Diagnostic and predictive factors of perioperative comorbidities in the treatment of hydrocephalus

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Introduction: The objective of this study was to demonstrate the predictive value and the presence of diagnostic comorbidity and perioperative factors in the outcome of shunt surgery for hydrocephalus.

Methods: We retrospectively analyzed a series of 32 patients who underwent surgery for NTH on Neurosurgical Service KBC Zemun in the 2006-2012 period year. Diagnostic factors were analyzed: clinical signs (gait disturbance, cognitive deficits and incontinence), Evans’ index and lumbar puncture. Perioperative comorbidity factors analyzed were: arterial hypertension, diabetes mellitus, and cerebrovascular insult.

Results: Of the total of 32 operated patients had gait disturbance, cognitive deficits 24 and 23 urinary incontinence. Improving gait disturbance had 20, 13 had cognitive deficits and 11 urinary incontinence. Improvement of gait disturbance was significantly different (p<0.05) than the other two improve clinical signs. Of the factors of perioperative comorbidities, hypertension was the most common 24, with diabetes mellitus showed a statistically significant predictor of unfavorable outcome (p = 0.029).

Conclusions: gait disturbance proved to be the most common diagnostic NTH factor and the factor that has the best prognosis in patients operated for NTH, while DM is the most common factor of perioperative comorbidities.

Key words: normotensive hydrocephalus, treatment outcome, comorbidity

INTRODUCTION

Hydrocephalus is a term that is well known in medicine since the time of Hippocrates and by itself does not represent a particular disease, but a manifestation of various etiological factors that lead to disruption of production, circulation and resorption of cerebrospinal fluid. The first morphological description of hydrocephalus, which it defines as the ventricles enlarge at the expense of reduction of brain tissue, gave Andreas Vesalius in the sixteenth century. The first modern classification of hydrocephalus was proposed by Dandy:

1. hydrocephalus due to hypersecretion of CSF,
2. hydrocephalus due to disturbed CSF circulation and hydrocephalus due to third disorders of CSF absorption.

Dandy and Blackfan in the early decades of the twentieth century, with limited diagnostic procedures such as lumbar puncture, ventricular puncture and skull radiography, established a division of hydrocephalus, which based on the existence of communication between the chamber system of the brain and lumbar bag (which was checked by inserting color intraventricular and a subsequent lumbar puncture) to communicating and non-communicating hydrocephalus. Ransohoff et al have supplemented this division; they noticed that the site of obstruction can be Silvio’s aqueduct and outlet fourth ventricle, and named it non-communicating or intraventricular obstructive hydrocephalus. Hydrocephalus in which there was communication between the ventricular and lumbar bags, but there was an obstruction at the level of the basal subarachnoid cisterns or in an area of the terminal absorption of cerebrospinal fluid called the extraventricular obstructive hydrocephalus. Depending on whether the expanded ventricular or subarachnoid cerebrospinal fluid compartments hydrocephalus is divided into internal and external. According to the course, hydrocephalus is divided into acute, subacute and chronic, and in relation to before and postnatal occurrence of the congenital and acquired. Normotensive hydrocephalus (NTH) allocates a unique clinical entity, which was introduced into modern medical practices of the 60’s of the twentieth century in the works of Hakim and Adams that define it: the classic clinical triad (dementia, incontinence, gait disturbance),
enlargement of the chamber system of the brain normal intracranial pressure\textsuperscript{5,6}. It belongs to a group of acquired chronic communicating hydrocephalus, and depending on whether is known or unknown causes, it is divided into primary (idiopathic) normotensive hydrocephalus (pNTH) and secondary normotensive hydrocephalus (sNTH). Secondary normotensive hydrocephalus occurs on the basis of a previous subarachnoid hemorrhage, meningitis and traumatic brain injury. Normotensive hydrocephalus is considered one of the treatable causes of dementia and represents 6\% of all causes of dementia\textsuperscript{1}. The incidence of hydrocephalus at the global level varies from 0.2 to 5.5 newly formed cases per 100 000 inhabitants per year, while the prevalence in children up to 65 years 0.003\%, and age over 65 years from 0.2 to 2.9\%\textsuperscript{7,8}. Normotensive hydrocephalus is a significant health disorder which adequate and timely treatment leads to improved quality of life for elderly people. Cerebrospinal fluid (CSF) is produced by ultrafiltration and active secretion in the choroid plexus of the brain chamber system\textsuperscript{9,10}. A smaller amount of CSF is produced in ependymoma ventricles and brain parenchyma. Daily create about 400-500ml fluid (0.35ml/min). The volume of cerebrospinal fluid varies from 130-170ml and changes with age, while the volume of CSF in the brain ventricles around 15-20ml and represents about 25\% of the total amount of CST's. The average pressure of the cerebrospinal fluid in the newborn is 40-50mmH\textsubscript{2}O, while in adults ranges from 100-200mmH\textsubscript{2}O\textsuperscript{11,12}. Once created CSF, pulsatile circulated through the chamber system of the brain and through openings fourth ventricle (Luschka and Magendie) exceeds supply the cistern in the basement of the brain, where it circulates mainly in the spinal subarachnoid space and back, and partly through the basal cisterns of the brain in the subarachnoid space of the convexity of the brain, to place their absorption into dural venous sinuses through the arachnoidal villi. A smaller part of the cerebrospinal fluid is absorbed directly into the venous capillaries and lymph through the spinal and cranial nerves\textsuperscript{13}.

\textbf{MATERIALS AND METHODS}

The study included 32 patients who were surgically treated for hydrocephalus in the Neurosurgery Service KBC Zemun, in the period from January 2006 to June 2012. The study includes all patients who were operated within the specified period, regardless of whether it was a primary or secondary hydrocephalus normotensive normotensive hydrocephalus. Diagnosis NTH-and was based on the presence of a minimum of two cardinal clinical signs: CT or MR examination finding. All operated patients were treated with ventricular-peritoneal shunt surgery, where the used systems with flow-regulated valvular medium pressure without additives anti-siphon equipment. The study was designed as a retrospective descriptive case series study.
### DISCUSSION

Half a century has passed since Hakim in 1965 in a series of three patients (two with sNTH and one with pNTH) singled NTH as a distinct clinical entity, but the validity of its concept is still the subject of much debate stemming from numerous clinical studies of NTH since the 60s of the twentieth century until now.\(^{15-19}\) It is still accurate incidence and prevalence NTH's unknown, clear diagnostic criteria have not been established, studies of pressure on cerebrospinal fluid were not for all patients with NTH's uniform and there is no systematic analysis of the natural course of NTH’s.

Although the extended lifespan and development of medical science dictates that the number of patients who are hospitalized and operated because of NTH from year to year grows, there is no consensus on the most important issues such as: etiology, pathogenesis, diagnosis and prognosis of NTH's. Regarding the etiology and pathogenesis of authors described the various morphological changes such as thickening and fibrosis arachnoida, inflammatory changes in the arachnoid granulations,ependymal disruption chamber, subependimal gliosis, multiple infarcts caused by atherosclerosis and pathological changes (senile plaques and loop neurofibrila characteristic of Alzheimer's disease), generally accepted standards for post-mortem neuropathological confirmation of the diagnosis of NTH-a for now still doesn’t exist.\(^{20}\) Even the gold standard in the diagnosis of NTH, the favorable outcome of shunt surgery, is called into question, since it is assumed that there is a lot of false negative and false positive results.\(^{20}\) False-negative results largely unrecognized condition coexisting neurodegenerative diseases (Alzheimer's disease and Parkinson's disease) and shunt malfunctions, while the false-positive results associated with chronic compensated hydrocephalus and other chronic communicating hydrocephalus which by definition does not belong in NTH, such as long-open adult ventriculomegalgy and Blake's posterior fossa cyst. As for the long-term prognosis and treatment of NTH and how NTH's disease of older age, for now doesn’t exist proper prospective, controlled study with the level of evidence 1 or 2 on long-term outcome of operative treatment. For now, all studies show that the initial positive treatment outcome, some authors claim up to 95% in the later course of the disease significantly reduced. The average adherence to the treatment pNTH is around 66%, and sNTH's about 87%\(^{21}\). In our series, all the surgical patients have had a stroke disorder in the clinical picture. The representation of gait disturbances as a clinical sign ranges from 94-100%\(^{22}\). Ojeman et al were the first group of authors who are back in 1969, noted that the walk disturbance is the most common and earliest sign of NTH-a\(^{19}\). From these first studies until now, most authors reported that the walk disturbance is clinical signs that are usually occurs first, and as such is a good sign of treatment pNTH-a\(^{24-25}\). Gait disturbance after the appearance of the other two cardinal clinical sign has a bad prognostic sign, and according to Blake & Associates has a negative predictive value of 83%\(^{26}\). In our series of 32

### TABLE 1

<table>
<thead>
<tr>
<th>Disruption</th>
<th>Cognitive deficit</th>
<th>Incontinence</th>
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<tbody>
<tr>
<td>Present</td>
<td>32(100%)</td>
<td>24(75%)</td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
<td>8(25%)</td>
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**THE RESULTS**

In a retrospective analysis are shown in 32 patients operated for NTH-a (VP shunt) in the period from January 2006 to June 2012 in Neurosurgery KBC Zemun. All patients were between 45 and 74 years, the average age of the patients was 65.45 g (SD 6.6 g). Median age was 66 years. Most of the respondents were in the seventh decade of life and that 20 of them or 62.5%. 20 of them or 62.5% had a positive treatment outcome (neurological improvement) while 12 or 37.5% had no changes in neurological status after operative treatment. The average age of patients with a positive outcome of treatment was approximately 62 years (n=20, x=62.6, Med=66, SD=6.43, CVI=10%), and the average age of patients with no change in the postoperative was 70 (n=12, x=71.25, SD=2.78 CV=3%, Med=70). Student's T-test demonstrated a statistically significant difference in relation to the age of patients with improvement after operative treatment of NTH and patients without changes in neurological status after operative treatment of NTH-a (t=3.785, df=30, p<0.05). (Figure 1) From the total number of treated patients, 32 (100%) patients had a stroke disorder, 24 (75%) cognitive deficits and 23 (72%) urinary incontinence. (Table 1) Diabetes mellitus as a factor of preoperative comorbidity is an adverse prognostic factor in anticipation of recovery of cognitive and sphincter function, and functions coordinated movements of walking. With the Fisher exact test is shown a statistically significant difference between the groups of patients with DM and patients without DM in relation to the outcome of treatment. (p=0.029, p<0.05). Patients with gait deficits had improvement in 20 cases, or 62.5%, cognitive deficit improved in 13 patients or 54.17%, and urinary incontinence in 11 patients or 47.82%. Improvement of walking statistically significantly different compared to the other two cardinal signs (χ² = 4.941, df = 1, p<0.05). From 32 patients operated because of NTH, in our series of 9 patients or 28.12% had complications of operative treatment in terms of symptomatic subdural collection and audit of the shunt due to hypofunction of the shunt. Of these, 6 patients or 18.75% had symptomatic subdural collection, while 3 patients or 9.37% had hypofunction shunt later in the postoperative period for which has been performed shunt revision.
patients, 20 of them or 62.5% had an improvement of walking in the postoperative treatment. According to the latest Japanese clinical guidelines for pNTH’s from 2012, the percentage ranges from 58-90%, so that our series fits in this average. Also, the outcome of treatment in our study were followed for an average over a short time interval (average 8 months), and the walk is a neurological disorder deficit which significantly improves previously in relation to two other clinical signs. Cognitive deficit (dementia) was present in our series at 24 and 75% of patients. Average of cognitive deficit at diagnosis NTH’s ranges from 78-95%. Cognitive deficit is a clinical sign NTH, which is the weakest and the latest recovery after shunt surgery and for its adequate preoperative assessment and postoperative follow-up is necessary to improve the use of quantitative neuropsychological measures. In our series of assessments of cognitive deficit was qualitative, based on a review of examiners and heteroamnestic, which should be taken into account when analyzing the data. According to Thomsen et al improvement of cognitive deficit is at pNTH’s around 40-60% while in sNTH’s about 90%25. Japanese clinical guidelines for the treatment pNTH’s says that this percentage varies from 28-90% for pNTH’s. In our series, improvement of cognitive deficit had 13 or 54% of the patients (the study was retrospective), cognitive deficit was not detected quantitatively rather than qualitatively before and postoperatively, and the mean follow-up of 8 months is not enough to obtain a true picture of the outcome of treatment for cognitive deficit. It is believed that the optimum year follow-up in order to obtain reliable data on the improvement of cognitive deficits following surgery pNTH’s. Urinary incontinence as a clinical sign in the diagnosis of NTH is represented by 45%-90%. In our series, 23%/72 patients had any of the three degrees of urinary incontinence. The presence of urinary incontinence with any of the clinical signs of NTH and reduces the chance of long-term functional recovery of patients with NTH-after shunt surgery with a positive predictive value of 32-37% as a predictor31. Nevertheless, the clinical manifestation of incontinence, which is earlier and better recovery in patients with NTH than in patients with dementia. Improvement of incontinence after shunt surgery in our series had 11 ili 48% of the 23 patients who had had in the preoperative period.

CONCLUSION

Our results over the cumulative follow-up of 276 months, indicating that in two thirds of patients after placement of the VP shunt is expecting a significant recovery: improving the coordination of walking 62.5%, of the cognitive deficits in 54.17% and urinary incontinence in 47.82% of cases. Based on the statistical evaluation justified predictors of placement of ventriculo-peritoneal shunt and good outcomes were defined: age of 60 years, absence of diabetes mellitus and the dominance of gait disturbances in a clinical trias.

SUMMARY

EPILEPSIJA KAO INICIALNI FAKTOR KLINIČKE PREZENTACIJE ARTERIOVENSKIH MALFORMACIJA MOZGA – PRIRODNI TOK I FAKTORI RIZIKA

Cilja rada: Cilj rada je bio da se pokaže prediktorna vrednost i zastupljenosti dijagnostičkih i perioperativnih faktora komorbiditeta u ishodu šant operacija zbog normotenzivnog hidrocefalusa.


Rezultati: Od ukupnog broja operisanih pacijenata svih 32 su imali poremećaj hoda, 24 kognitivni deficit i 23 urinarnu inkontinenciju. Poboljšanje poremećaja hoda je imalo 20, kognitivni deficit 13 i inkontinenciju 11. Poboljšanje poremećaja hoda je statistički značajno razlikuje (p<0,05) od poboljšanja druga dva klinička znaka. Od faktora perioperativnog komorbiditeta hipertenzija je bila najzastupljenija 24, dok se diabetes mellitus pokazao kao statistički značajan prediktor nepovoljnog ishoda lečenja (p=0,029).

Zaključak: Poremećaj hoda se pokazao kao najzastupljeniji dijagnostički faktor NTH-a i faktor koji ima najbolju prognozu kod pacijenata operisanih zbog NTH-a, dok je DM najzastupljeniji faktor perioperativnog komorbiditeta.

Ključne reči: normotenzivni hidrocefalus, ishod lečenja, komorbiditet.

REFERENCES:


