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New opportunities in glioma therapy - awake craniotomy

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Abstract:

In some populations over the past 30 years there has been an increase of 30% in brain tumors morbidity, in Poland, over two-fold increase within three decades. Even though the diagnostics is significantly increasing, the mortality still remains high - general statistics of survival is 34%, for the most malignant cases - less than 5%. Brain tumor resection is essential not only for the overall survival, but the post-operative quality of life is as important as the survival rate. Especially in motor and language area lesions, the greater resections with lesser post-operative complications are required. The modern opportunity in favour of such circumstances is tend to grow within awake craniotomy technique.

The aim of the study is to present the newest achievements in field of neurosurgical awake surgery. For the purpose of this study, most significant works have been reviewed in period 2000-2015.

Study reveals the growing importance of awake surgery with simultaneous necessity for new pre-operative technologies, which can support the greater outcomes of the surgeries. Apart from that, the concerns of the ethical matter can be withdrawn if the valid algorythms and guidelines are applied for this procedure.

Keywords MeSH: awake craniotomy, glioma, neurosurgery

Background

The fight against tumors of the Central Nervous System dates back to the days of modern medicine and the nineteenth century, when it was the first time in 1879 that surgeon William Macewen conducted a brain tumor removal operation solely on the basis of neurological symptoms. [1] Then neurosurgery blossomed under the leadership of Harvey Cushing and Ernest Sachs, Fathers of Neurosurgery, with the development of electrophysiology, neuropathology of stereotaxis, and in the 70s and 80s, with the development of CT and MRI imaging. [1;2]

CNS tumors are the most unusual type of human cancer. First and foremost, the etiology of these hyperplasia is largely unknown, although it is attributed to many factors, including genetic factors, immunosuppression (greater probability of the primary lymphoma of the CNS) and cranial radiation (which increases the probability of astrocytoma and glioma). Their malignancy is not measured only histologically as for other tumor groups, but also within the localization - histopathologically benign tumor may be nonoperative due to the location in a critical area of the brain, such as the pons or the medulla oblongata. The hyperplasia can cause a very rapid onset of symptoms, due to the effect of mass and compression of many structures within the small area of the organ, in addition to armour of the skull. [3]

Among adult cancers, CNS tumors now account for more than 2.5% of the cases. [1] In a higher proportion of cases children are affected, with more than 20% of the cases. In some populations over the past 30 years there has been an increase of 30% in brain tumors morbidity, which shows the scale of one of the greatest plagues of the 21st century. [4] According to the National Cancer Registry, over two-fold increase in cases has been reported in Poland over the past three decades, especially in 50-year-old patients. [5] The average survival rate is unfortunately still low, with an average of about 34%, for the most severe of the CNS, glioblastoma multiforme, only 5.1%. In the United Kingdom, 10 people die from brain tumors every day, and every two hours a patient is diagnosed with brain tumor in the UK. [4]

Within the diagnostics and treatment of CNS tumors, multidisciplinary approach to the patient is extremely important. Symptoms of brain tumor include neurological symptoms (headache, nausea and vomiting, cognitive impairment, imbalance); Psychological: (from impaired thinking, impaired consciousness, frontal cortex syndrome- impulsivity, emotional lability to abulia, aphasia in the case of temporal lobe injury). [6;7] Therapy, depending on the degree and severity at the histological and molecular level, is the result of the work of neurosurgeons and neurooncologists The assessment of the severity of certain cognitive or motor functions must be performed by a neuropsychologist, neurologopedist or a neurophysiologist.

The meanders of the human mind hide the greatest variety of functions and individual variability than any other organ. Therefore, in neurosurgery, a very important aspect is the postoperative Quality of Life indicator, which differs due to the location of the resection and its extent. In many cases, CNS tumors are located in the motor or language regions of the frontal and parietal lobes, the loss of which can significantly reduce the postoperative quality of life and prevent further proper functioning. In response to the challenge of increasing QoL and reducing iatrogenic complications following surgical operations, modern surgical mapping techniques such as awake surgery are emerging.

Objectives

The aim of the work is to present the greatest achievements in the field of awake surgery and the modern challenges associated with it.

Methods

Substantial articles on awake craniotomy and awake surgery from period 2000-2015 in the Asian, European and American regions have been analyzed.

Among 294 articles related to awake surgery in neurosurgical circumstances, 24 articles were selected for analysis.

Results

"Awake surgery" in neurosurgery or "awake craniotomy" is a type of neurosurgical operation where patient is awake during tumor resection, which can be used for direct mapping of the motor, sensory or linguistic cortex. [8] Awake surgery is an extremely demanding task with its simultaneous multidisciplinarity and collaborativeness of neurosurgeons, anesthesiologists and neuropsychologists that aims for the most accurate possible resection while minimizing iatrogenic effects, and performing the greatest psychological comfort for the patient.

Awake craniotomy was created in the 1980s in North America, later implanted in Europe and Asia. [9] Today is still popular the most in Asia and the United States. In Japan, the guidelines of the Japan Awake Surgery Conference in 2012 have developed the criteria by which the patient should be qualified for surgery. [10] The most important criteria are:

* Patient age - usually between 15 and 65 years old.

* Use in Primary Motor Cortex (PMC) and Language Cortex cancers

* Its use in epilepsy is justified if macroscopically no epilepsy focus can be isolated

* It is essential to simulate surgery before the actual operation in the patient's presence

* Determine the dominant hemisphere with a Wada test or with fMRI preoperatively

* Language barrier, patient refusal, significant neurological deficits are the main contraindications to the method.

Preoperative Diagnostics and Preparation

Preoperatively, a neuropsychologist and neurologist monitors the function of the cortex within which the tumor is located, also assessing their degree of deficit. In case of brain tumors, especially gliomas with frequent recurrences, reliable preoperative detection techniques are important. [10;11] The mapping of damaged areas is performed by fMRI (brain functional magnetic resonance imaging, in which, apart from the magnetic field and radio waves, the intensity of the signal is influenced by changes in metabolic activity) and tractography (where pathways mapping is based on measuring the direction of motion of water molecules, and can reveal microscopic histological differences). [12] In motor cortex regions, fMRI and DTI (with sensitivity to 88% and 87% specificity) are the most important. [13] For language regions, fMRI is currently the most important method of mapping, followed by rTMS (Repetitive Transcranial Magnetic Stimulation), which has been shown to be able to detect partially-negative language regions before surgery and is one of the tools for routine follow-up of these patients with recurrent glioma. [14;15]

The surgical procedure

The anesthesiologist evaluates the patient and selects the most appropriate anesthetic technique "asleep-awake-asleep", "asleep-awake", "awake-awake-awake" or variants. With Asleep-Awake, general anesthesia is given at the beginning of surgery, the patient is awake from mapping to resection and termination of surgery. Asleep-Awake-Asleep (AAA) technique uses general anesthesia (Propofol / dexmedetomidine + remifentanil) at the beginning and at the end of surgery - including resection, the patient is awakened with local anesthesia while mapping strategic areas of the lesion. [16;17]

During surgery, the patient in all of the above variants is awake during intraoperative mapping, which consists of performing specific actions referred to by a neuropsychologist / neurotherapeutist such as limb movement, repetition of specific words, and even - for outstanding musicians - playing an instrument - while brain function is being monitored and mapped with electric stimulation directly on the lesion by a neurosurgeon, which allows for the most accurate localization of cortical function and removal of the tumor with the necessary margin while maintaining essential vital functions. [10;18]

The entire operation is performed under the control of the IEMAS - intraoperative screening evaluation for awake craniotomy, which simultaneously monitors mimetic response and patient behavior, neurosurgical microscope operating field, stereotaxis, vital signs and progression of neuropsychological examination. [19]

Postoperatively, the patient is also monitored neuropsychologically and neurotherapeutically to check the postoperative function of the operated brain areas.

Challenges and controversies of the method

The most controversial aspect is the patient's consciousness when performing surgery on such a sensitive and important organ. However, studies have shown a significant efficacy of awake craniotomy (AC) compared with general anesthesia (GA) in terms of greater total tumor resection (100% removal in 26% in AC versus 6.5% in GA), to higher postoperative results in Karnofsky scale in awake craniotomy and lesser hospitalization time than in patients under general anesthesia. [20-22]

With the introduction of modern preoperative mapping techniques, the next question is if it is possible to replace intraoperative awake mapping with preoperative mapping in its entirety. However, along with the current protocol, fMRI, rTMS and other imaging techniques are still insufficiently accurate to reduce the importance of awake surgery and direct intraoperative mapping, as evidenced that the value of the preoperative mapping value is less efficient than the intraoperative version (59% sensitivity and over 97% specificity of fMRI mapping in linguistic areas) as well as changes in brain volume and displacement of areas as the progress of operations is already evident in stereotactic measurements and inevitable. [23-25]

Another aspect is the perspective of the patient while performing the above neurosurgical technique so that it remains as a patient's life-saving operation and does not create traumatic experience and consequently reduce the quality of life after surgery. In recent observations of the patient's perspective on awake surgery, it has been shown that all patients tolerate the surgery well, judging by their subjective assessment the procedure is less painful than expected. The most painful was the fixation of the skull and the feeling of cold, dry mouth and long-term lying in an inconvenient position, while neurosurgery maneuvers during resection and stimulation of the areas were not painful at all. [26]

Summary

Awake surgery improves the probability of maximum tumor resection while retaining functionality for which the lesion region is responsible and reduces intraoperative mortality associated with complications (aneurysm rupture, air embolism). [27] As a result of intraoperative mapping, the likelihood of secondary focal neurological deficits is reduced. Modern non-invasive imaging techniques and cortical stimulation in the near future will be an ancillary method of preoperative mapping of the resection area. Concerns about the painfulness of a procedure are in most cases groundless when the valid algorithms are being used.

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