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The Outcomes of Endoscopic Third Ventriculostomy in the Treatment of Hydrocephalus: 317 Pediatric and Adult Cases

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ABSTRACT

AIM: To evaluate the role of endoscopic third ventriculostomy (ETV) as a primary or secondary treatment for hydrocephalus and factors affecting ETV success.

MATERIAL and METHODS: Pediatric and adult patients with symptomatic hydrocephalus treated with ETV during 11 years (2008–2019) in our clinic were retrospectively evaluated. Patients were divided into primary ETV group, in which ETV was the first method of hydrocephalus treatment, and secondary ETV group, in which cerebrospinal fluid (CSF) drainage procedures were initially attempted. Statistical data analyses were performed to compare the outcomes of primary and secondary ETV groups.

RESULTS: In total, 317 patients treated with ETV [140 (44%) patients aged 3–18 years and 177 (55%) aged 19–80 years] were followed-up for a mean duration of 60 months. Primary and secondary ETV groups comprised 207 and 110 patients, respectively. Further, 170 (82%) patients in the primary ETV group and fifty-nine patients (53%) in the secondary ETV group benefited from ETV. Primary ETV was associated with the highest probability of success (OR: 11.87). Increasing age (OR: 0.97) and male sex (OR: 4.719) increase the probability of achieving success. The overall prediction accuracy of the model was 72.2%. Kaplan–Meier survival analysis showed no significant difference between categorical groups in terms of time to failure (1.3 and 5 years), sex, ETV type, and categorized age (below 18 and above) ($p > 0.05$). Complications occurred during or after ETV in 14 patients.

CONCLUSION: Unlike most studies, our study includes both adult and pediatric groups. According to the findings obtained in our study, the recovery rate was higher in the primary ETV group (82%) than in the secondary ETV group (53%). According to the model we created, our prediction rate of recovery was 72%. Primary ETV, male sex, and advanced age are important predictors of success in ETV.

KEYWORDS: Hydrocephalus, Endoscopy, Third ventriculostomy, Primary ETV, Secondary ETV

INTRODUCTION

Endoscopic third ventriculostomy (ETV) was performed for the first time by Mixter in 1923 (21). It was performed using an urethroscope in pediatric patients with obstructive hydrocephalus. Putnam modified this urethroscope for intracranial use (25). However, high error rates, poor outcomes, and progression in ventricular shunting have been the most significant obstacles to the process in terms of ETV applications. ETV applications have increased in number with technological advances in surgical techniques and instruments and increased imaging quality (14,15). ETV is the most commonly used neuroendoscopic procedure in the management of hydrocephalus (1,6). Although it is most commonly used for the treatment of hydrocephalus due to aqueductal stenosis, its use has increased in recent years for

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the treatment of other cases of communicating hydrocephalus. In addition, although this practice has become traditional among neurosurgeons, there is a significant learning curve of the procedure in terms of reducing complications (1,6), and most of the complications can be very serious in nature. These complications can occur intraoperatively (bradycardia, hemorrhage, and damage to the neural structure) and postoperatively (hygroma, hematoma, cerebrospinal fluid (CSF) leakage, infection, and seizures). It is mandatory for surgeons to get full insight into these threats.

There are now numerous studies in literature regarding the long-term outcomes of ETV in the pediatric population, and some case series have reported data on mixed study groups including pediatric and adult patients (3,18,23). However, large population studies focusing only on the role of ETV in adult hydrocephalus are relatively inadequate, except for few studies reporting only with a limited duration of follow-up (5,8).

There is evidence suggesting that young age in children predicts poor outcomes after ETV (7), and some evidence suggests a role for the etiology of hydrocephalus on the outcomes after ETV (5,7,11,17). The role of ETV in the management of hydrocephalus in adults has been less extensively studied. Given the different physiology of cranial development, intracranial adaptation and production, and absorption of CSF, the findings of pediatric studies may not be applicable to adults (20).

This study aimed to investigate the efficacy of ETV in hydrocephalus treatment in a mixed group of patients including adult and pediatric patients and to evaluate the predictors of ETV success according to primary and secondary ETV, categorized age (0–18 and 19–80 years), and sex by creating a regression model owing to the high number of cases.

MATERIAL and METHODS

Patient population

We retrospectively evaluated cases undergoing ETV due to hydrocephalus in Adana Numune Training and Research and Adana City Hospitals between 2008 and 2019. The study site together with the neighboring provinces has a population of as high as 10 million. All cases of hydrocephalus are referred to our hospital, which is a reference hospital for ETV procedures. Considering the above, we have increased our experience owing to a sufficient number of cases from all adult and pediatric age groups and presence of only one surgical team. The study group comprised patients who exhibited clinical signs of increased intracranial pressure and who were diagnosed for the first time with hydrocephalus based on the imaging methods and who underwent ventriculoperitoneal (VP) shunt placement. In radiological workup, all patients underwent preoperative 3T magnetic resonance imaging. Disease etiology was investigated using MRI scans, if present. All structures, including the third ventricle and prepontine cisterns, were examined. Patients with hydrocephalus who did not preciously undergo any form of CSF drainage were included in the primary ETV group, and those with recurrent hydrocephalus after undergoing VP shunt placement were included in the secondary ETV group. Patients under 3 years of age were not included because of the presence of a persistent open fontanelle and physiological differences.

Duration of Follow-up

Patients with a follow-up period of at least 1 month were included in the study. The persistence of hydrocephalus findings after surgery and the need for revision surgery were defined as failure. This does not include temporary CSF drainage measures such as ventricular puncture, lumbar puncture, and external ventricular drainage placement. Postoperative duration of follow-up was calculated from the initial ETV to ETV or end of follow-up period.

Statistical Analysis

Demographic characteristics of the patients and surgical characteristics were summarized using descriptive statistics. Kolmogorov–Smirnov test was used to check whether continuous variables were normally distributed. Furthermore, chi-square test was used in univariate analysis of categorical variables. Kaplan–Meier curves (Figure 1A-C) were used to predict failure-free ETV survival and success scores at 1, 2, and 5 years. Binary logistic regression analysis was used to evaluate the relationship between the independent variables and ETV success as the dependent variable. P-value of less than 0.05 was considered statistically significant.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee (Adana City Training and Research Hospital Ethical Committee, KY2020-58-890) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

RESULTS

Patient Characteristics

A total of 329 patients underwent ETV. The procedure was terminated during surgery in 12 of them (3.6%). The ETV procedure was abandoned due to bradycardia in five, severe obstruction in the foramen of Monro in two, lack of anatomical landmarks in the base of the third ventricle in three, and possible presence of the posterior cerebral artery protruding from the tuber cinereum in two. These patients underwent VP shunt placement. With the exclusion of these 12 patients, 317 patients were analyzed in terms of ETV procedure (185 men and 132 women). In total, 207 (66%) patients underwent primary ETV and 110 (34%) underwent secondary ETV.

All patients presented with the symptoms of hydrocephalus, including intracranial hypertension and other typical neurological symptoms such as cognitive dysfunction and difficulty in walking. Factors causing hydrocephalus are shown in Table I. There were complications during and after ETV in 14 patients, 3 of whom had mild hemorrhage during the procedure, 3 had CSF leakage, 1 had intraparenchymal abscess (Figure 2A-H), 1 had transient oculomotor nerve palsy (Figure 3A-D), 3 had transient abducens paralysis, 2

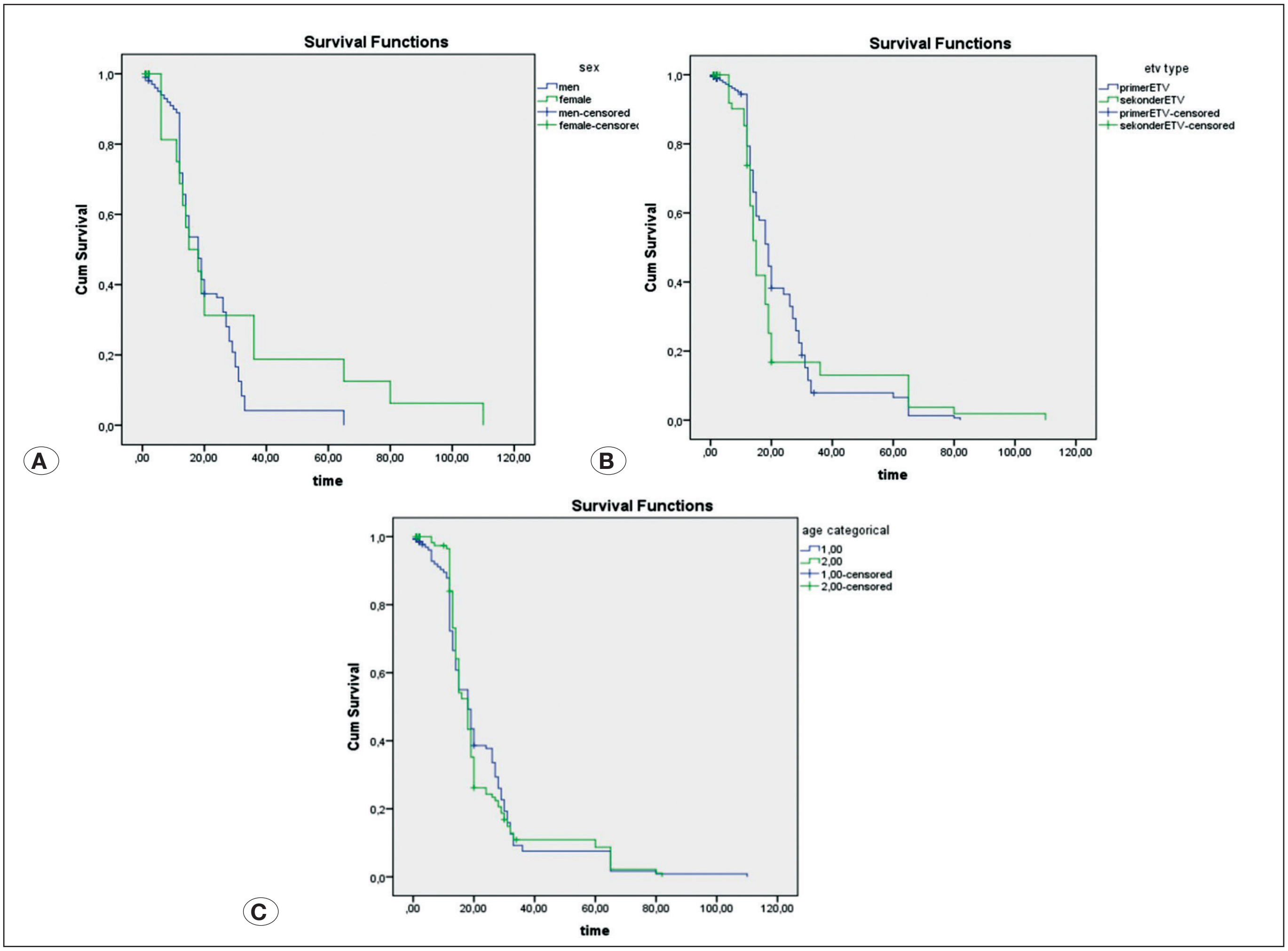

Figure 1: Kaplan–Meier curve: comparison by **A)** sex, **B)** ETV type, and **C)** categorized age.

had asymptomatic subdural hematoma, and 1 died of basilar artery injury during the procedure.

The mean duration of follow-up was 62 months (range 1–82 months). in the primary ETV group and 42 months (range 1–110 months). in the secondary ETV group. In independent samples t-test that was performed to evaluate whether primary and secondary ETV types influenced the mean duration of follow-up (during the period until the first revision or time period when there was no hydrocephalus attack), no significant difference was observed between the mean duration in the primary ETV group ($\bar{X}$A: 19.16) and that in the secondary ETV group ($\bar{X}$A:12.68) ($t_{(317)}$ = 3.36, p>0.05).

Patients showing no improvement after ETV underwent repeat ETV within the first month. Fifty patients in the primary ETV group underwent repeat ETV within the first month owing to clinical and radiological findings of hydrocephalus. Of these patients, 37 underwent shunt placement due to procedural failure. Twelve patients benefited from ETV. One patient died during surgery due to basilar artery rupture. Moreover, 60 patients in the secondary ETV group underwent repeat ETV within the first month owing to recurrent clinical and radiological findings of hydrocephalus. Clinical improvement was noted in 10 patients, and 51 patients underwent shunt revision due to failure in repeat procedure.

The mean age was 33 ± 22 years (median 29 years, range 3–80 years) in the primary ETV group and 16 ± 11 years (median 14 years, range 3–48 years) in the secondary ETV group. The regression model in binary logistic regression analysis of age, ETV type, and sex, which are assumed to be independent predictors of ETV success, was found to be statistically significant ($x^2_{(3)}$ = 84.888, p<0.05). The independent variables, particularly primary ETV, age, and sex, were significant predictors with an alpha of 0.05. Among these factors, primary ETV had the highest probability of achieving success (OR: 11.87). Increasing age (OR: 0.97) and male sex (OR: 4.719) increased the probability of achieving success. The overall prediction accuracy of the model was 72.2%.

Kaplan–Meier analysis showed significant differences between males and females in terms of time to failure (log rank (Mantel–Cox), p=0.113; Breslow (generalized Wilcoxon), p=0.851; Tarone–Ware, p=0.458; p>0.05) (Figure 1A).

Table I: Demographic distribution of ETV patients according to categories

	Primary ETV	Secondary ETV	Total
Number	207	110	317
Sex Male Female	120 86 1 (dead)	65 45	185 131 1 (dead)
ETV Success Rate	81.6%	53.64%	72%
Patients undergoing shunt placement	37 (17.8%)	51 (46.36%)	88
Mean age (years)	33 (3–80)	16 (3–48)	
Mean duration of follow-up (months)	62	42	60
# of patients in accordance with age group 3–18 years 19–80 years	52 155	88 22	140 (44%) 177 (55%)
Hydrocephalus			
Aqueductal stenosis	131	64	195 (61.5%)
Tumor	36	21	57 (17%)
IVH	19	4	23 (7%)
Communicating hydrocephalus (NPH, non-NPH, Skull trauma, and postop craniotomy)	14	8	22 (6.9%)
Other causes	12	8	20 (6.3%)

***IVH:** Intraventricular hemorrhage, **NPH:** Normal pressure hydrocephalus.*

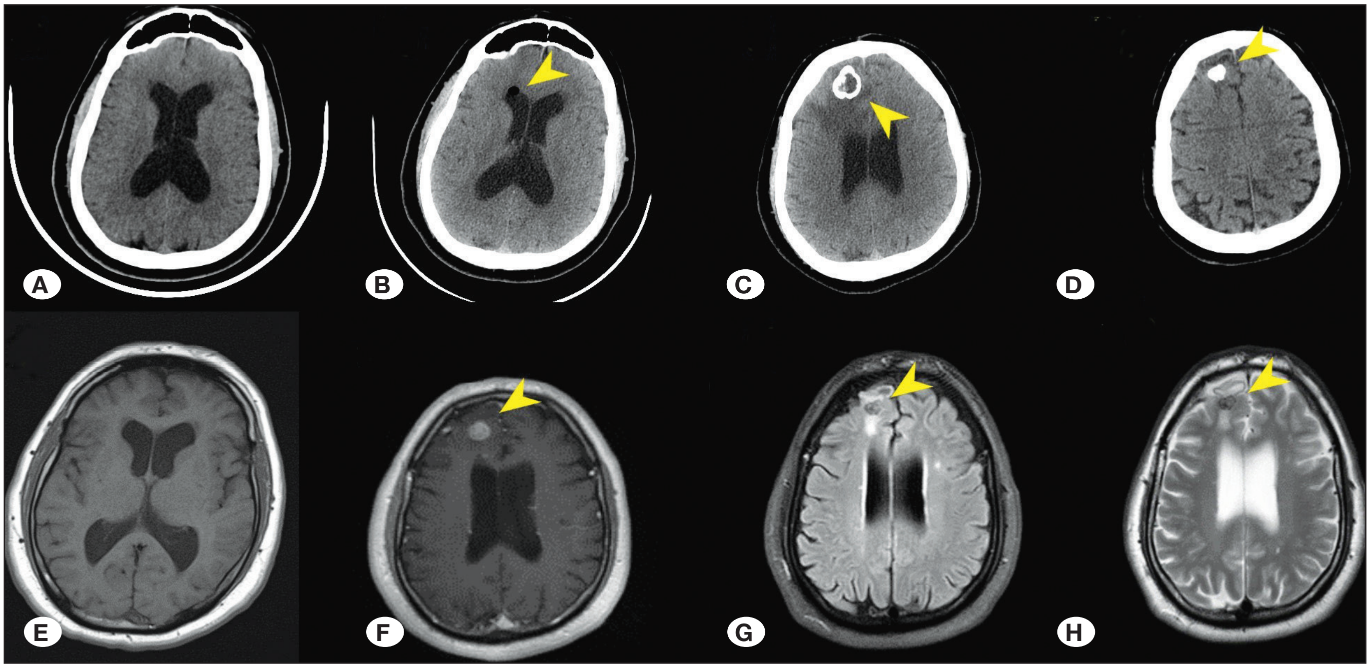

Figure 2: A–E) Preoperative: CT and MRI; **B)** postoperative day 1 CT; arrowhead shows pneumocephalus; **C)** postoperative 1 month CT; arrowhead shows abscess; **D)** postoperative 1 year CT; arrowhead shows residual abscess; **F)** postoperative 1 month MRI; arrowhead shows abscess; **G-H)** postoperative 1 year MRI; arrowhead shows traces of sclerotic abscess.

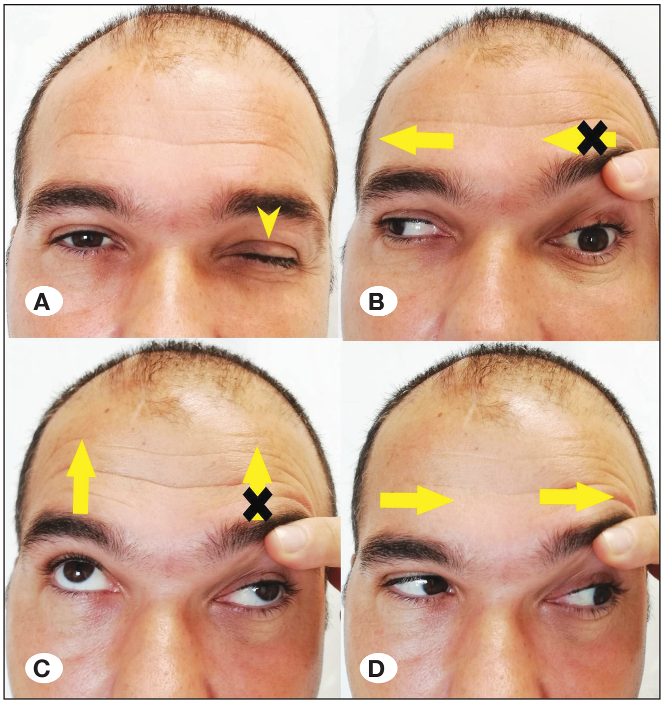

Figure 3: Oculomotor nerve palsy: **A)** lowered left eyelid in the neutral position (indicated by the arrowhead), and **B)** no movement in the left eyeball at the right gaze (indicated by the mark). **C)** At the upper gaze; there is no movement (marked). **D)** There is movement in both eyeballs at the left gaze.

There was no significant difference between primary and secondary ETV groups in terms of time to failure (log rank (Mantel–Cox), p=0.393; Breslow (generalized Wilcoxon), p=0.035; Tarone–Ware, p=0.074; p>0.05) (Figure 1B). There was no significant difference between patients aged younger and older than 18 years in terms of time to failure (log rank (Mantel–Cox), p=0.838; Breslow (generalized Wilcoxon), p=0.804; Tarone–Ware, p=0.962; p>0.05) (Figure 1C).

DISCUSSION

In this study, we summarized our ETV experience and presented our results that are based on a mean follow-up duration of 60 months. We achieved success with ETV in 317 patients (72%), a rate consistent with that reported in the literature (6,12,20,31). Owing to a high number of cases in our series, we created a model to predict ETV success. In this model, we tested whether age, sex, and primary and secondary ETV were predictors of ETV success.

In a multivariate analysis of 168 adult and pediatric patients (age, 3–85 years), Labidi et al. evaluated conditions that are related to the success of primary ETV (19). They identified hydrocephalus and sex as the only preoperative factors associated independently. Compared with male sex, female sex was found to be a predictor of good outcomes. In a study involving 190 patients undergoing either primary or secondary ETV (age, 16–79 years), Waqar et al. identified young age, secondary ETV, and hydrocephalus after an infection as the predictors of poor outcomes in a model that was created to predict success (31). In a study involving patients aged less than and older than 18 years, Chhun et al. identified no predictors of poor outcomes among the factors predicting ETV success, such as primary ETV, secondary ETV, and causes of hydrocephalus (3). Different from their study, the present study involved a larger number of patients and patients undergoing secondary ETV in addition to those undergoing primary ETV. The model used in this study identified not only primary ETV as an important predictor of ETV success but also male sex and advanced age as important predictors. Chiba et al. reported that a visible folding sign in the tectal region is a good predictor of ETV's operational success (4).

Kaplan–Meier survival analysis of our database showed no significant difference (p>0.05) in terms of time to failure at 1.3 and 5 years according to sex (female and male), categorized age (above and below 18 years), and ETV type (primary and secondary) (log rank (Mantel–Cox), Breslow (generalized Wilcoxon), Tarone–Ware). In a study by Waqar et al. (31), survival was longer in the primary ETV group than in the secondary ETV group, whereas the time to failure did not significantly differ between the groups.

In the study by Bouras and Sgouros, 2,985 ETV procedures were performed in 2,884 patients (1). The cause of hydrocephalus was aqueductal stenosis in 29.3%, tumor in 37.6%, meningomyelocele in 7.6%, cyst in 2.6%, cerebellar infarction in 0.9%, Dandy–Walker malformation in 0.6%, Chiari malformation in 0.4%, post-hemorrhagic hydrocephalus in 7.4%, post-infectious hydrocephalus in 1.8%, and normal-pressure hydrocephalus in 1.2%. Hydrocephalus resulted from other causes in 1.3% of cases, and the rate of cases with an unidentified cause was 9.8%. Of the patients in our series, 61.5% had aqueductal stenosis, 17% had a tumor, 7% had IVH, 6.9% had communicating hydrocephalus, and 6.9% had other causes.

Of 207 patients who underwent primary ETV, 50 underwent repeat ETV within 1 month after initial surgery owing to recurrent clinical and radiological findings of hydrocephalus. The procedure was successful in 12 patients, whereas 37 underwent shunt placement. No decision for performing repeat EVT was made. The procedure was successful in 169 of 207 (81.6%) patients. It was determined during the procedure that the opening created in previous surgery had been occluded in one patient. This patient died due to basilar artery injury during repeat ventriculostomy attempt. It was considered the cause of injury to the basilar artery that recurrent adhesions also involved the basilar artery. The success rate of primary ETV was found to be 80% in the study by Waqar et al. (31).

Of 110 patients who underwent secondary ETV, 60 underwent repeat ETV within the first month after initial surgery owing to recurrent clinical and radiological findings of hydrocephalus. The procedure was successful in 10 patients, and 51 patients underwent VP shunt revision. The procedure was successful in 59 of 110 (53%) patients. The success rate of secondary ETV was found to be 59% in the study by Waqar et al. (31).

The patients requiring repeat surgery manifested with the symptoms of hydrocephalus within the first month. In a study by Lam et al., the time to repeat surgery was reported as 25 days in a series of 525 patients (20).

Our case series involved patients aged 3 years and older. Because there is a controversy over the success of ETV in infants. Some authors found that ETV success does not depend on the age of the patient (8). El Damaty et al. reported a success rate of 44% for ETV in children aged less than 2 years (9). Shim et al. suggested that simultaneous ETV and VP shunt placement must be performed in patients with infantile hydrocephalus only due to poor outcomes of ETV (28). In a study involving patients aged younger than 3 years with obstructive and communicating hydrocephalus, Zhao et al. reported a success rate of 60% for ETV (33). The present study excluded patients aged younger than 3 years undergoing ETV. These cases will be further evaluated in a future study.

Complications

The rate of all complications after ETV ranges between 0% and 15% (12,18,27,29,30) but long-term complications are rare. Various anatomical factors and specific ventricular configurations play an important role in the success of ETV surgery. Similar to previous reports (10,24), third ventricular adhesions and prominent tuber cinereum is the most challenging situations for us in ours series. Also, interhypothalamic adhesions, thick and prominent massa intermedia, and narrow tuber cinereum were the other anatomical variations for surgical difficulty.

However, complications such as fever, bleeding, hemiparesis, gaze palsy, memory disorders, change in consciousness, diabetes insipidus, weight gain, and early puberty have been reported (32). Intraoperative neural damage, such as injury to the thalamic, forniceal, hypothalamic, and midbrain structures, can also be observed. Intraoperative bradycardia and hemorrhages including life-threatening bleeding due to basilar artery rupture have also been reported. Attempts to perforate the base of the ventricle, especially in case of hydrocephalus secondary to an infection and bleeding, can lead to bleeding. In a series of 2,884 cases, Bouras and Sgouros reported an early mortality rate of 0.21% after surgery (6 patients died, 2 had sepsis, and 4 had bleeding) (1). In terms of late mortality, “sudden death” (25 and 60 months after surgery) due to acute hydrocephalus secondary to stoma obstruction occurred in two children. In a study involving 336 pediatric patients, the mortality rate was reported to be 0.3% by Kulkarni et al. (18). In a series of 129 patients, Wang et al. reported 0% mortality and morbidity rates. In our series, one patient died of bleeding from the basilar artery that was injured during perforation because the base of the third ventricle was thick and slightly opaque during the second ETV (0.31%) (30). The rate of basilary artery injuries is 0.49 % in literature (11,16). The procedures we have conducted to prevent basal artery damage during the procedure include the following.

1- Preoperative MRI carefully is evaluated. A surgical approach is determined in consideration of prepontine cistern, basilary artery position, tuber cinereum and their surrounding anatomical structures.

2- The membrane is opened by blunt dissection between both mammillary bodies under clear visible transparent tuber cinerum

3- In the presence of thick and raised tuber cinerum, suitable landmarks are used. After entry with correct position and orientation (transition from the foramen Monro to the midline), we proceed to the midline in the 3rd ventricle and carefully enter through the midpoint between the raised mammillary body and the infundibular recess by blunt dissection.

4- In the presence of the opaque liliquist membrane at the bottom after the tuber cinerum is opened, the endoscope is not advanced further and the membrane is not forced to open with blunt dissection.

5- Schmidt proposed the use of the Doppler probe during the procedure in order to determine whether existency of basilary artery under the membrane (26).

6- In other studies, the position of the basilar artery is determined with neuronavigation preoperatively (22). During ETV, the basilar artery is viewed on the screen at the time of opening of the stoma by using probes and the procedure is completed.

No late mortality occurred among the studied patients in the late term. However, this is probably caused by the fact that the study center is a reference hospital for ETV procedures and the patients attend control visits in another hospital after discharge. As a result, data on late mortality if occurred in any patient could not be accessed because they were already dropped out of our clinic.

One of our patients developed intraparenchymal abscess (Figure 2). This is a very rare case, and our literature search using the keywords of “abscess” and “ETV” returned only one study (12) reporting abscess formation after ETV. In a series of 250 patients, Grand et al. reported surgical treatment of abscess only in one patient but without presenting any case images (12). Our patient developed intraparenchymal abscess that was treated with medical therapy after 1 month. The images at 1 year showed sclerotic tissues. One of the patients had transient oculomotor nerve palsy (Figure 3). As already suggested in the literature (2,15,23), it was considered that opening the base of the ventricle while it is bulging downward or deviation from the midline while perforating the base of the ventricle may cause third cranial nerve paralysis. Our patient with paralysis recovered after 3 months. Cranial nerve paralysis is very rare in the literature (1,13,23,33). Other complications include CSF leakage, asymptomatic subdural hematoma, and mild intraventricular bleeding during the procedure. These do not affect a patient’s prognosis.

Limitations

The limitations of this study include retrospective study design and the fact that patients are referred to our center from other hospitals because our center is a reference hospital for ETV procedures. Patients are not followed-up for long periods after surgery because they continue their follow-up program in the referring hospitals. Thus, we do not have data on the long-term complications.

CONCLUSION

We reported our experiences of ETV procedures in our center, which witnesses a high volume of patients undergoing this procedure owing to the fact that the study center serves as a reference hospital to a population of 10 million people. In logistic regression analysis of the data obtained from a series of 317 patients, primary ETV was identified as a factor with the highest probability of being associated with procedural success. Advanced age and male sex also increase the probability of ETV success but to a lesser extent. The prediction accuracy of the model was 72.2%. Complications occur at a low rate but can lead to serious consequences. For example, two complications reported in the present study have been mentioned in the literature but have not been clinically and radiologically documented. Thus, these cases are presented in this manuscript. In conclusion, ETV should be the first-line procedure for the treatment of hydrocephalus. The outcomes can be estimated using the models to predict success.

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