Oiginal article

Ukr Neurosurg J. 2021;27(4):
doi: 10.25305/unj.239697

Microvascular decompression for trigeminal neuralgia, long-term follow-up results and assessment of possible prognostic factors: a single-center retrospective cross-sectional cohort study

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Received: 07 September 2021
Accepted: 11 November 2021

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Aim: Prognostic factors detection and analysis of long-term results of microvascular decompression for trigeminal neuralgia.

Materials and methods. 161 cases of trigeminal neuralgia (TN) treatment by MVD technique without preliminary invasive interventions within 10 years were analyzed. Two blocks of information were designed which included objective case data (8 factors) and patient satisfaction survey (5 questions). Follow-up minimal cut-off was 1 year (median 5.8 years). The primary end point is the proportion of pain free patients and BNI (Barrow Neurological Institute) score at last follow-up. The secondary end point is the assessment of possible risk factors of treatment failure: symptoms duration, decompression type, affected nerve branches, neurovascular conflict visible on MRI, different indications for surgery. Logit-regression analysis was carried out. Significance level was set at $p<0,01$.

Results. Among the studied factors as predictors for pain recurrence all but one failed to reach significance threshold. Conflict on MRI ($p=0,231$), involved nerve branches ($p=0,340$), indications for surgery ($p=0,659$), number of involved vessels ($p=0,834$), achieved decompression type ($p=0,157$), venous compression ($p=0,143$), gender ($p=0,150$), affected side ($p=0,934$) did not reach the significance level. For symptoms duration $p=0,0012$.

Conclusions. As a result of multifactorial analysis of study results, the only significant prognostic factor for treatment failure (pain recurrence or worsening of obtained result) was symptoms duration at the time of surgery.

Key words*: trigeminal neuralgia; microvascular decompression; prognostic factors*

Introduction

Trigeminal neuralgia (TN) is an extremely painful, disabling condition that is difficult to diagnose and treat. Its social and economic burden determines the urgency of the problem of TN treatment. The incidence is 40-50 cases per 1 million population. The most vulnerable are people aged 35 to 65 [1, 2]. The epidemiology of the disease against the background of the demographic situation in Ukraine and Europe creates the preconditions for increasing the number of patients in the future [1, 3]. Despite the significant evolution of therapeutic approaches since the first attempts, many fundamental issues remain unresolved [4].

Published in 2019, updated guidelines that correspond to high standards of evidence of the GRADE system, specified the treatment approaches for TN [5]. It is worth noting that the data on which the guidelines are based, due to a certain inertia of the system, although have been available for a long time, have been analyzed only recently. Thus, there is a need for further profound inquiry study of this problem.

The motive for the study is a pool of data, indicating the probable negative predictive value of some factors that, according to the modern approach, are not influenced [6–8]. The validity of a step-by-step therapeutic approach from pharmacotherapy to invasive techniques with uncertain criteria and terms is questionable. Firstly, the use of the gold standard of treatment of carbamazepine has significant limitations due to its side effects. Secondly, according to randomized clinical trials data, after 5–16 years, only 22% of patients had an effect from carbamazepine, and 44% required additional or alternative treatment [9].

The assumption that constant irritation of a nerve or its entry zone can lead to irreversible damage, and that early microvascular decompression (MVD) may be

the key to more effective treatment, raised a number of questions: is it necessary to achieve complete transposition of the vessel, is the interposition of the insulating material sufficient? Do the number and nature of the vessels and nerve branches involved affect the outcome of the operation? Does the difference in indications for surgery affect the treatment outcome?

Objective: to identify prognostic factors and analyze long-term results of the treatment of trigeminal neuralgia by microvascular decompression technique.

Materials and methods

The study was carried out as a part of the research work of Subtentorial Neurooncology Department and is a part of a multicenter study. The study was approved by the Committee on Ethics and Bioethics of the Romodanov Neurosurgery Institute (Minutes №3 of June 6, 2016). Informed and voluntary written consent was obtained from all patients to participate in the study.

The main group was formed of patients with classical and idiopathic TN, who underwent MVD surgery as the primary invasive method of treatment.

Inclusion criteria: patients diagnosed with TN, MVD surgery at any stage of treatment, the presence of follow-up data for more than one year. The archive depth is 10 years. Exclusion criteria were formed on the basis of compliance of final diagnoses with the criteria of the International Classification of Headaches of the third edition for the group of diagnoses 13.1.1 "Trigeminal neuralgia" [10]. Patients whose diagnosis at the time of the first visit did not meet these criteria, as well as those whose MVD was supplemented by one of the types of rhizotomy, were excluded from the study.

161 patients (57% women and 43% men) met the criteria for enrolment. The age of patients was from 27 to 77 years (median - 59.7 years, interquartile range (IQR) - 13 years).

The data were divided into two blocks: the first - with the objective component of the case, data on the history, duration of the disease, involvement of nerve branches, findings during magnetic resonance therapy (MRI) and surgery, volumes of interventions, complications, assessment of the result according to the BNI scale (Barrow Neurological Institute) [11–14], duration of relapse-free period, etc.; the second is the assessment of the patient satisfaction with the treatment and the current state of health. Data collection was carried out by studying medical records and questionnaires of patients during follow-up examinations, by phone or mail.

The primary endpoint is the proportion of patients without pain and the score of BNI scale during last follow-up, the secondary endpoint - assessment of probable risk factors for treatment failure (duration of symptoms, type of decompression, number and location of affected branches, presence of neurovascular conflict according to MRI, difference in indications for surgery). Pain relapse was considered an increase in the score of BNI scale or grade IIIb and above at any time after surgery.

Indications for surgery were divided into two groups: ineffectiveness and intolerance to medication treatment.

According to MRI data neurovascular conflict was verified in 90% of cases.

The procedure of the MVD was carried out according to the standard technique. Surgical position is on the side. Three-point rigid fixation of the head. Combined multicomponent anesthesia. Surgical approach by ipsilateral retrosigmoid craniotomy. Wide arachnoid dissection and 360º revision of the entire cisternal portion of the root from the entry zone to the trigeminal cavity. Endoscopic assistance was used if necessary. The criterion for the presence of neurovascular conflict was the dislocation or deformation of the root as a result of contact with the vessel [5, 15, 16]. The decompression result was evaluated according to the operation report in three gradations: artery transposition, Teflon interposition, coagulation and vein cross-section. Cases with rhizotomy of any volume were removed from the analysis.

Study design: a retrospective cohort cross-sectional single-center.

The data analysis at the first level was carried out by methods of descriptive statistics with the subsequent corresponding processing. A Logit-regression analysis was used to assess the probable risk factors for treatment failure. Data processing was performed using R-statistics, StatPlus MS Excel® and SPSS packages.

Results and discussion

The majority (62.7%) of patients had a multivascular conflict. The superior cerebellar artery was involved in 81.4% of cases. The venous component was present in 61.5% of conflicts ***(Fig. 1)***. The most common combination was the involvement of the SCA and the vein in the form of a conflict of the type "hammer and anvil".

The duration of symptoms before surgery ranged from 6 to 480 months (0.5 to 20 years, median - 60 months (5 years), IQR - 72 months (6 years).

The median follow-up after surgery was 70 months (5.8 years), (IQR - 60 months (5 years)). Observation range is from 12 to 180 months (from 1 to 15 years).

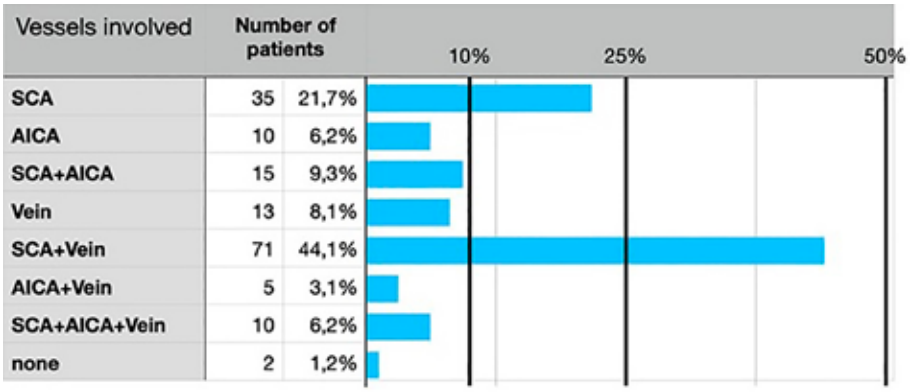
Data on the involved branches of the trigeminal nerve are given in ***Fig. 2.*** In 96 (60%) cases the right-sided localization was found, in 65 (40%) - the left-sided.

The incidence of postoperative complications was 24.2% (***Fig. 3***). Among them, facial hypoaesthesia prevailed, which persisted at the time of discharge, hearing loss, cerebrospinal fluid leak, meningitis, reactivation of herpes simplex infection, persistent headaches, and hydrocephalus were less common. One patient had more than one complication.

Assessment of the probability of painless course is shown in ***Fig. 4***. In 6 patients there was a relapse or incomplete regression of pain in the early postoperative period. In 2 cases, repeated operation was performed during the same hospitalization.

BNI pain control data are shown in ***Fig. 5***. In particular, 114 (71%) patients had no pain and did not take medication, 16 (10%) had episodic pain that

This article contains some figures that are displayed in color online but in black and white in the print edition



NVC - neurovascular conflict; SCA - superior cerebellar artery; AICA - anterior inferior cerebellar artery

Fig. 1. The nature of the NVC.

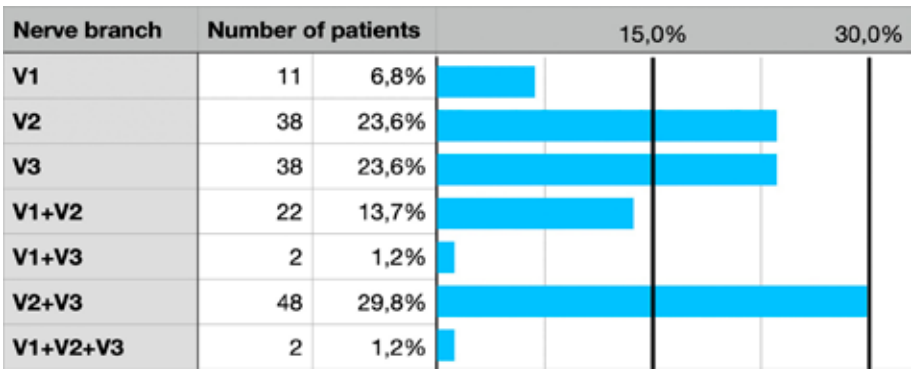


Fig. 2. Distribution of patients according to the involved branches of the trigeminal nerve

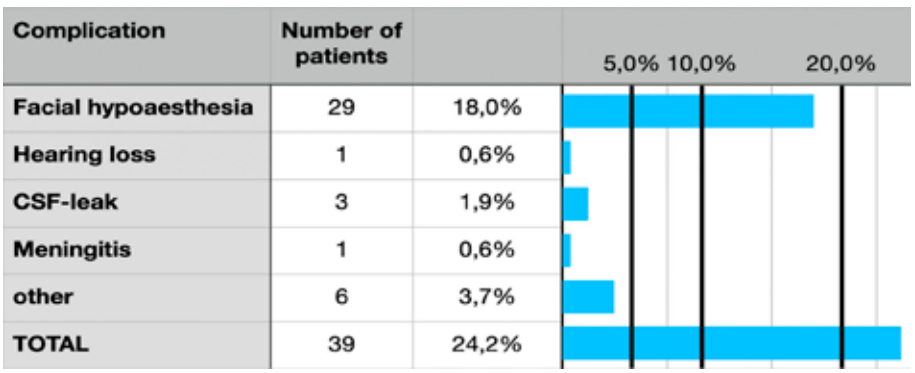


Fig. 3. Postoperative complications

did not require medication, 18 (11%) had satisfactory pharmacological control, 5 of them had no pain, significant or uncontrolled pain was registered in 12 (7%) patients.

The results of the study of patient satisfaction with the current state of health and treatment are shown in ***Fig. 6.***

When studying possible predictors of pain relapse among the studied factors, the level of significance overcame only by the indicator of the duration of symptoms (p = 0.0012). Conflict according to magnetic resonance imaging (p = 0.231), involvement of nerve branches (p = 0.340), indication for surgery (p = 0.659), number of vessels involved (p = 0.834), achieved type of decompression (p = 0.157), the presence of venous compression (p = 0.143), gender (p = 0.150) and the side of the lesion (p = 0.934) did not reach the critical level of significance.

A limitation of the study is a single-center nature, which can affect representativeness of the sample, high-volume center bias, single-surgeon bias, exclusion of a large proportion of patients, in particular including clarification of diagnostic criteria, and imperfection of data collection system.

The advantages include long-term follow-up, the median of which exceeds the 5 years typical for most studies. A large number of observations for studies of this design indirectly indicates a small Type II error.

The high frequency of venous conflict detection compared to the literature data may be due to difference

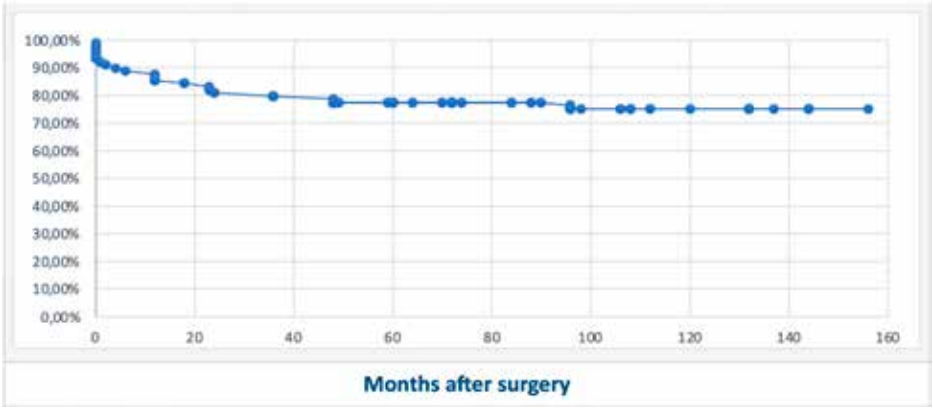


Fig. 4. Percentage of patients without pain at different stages after surgery

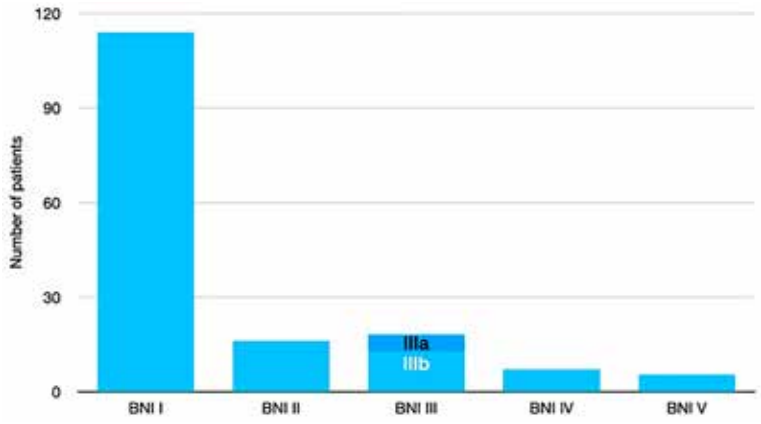


Fig. 5. Assessment of pain on the BNI scale during the last control

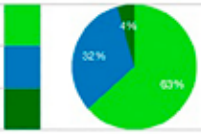
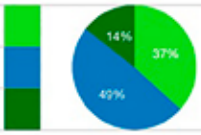
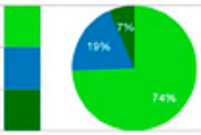
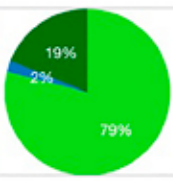
Looking back now, how would you consider the timing of your surgery?			
Should have been earlier	102	63,3%	
About right	52	32,2%	
Could have been delayed	7	4,4%	
How long did it take you to completely get over the operation?			
Average, weeks	11,7	3 patients reported: - «still not».	
Median, weeks	4		
IQR, weeks	0-104		
How well did this operation meet your expectation?			
Better than expected	59	36,7%	
Just as expected	79	48,9%	
Worse than expected	23	14,4%	
Overall, how satisfied are you with your current situation?			
Satisfied	120	74,4%	
Slightly Unsatisfied	30	18,9%	
Unsatisfied	11	6,7%	
If you needed treatment again, what treatment would you choose?			
The same surgery	127	78,9%	
Other surgery	0	0,0%	
Drug therapy	4	2,2%	
Unsure	30	18,9%	

Fig. 6. Patient satisfaction with health and results

in the alertness of surgeons from different schools [17–19], this may result in both overdiagnosis and underdiagnosis. This requires the development of more objective criteria and tools with high interobserver agreement.

A significant disadvantage of the study is the absence of blinding both in relation to the side of the lesion in the analysis of magnetic resonance imaging, and the surgeon on the results of MRI. This probably explains the fact that the percentage of detected neurovascular conflicts according to MRI was 90% with 100% specificity, which is consistent with the literature on sensitivity, but significantly exceeds the specificity of the method.

Data of other authors, the results of morphological studies and modern ideas about the mechanisms of pathogenesis [6, 20, 21] indicate the need to study the role of early MVD in the treatment of patients in spite of the current therapeutic paradigm.

Known prognostic factors of long-term effectiveness of the MVD (neurovascular conflict according to MRI, age, gender, number and nature of involved vessels, etc.) [22], according to our data, did not demonstrate a significant impact on long-term outcome. This requires randomized clinical trials to determine the actual strength of the effect of a particular factor and the significance of its minimal clinical effects.

Conclusions

In a multifactorial analysis of the study results, it was found that the only significant prognostic factor for treatment failure (pain relapse or worsening of obtained result) was the duration of symptoms at the time of surgery ($p = 0.0012$).

It is important to observe the principles of modern classification and diagnosis of the disease, which allows for a more careful stratification of patients when choosing treatment methods and for conducting the research, as a large number of patients were excluded from the study due to non-compliance of the determined diagnosis with modern criteria for trigeminal neuralgia, including classical.

Disclosure

Conflict of interest

The authors declare no conflict of interest.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

The written informed consent was obtained from each patient or appropriate family member before the surgery.

Funding

The research had no sponsor support.

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