as cerebral infarction. Definitive diagnosis was established with further imaging studies when the symptoms worsened. To overcome uncertainty in diagnosis, some other studies suggest the use of C-methionine PET that supports the MRI findings [21]. Along with the imaging modalities, serum tumor markers have a somehow limited but useful function because of the non-invasive nature[11,22].

A tissue diagnosis, through biopsy or a more aggressive surgical approach, is the accepted method of diagnosis of germinomas. After histologic diagnosis, germinomas have a high potential for curative treatment with RT. RT alone in relatively high doses and volumes frequently affords a curative choice for most patients. However, the late effects of RT have urged investigators to examine the efficacy and safety of adjuvant CTx to reduce the RT dose or field and the associated morbidity while maintaining the excellent overall survival (OS)[23,24]. The current proposed treatment includes four cycles of CTx with carboplatin and etoposide succeeded by lower dose whole ventricular RT with a boost to the tumor[25].

The outcome for subjects with germinomas is highly favorable, and several trials reported a 5-year OS of over 90%. Lesion size and pathological classification influence OS in GCTs[26]. While pineal germinomas are usually diagnosed earlier due to distinctive symptoms, BGGs are generally detected at a later stage with larger tumors due to mild or non-specific symptoms. It might be expected that BGGs would have a worse prognosis compared to pineal counterparts. However, previous studies of BGGs also revealed good OS and prognosis with CTx and RT. Among the bilateral BGGs in the literature, only Phi et al.[9] reported that one patient died after 35 months of follow-up (***Table 2***). This article also stated that treatment with only CTx frequently leads to tumor recurrence[10]. Even after treatment, symptoms generally remain unchanged, with deteriorated motor functions and cognitive and behavioral disturbances[9]. Improvement in these symptoms is strongly dependent on their severity, which is correlated, to some extent, with the diagnostic and treatment delay. For this reason, early diagnosis is crucial to maximize the potential for symptomatic improvement.

Conclusion

BGGs are mostly unilateral, but bilateral entities are also rarely seen. Despite excellent survival rates, symptomatic outcomes are often ufavorable. It is crucial to recognize the initial MRI findings and diagnose these tumors early to maximize symptomatic relief while minimizing complications.

Disclosures

Conflict of Interest: All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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NEUROSONOLOGY X NEUROSURGERY

Intraoperative ultrasound use in cranial neurosurgery- The basics and initial experience

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Abstract

Reliable spatial orientation in neurosurgery is of utmost importance. Anatomical landmarks-based orientation or sulcal identification is insufficiently accurate for the requirements of modern times neurosurgery

Intraoperative ultrasound (IoUS) is affordable and widely available, easy to use, does not require additional equipment nor installation, and does not use additional any expendable material. It is mainly used (but not limited) to localize, optimize approach and evaluate resection of expansions of all origins, but also in vascular neurosurgery, hydrocephalus and malformations.

The paper reviews the possibilities of intraoperative ultrasound use in cranial neurosurgery, and also introduces the basic aspects of intraoperative use.

The significance of IoUS in contemporary neurosurgery is improving with the technical development and advances within the field. The basic role in localization of the lesions is still not used to the extent it deserves, or should be used, while there are already numerous other possibilities providing exceptionally reliable intraoperative information regarding all aspects of surgical substrates and treatment.

Keywords: intraoperative ultrasound; neurosurgery; cranial

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Introduction

Reliable spatial orientation in neurosurgery is of utmost importance. Anatomical landmark-based orientation or sulcal identification is insufficiently accurate for the requirements of modern neurosurgery [1]. Neuronavigation has been designated as one of the most important breakthroughs in surgery, and it is certain that high-profile neurosurgery cannot be performed without one such system. On the other hand, there are numerous system flaws, particularly with orientation in real time intraoperatively, when all structures change and/or move relative to the pre-programmed state of the neuronavigation [2].

Intraoperative use of magnetic resonance imaging (MRI) and computed tomography (CT) allows neurosurgeons to overcome these limitations by complementing the initial findings with subsequent intraoperative assessment uploaded into the navigation system, increasing the reliability of the system [3]. However, intraoperative diagnostics have a number of limitations, most of which are financial but also encompass spatial orientation and overall examination complexity [4]. Above all, intraoperative MRI and CT devices are extremely expensive, which is a problem in less developed centers and low- and middle-income countries. Moreover, even though intraoperative imaging increases the safety and improves surgical treatment in general, it is not recognized by the recommendations and guidelines of regulatory bodies [5]. Therefore, it is impossible to charge for this additional intraoperative tool, perhaps representing the primary issue in high-income countries and commercially oriented centers, which can afford these systems [6,7].

In contrast, intraoperative ultrasound (IoUS) is affordable and widely available, easy to use, does not require additional equipment or installation, and does not use any additional expendable material. It is mainly used to localize lesions, optimize the operative approach, and evaluate the extent of resection but not limited to these purposes [1]. Although IoUS was initially introduced into neurosurgery in 1978 by Reid [8], this technology has largely been unexplored due to its limitations in terms of bone interference, poor image quality (of that times systems) and lack of familiarity among neurosurgeons [9].

Most of these limitations have now been overcome. This article article emphasizes the important role IoUS may have in neurosurgery. Despite its steep learning curve, IoUS may facilitate neurosurgery.

Ultrasound basics and practical adjustments for intraoperative use

The basic principles of general ultrasound examination and neuroultrasonography apply to its intraoperative use.

Beginner users should expect to see images similar to those obtained from T2 MRI sequence, albeit somewhat between the native and contrast-enhanced series, or contrast-enhanced CT. IoUS exceeds the quality of native CT images, but it does not replace CT and should not be used to intraoperatively complement insufficient native CT findings.

Transducer selection

Prior to IoUS use, an adequate transducer should be selected based on the desired features.

1. Frequency: High frequency allows improved image resolution. Low frequency allows improved penetration.
    a. 3 MHz: good penetration, but poor resolution; capable of penetrating a thin temporal bone or skull in children
    b. 7 MHz: acceptable balance between resolution and penetration; most used in neurosurgery
    c. 10–12 MHz: better resolution at the cost of penetration; used for the superficial lesions
2. The size of the transducer: Larger transducers often provide better image quality but are difficult to access. There are four general types of intraoperative probes for use in neurosurgery:
    a. craniotomy (approximately 30x10 mm)
    b. burr-hole (approximately 10x10 mm)
    c. "hockey stick" with flexible tip (approximately 30x10 mm)
    d. minimally invasive (approximately 6-7 mm radius)

Although dedicated probes exist, the exam may often be performed using the usual probes which are widely available. The frequent lack of access to dedicated probes should not be considered a limitation to regular use. Linear probes penetrate more superficially and may be more suitable for beginner use, although they might require craniotomy enlargement due to their larger size.

Navigated ultrasound is a powerful tool that combines the benefits of real-time ultrasound imaging with the ability to track the probe, facilitating image-guided navigation (10, 11).

Approach to the patient

Fully immersive dedicated probes for intraoperative use may be sterilized and used within the watery environment without the use of gel. When using regular or older generation intraoperative transducers, the probe requires gel and should be placed into watertight sterile protection foil to prevent gel spill into the operating field. There should be enough gel between the probe and the sterile foil to enable proper functioning of the IoUS.

After preparing the probe in sterile fashion, the operating field should be prepared, and there should be no air between the probe and the tissue (1).

- The operating table should be maneuvered to position the patient's head and craniotomy transducer at the highest point, allowing for saline filling, reducing artifacts, and expanding the field visualized by the probe.
- The control panel should be covered with sterile foil to facilitate manipulation.
- The craniotomy should be large enough to enable visualization of the entire lesion.
    e. A slightly larger craniotomy allows for better visualization, while the dural opening can be adjusted according to the transdural IoUS findings.
    f. The dual craniotomy technique is an alternative to a larger craniotomy and includes an additional mini craniotomy sufficient in size to accommodate the transducer that is separate from the main craniotomy.
    g. For an ultrasound-guided biopsy, a craniotomy should be large enough for both the transducer and a biopsy needle.
- Initial ultrasonography is performed in the standard planes until the target structure is visualized. Then, the probe moves according to the neurosurgeon's need to visualize the structure from different angles.
- If available, the transducer should be registered with intraoperative neuronavigation. This co-registration may be combined with preoperative imaging (12).

Device Settings

Depending on the IoUS system used, there are several features which may be used to further enhance the acquired images:

- *Tissue Harmonic Intensity*: This option, which improves picture quality, should be active if available.
- *Image gain* and *brightness* are set at the beginning of the ultrasonography and may be corrected during the exam.
- The exam begins without field enlargement. The depth should be set according to the preoperative images for optimal anatomical orientation and resolution. Once the structure is localized, magnification is adjusted if needed.
- *Color Doppler* and *PowerDoppler* may be used to evaluate vascularization.

Ultrasonic display features

Normal structures of the brain and surrounding structures are seen as:

1. Hyperechoic: falx, tentorium, choroid plexus, and pineal gland.
2. Isoechoic: normal brain tissue.
3. Hypoechoic: brainstem
4. Anechoic (no signal): ventricular system and basal cisterns, CSF, and liquid.

Pathological structures:

1. Hyperechoic lesions: blood, solid intracranial tumors, vascular lesions (arteriovenous malformations, cavernomas, hemangiomas, and so on), capsules of cystic lesions, calcifications, high-grade gliomas, metastases
2. Moderate hyperechoic lesions: low-grade brain tumors, some metastases
3. Hypoechoic or anechoic lesions: cysts, chronic and subacute hematomas, necrotic zones of glioblastomas, abscesses

Foreign bodies (metal, glass, plastic, bone fragments) are usually hyperechoic. However, as most ultrasound signals are reflected from the surface of these objects rather than spread through them, only a probe-oriented surface can be visualized. The quality of the images may change substantially due to artifacts.

Mair et al. proposed stratifying neoplastic lesions into one of four grades (grades 0–3) on the basis of their ultrasonic echogenicity and border visibility.

- Grade 3: clearly identifiable with a clear border with normal tissue
- Grade 2: clearly identifiable but without clear border with normal tissue
- Grade 1: difficult to identify and without clear border with normal tissue
- Grade 0: lesions that could not be identified

High-grade gliomas, cerebral metastases, meningiomas, ependymomas, and haemangioblastomas demonstrated a median ultrasonic visibility grade 2 or greater, while low-grade astrocytomas and oligodendrogliomas demonstrated a median ultrasonic visibility grade 2 or less. (13)

Intraoperative ultrasound in cranial surgery

IoUS is commonly used in neurosurgery for the following surgeries:

- Tumors: localization, biopsy, resection, identification of feeders or drainage blood vessels in vascular tumors, as well as for assessment of the preciosity of venous sinuses)
- Infection: localization, identification, and aspiration driven by ultrasound, as well as completeness of evacuation
- Vascular lesions: localization and identification of lesions, identification of feeders and drainage blood vessels, transience of blood vessels postoperatively
- Hydrocephalus: catheter placement
- *Arnold-Chiari* malformation: decompression assessment

Lesion localization and optimal approach planning

Ultrasound examination can provide information about the location, size of lesions, as well as the interposition or proximity of blood vessels or ventricles. Small subcortical lesions are easily identified and clearly demarcated from the surrounding parenchyma (14) (***Figure 1***).

Recently, these features were used in patients with intracerebral hematoma to complement endoscopy for minimally invasive treatment. (15)

Resection Control

During brain tumor resection, IoUS provides a quick and accurate real-time assessment and allows for optimal safe resection and confirmation of the completeness of resection of solid lesions (10).

IoUS fusion with MRI through the neuronavigation system is particularly useful for intraoperative orientation and evaluation of tumor resection and is the best method for correction of errors from neuronavigation (***Figure 2***).

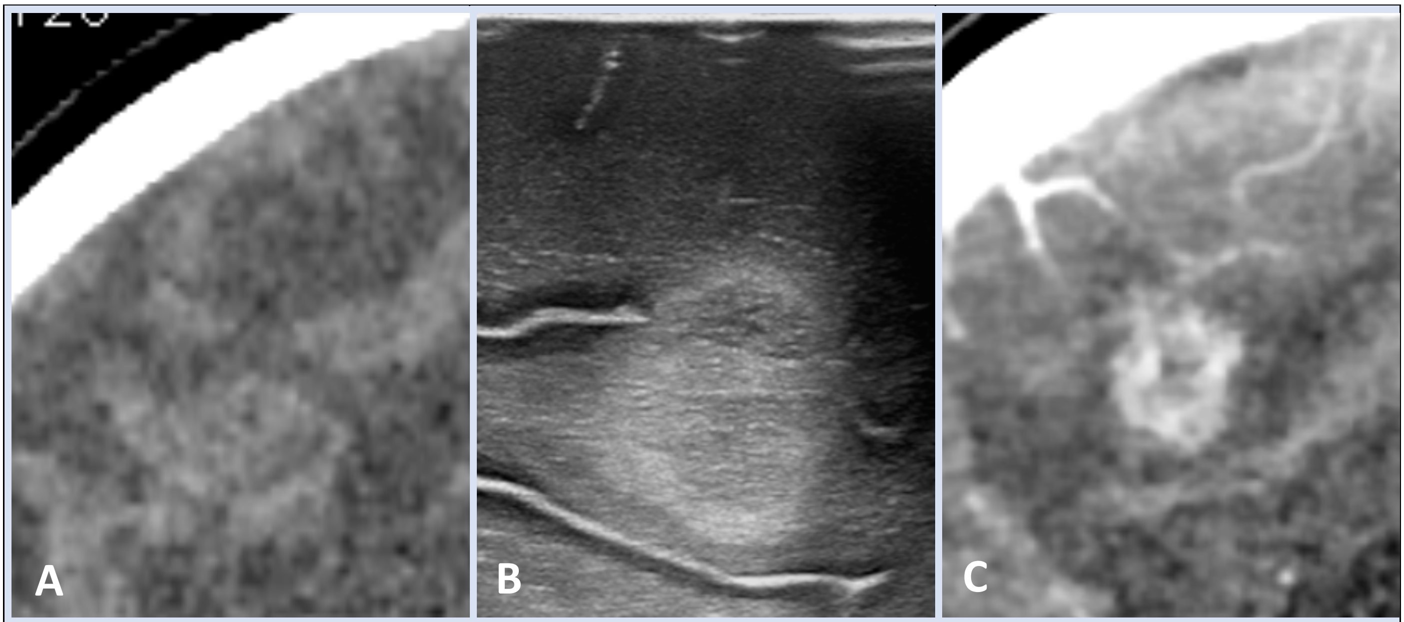

Figure 1. Comparative view of a frontal region metastasis.
A. CT without contrast enhancement; B. IoUS; C. CT with contrast enhancement.

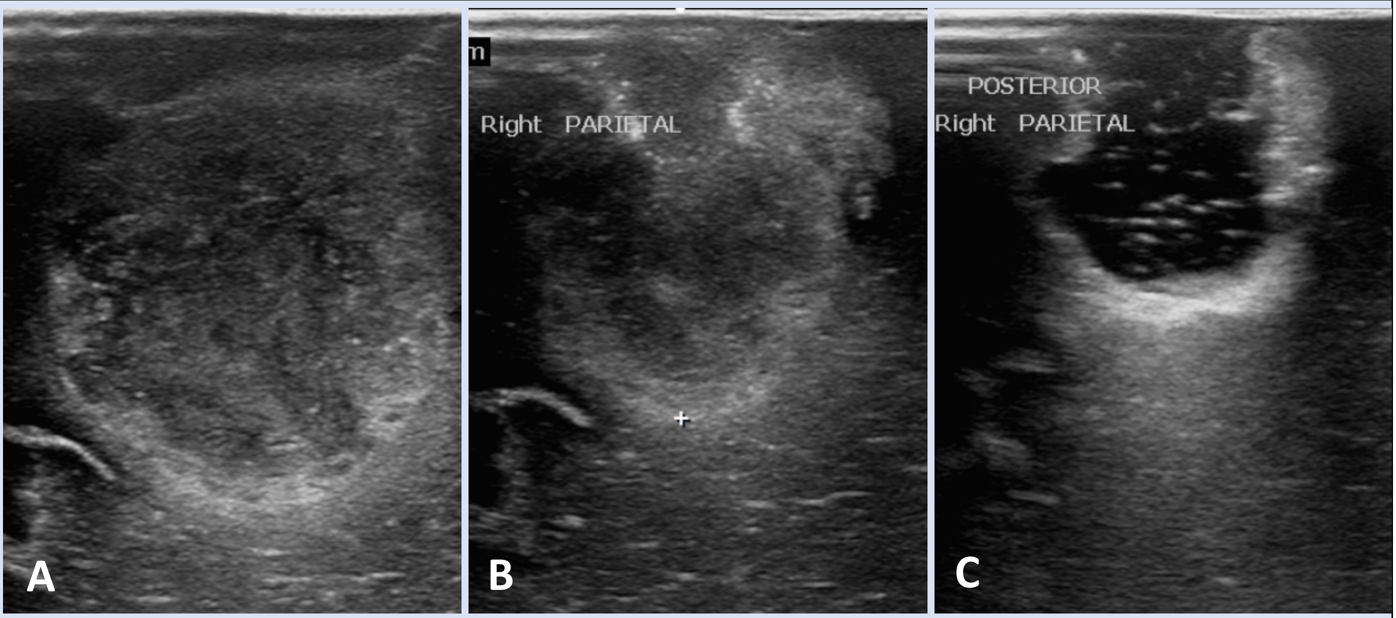

Figure 2. Intraoperative images obtained at different stages of brain tumor surgery shown in identical planes. A) before resection; B) during resection with the remainder of the tumor; C) after a complete resection.

In high-grade gliomas, contrast-enhanced IoUS in addition to 5-aminolevulinic acid guided resection allows for additional refinement and the greatest possible extent of resection (16, 17).

Vascularization and tumor features

Doppler sonography evaluation in tumor surgery allows for evaluation of the general vascularization of the lesion, localization of major arterial feeders and veins, and determination of venous sinuses patency or obliteration of the sinuses (18).

IoUS elastosonography has also elucidated key features of intracranial meningiomas, including meningioma consistency and the brain-meningioma interface, especially for hard-consistency meningiomas and those presenting with an adherent slip-brain interface (19).

Vascular neurosurgery

Micro Doppler provides information about blood flow and is useful in arteriovenous malformation and aneurysm surgeries because it enables real-time visualization of blood vessels and flow (20). This technology can also verify disruption of flow after aneurysm occlusion and identify an aneurysm inside a hematoma (21)

Early postoperative complications

After dural closure and just before repositioning of the bone flap, the final IoUS scan allows for the identification of early intracerebral hemorrhage or hydrocephalus formation (1).

Biopsy

The previously mentioned artifact feature may be used to visualize a needle in real time when performing a biopsy, and adding small dents to the top of the biopsy needle creates a visible and recognizable artifact (1). IoUS is therefore used to accurately locate a needle in the tissue when taking samples for a biopsy with results comparable to a stereotaxic biopsy while allowing additional monitoring of perioperative complications (22).

A biopsy can be performed in deep structures because real-time visualization allows for identification of the target structure and biopsy needle, while facilitating avoidance of deep anatomical structures such as the choroid plexus or large blood vessels. A three-dimensional ultrasound has proven to be the most adequate for this technique (1, 23). This technology also allows for monitoring of perioperative complications (22).

Catheter placement in hydrocephalus

The use of IoUS for the placement of permanent cerebrospinal fluid shunt catheters is associated with a decreased risk of shunt revision and may apply to temporary catheters as well (24). A burr-hole probe should be used through the same burr hole as the cather, although different burr-holes for the probe and catheter may also be drilled (25, 26).

In a study by Crowley et al., the use of IoUS was associated with a statistically significant decrease in shunt revisions, such that 21.7% of shunts required revision when the IoUS was used compared with 29.3% when IoUS was not used. The benefit of US was found to be more profound for occipital shunts (26). Recently, a study comparing the results with the use of IoUS and stereotactic navigation was started (27).

In children, neonatal acoustic windows allow quick assessment of the existence of intracranial lesions. The acoustic window has long been used in the evaluation of hydrocephalus or ventricular catheter position both intra- and postoperatively (28).

Evaluation of decompression in surgery *Arnold-Chiari* malformations

In patients with Arnold-Chiari type I malformation, decompressive surgery can be performed under IoUS surveillance, which allows assessment of ventral and dorsal decompression. Although morphological assessment is possible, evaluation of CSF flow is not, and the real impact of decompressive surgery may not be examined (29).

Education and Training

In addition to official courses endorsed by the professional societies and led by a few pioneer groups, it is important to mention that self-training options are available as well. Currently, two initiatives exist.

USim - developed by Camelot Biomedical Systems, Genova, Italy, and the Besta NeuroSim Center, Milan, Italy, as a dedicated app that transforms any smartphone into a "virtual ultrasound probe." This may simulate the application of iUS neurosurgery through a series of anonymized, patient-specific cases of different central nervous system tumors for education, simulation, and rehearsal purposes (30).

Customized Low-Cost Model for Hands-on Training - developed by the group from Tata Memorial Hospital, Mumbai, India, as an agar-based, low-cost customizable model using commonly available echogenic objects as targets. This allows the clinician to perform various training tasks like depth ultrasonography, target localization, and biopsy and resection cavity ultrasonography (31). In addition, a recent Frontiers in Oncology Research Topic on “Intraoperative Ultrasound in Brain Tumor Surgery: State-Of-The-Art and Future Perspectives” may provide further useful references (32).

Conclusion

The importance of IoUS in contemporary neurosurgery has yet to become fully recognized. Its basic functionality in localizing lesions lesions is often unmobilized, and there there are already numerous other technologies that provide reliable intraoperative information regarding all aspects of surgical substrates and operative approaches.

However, we emphasize the ease of use and likely conceptual familiarity of IoUS for neurosurgeons. We encourage all neurosurgeons to use this technique when appropriate, particularly young neurosurgeons who may come to appreciate IoUS as an essential tool in their neurosurgical armamentarium.

We hope that this manuscript will raise awareness of IoUS and its features and promote its usage among neurosurgeons in clinical practice.

Disclosures

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НЕУРОХИРУРГИЈА
The Serbian Journal of Neurosurgery

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Dear colleagues, dear friends,

Welcome to EANS2022 – European Congress of Neurosurgery – and welcome to Belgrade!

The Congress theme – **Trends, Insights, Innovations: Neurosurgery beyond Technology** – addresses the complex relation between technological advances and human ingenuity in the field of neurosurgery. The age of rapid technological progress, artificial intelligence, machine learning and virtual reality in the 21st century has brought many benefits to neurosurgery, but also many challenges.

After two turbulent pandemic years, the Congress in Belgrade will represent the regathering of European and world experts in neurosurgery. It will provide an excellent opportunity for sharing experiences and exchanging ideas through the top-level scientific program, aimed at providing a comprehensive insight into these benefits and challenges and striking the right balance between technology and human (neurosurgeons') touch.

The opportunity to hold this event of utmost scientific and social importance in Belgrade is a special honour for the neurosurgical community in Serbia and a much-appreciated acknowledgment of the enhanced regional and international cooperation in the previous period.

The Congress host city, Belgrade, has been the venue of several noteworthy international neurosurgical events over the past years – that said, we are particularly delighted to be able to host the EANS2022 Congress, which encapsulates the reintegration of the region into the mainstream of European neurosurgery.

Offering a unique blend between West and East, North and South, past and future, Belgrade will surely greet you with an open heart and an open mind.

We very much look forward to seeing you all in person next October in Belgrade!

Welcome. Explore. Enjoy.

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President of the EANS

Lukas Rasulic
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