Neurosurgical Forum
LETTERS TO THE EDITOR**Can the ETVSS adequately predict success of repeat ETV?**

TO THE EDITOR: We read with interest the article on endoscopic third ventriculostomy (ETV) by Breimer et al.¹ (Breimer GE, Dammers R, Woerdeman PA, et al: Endoscopic third ventriculostomy and repeat endoscopic third ventriculostomy in pediatric patients: the Dutch experience. *J Neurosurg Pediatr* 20:314–323, October 2017) and would like to share some concerns. The paper presents a retrospective analysis of the effectiveness of re-ETV and validation of the ETV success score (ETVSS) for re-ETV. Based on their analysis of 93 cases in which re-ETV was performed, the authors consider that factors related to re-ETV success are similar to those related to initial ETV success (e.g., patient age and hydrocephalus etiology) and conclude that ETVSS can adequately predict the chance of successful re-ETV. We maintain, however, that patient age and hydrocephalus etiologies may not always be the critical factors affecting the success of re-ETV; we believe that the simple use of ETVSS in selecting re-ETV candidates is insufficient and analyzing the reasons for failure of the initial ETV should be emphasized.

Mahapatra et al.³ reported a re-ETV technical success rate of 93.2% in 32 patients and concluded that age and hydrocephalus etiology had no major effect on re-ETV success. Marano et al.⁴ analyzed 215 cases in which ETV failure was treated by reopening of the obstructed stoma and also concluded that age had no effect in re-ETV outcome. Furthermore, both groups of authors found a higher re-ETV success rate in patients with postinfectious hydrocephalus (PIH) than in those with hydrocephalus of other causes and hold that PIH is not a negative prognostic factor in re-ETV success. This finding seems to conflict with the ETVSS because postinfectious etiology is considered as an important negative prognostic factor in that scoring system. The higher success rate in PIH is ascribed to changes related to inflammatory response; stoma closure or arachnoid scarring due to inflammatory response in PIH can cause initial ETV failure, but the residual inflammatory response resolves over time, and a favorable outcome can frequently be achieved through re-ETV.^{3,4}

The ETVSS is a validated predictive model for estimating the chance of initial ETV success over a 6-month period, based on patient age, hydrocephalus etiology, and shunt history.² We believe, however, that some limitations apply to the use of the ETVSS for predicting the re-ETV

success rate and suggest that caution is warranted. Previous studies have demonstrated that failure of initial ETVs can be categorized into early failures and late failures. Whereas early failures are frequently caused by poor CSF absorption, patient selection error, and technical problems such as inadequate stoma size and unperforated Liliequist membrane; late failures are usually related to stoma closure caused by complete scarring, coaptation of redundant tissue at stoma margins, formation of new membranes, and residual inflammatory response of the intraventricular and subarachnoid space.⁴ Moreover, re-ETV in patients with early ETV failure has been associated with a low success rate, in contrast to the rate in patients with late ETV failure, in whom it has been found to be much higher.^{1,5} Based on our institutional experience and our review of the literature, we believe that the reasons for initial ETV failures should be emphasized in considering whether to perform re-ETV and that using the ETVSS alone is of limited value in selecting re-ETV candidates. First, when a patient experiences early failure of an initial ETV and postoperative MRI depicts a fluid flow void in the stoma and prepontine region, the failure may be caused by poor absorption of CSF;³ therefore, re-ETV should be avoided in these patients regardless of high or low ETVSS. Second if early failure of an initial ETV is caused by technical problems such as an inadequate stoma size or unperforated Liliequist membrane demonstrated on postoperative MRI, a re-ETV can be performed. Third, in cases in which hydrocephalus is adequately managed when the ETV is patent, it suggests that the absorption of CSF is normal and ETV is an effective treatment for these patients, and then failure due to ETV closure could be handled by reopening it either;^{3,4} therefore, when an initial ETV failure is due to stoma closure, a high re-ETV success rate can still be achieved regardless of patient age, hydrocephalus etiologies, or ETVSS.

In conclusion, the predictive value of ETVSS for re-ETV success seems controversial. When confronted with failure of an initial ETV, we believe that the reasons for and timing of ETV failure must be evaluated in the individual case in order to determine whether to treat the patient with re-ETV or CSF shunt placement. Further larger studies are needed to assess the predictive value of the ETVSS for re-ETV.

Qiguang Wang, MD
Yan Ju, PhD

West China Hospital of Sichuan University, Sichuan, China

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Disclosures

The authors report no conflict of interest.

Response

We thank Drs. Wang and Ju for their interest in our work. We appreciate their emphasis on the individual patients characteristics, and there are a few details on which we want to elaborate.

The suggestion that the ETVSS could be used for patient selection for re-ETV follows from the validation studies we performed. As a matter of fact, it would be surprising if the ETVSS would not work, as most of the basic characteristics that predict ETV success are unchanged. The main characteristic that has changed is age, as the child will have grown (at least a little bit) older. We do not suggest using the ETVSS alone for patient selection. In practice, we do not even expect surgeons to select patients for the initial ETV based on the ETVSS alone, as there will always be exceptions.

When a patient who has previously undergone ETV returns to the clinic with recurrent symptoms of hydrocephalus, a thorough investigation of the potential cause is essential. The treatment algorithm proposed by Drs. Wang and Ju is sensible. If the intraoperative data from the initial ETV and postoperative imaging suggest poor CSF reabsorption, then repeat ETV is not a good option. If that same data set suggests technical failure, such as inadequate ventriculostomy size, then repeat ETV is a good option. If a patient has fared well for some time after the initial ETV procedure and then experiences symptom recurrence, perhaps due to closure of the ventriculostomy site, then repeat ETV is a good option. Similar ideas have been put forth by other groups.^{1,5,7} Our findings align with this proposal. If a new membrane is formed that obstructs the flow over the initial ventriculostomy site, then reopening will achieve a higher success rate than when the ventriculostomy opening appears to be patent (probably because in the situation in which the ventriculostomy site is already open at reoperation, the cause of symptom

recurrence lies elsewhere). In our evaluation of ETV and re-ETV we did not analyze MRI/flow images. In a prospective study, this should be included.

We concur with the idea that a longer interval between initial ETV and re-ETV seems to be associated with higher chances of re-ETV success. Other cohorts have shown this trend. In our data set, however, we cannot find a significant difference. We did notice that on face value there is the suggestion that longer duration between the 2 treatments might be associated with success: median 12.1 months (interquartile range [IQR] 5.6–29.4 months) versus 7.6 months (IQR 1.6–29.7 months) ($p = 0.17$). We wrote this while realizing (and stressing in our paper) that the lack of a statistically significant finding might be a statistical power issue of this cohort.

In the studies cited by Drs. Wang and Ju different definitions for late and early failure are used: < 7 days versus > 7 days in one study and terms of months in other studies. Also, one of the studies involves a mix of pediatric and adult populations (among the 32 patients only 14 were pediatric patients).³ Furthermore, the population of the African study with 215 re-ETV patients has a different set of etiologies than the population one would typically find in a Western country.⁴ In the same study many of the patients received bilateral choroid plexus cauterization in combination with an ETV. In our study this was not the case. It is hard to perform a head-to-head comparison of studies with such different study populations and setups. For the proper comparison of success rates, one needs more complete data. First, either a survival table or a survival curve is needed. Second, we also need proper means to compare which patients are included and treated (such as mean or median ETVSS with standard deviations or IQRs), as one can expect better success rates in selected patient groups.

Our main finding is that there are similar success rates for ETV and re-ETV in this cohort. This is interesting as there is and has been much discussion on whether it is worthwhile to attempt a re-ETV. There are some limitations to this conclusion, as our study was relatively small and retrospective, with potential for selection bias. We are aware of these issues.

As Drs. Wang and Ju suggest, it would be interesting to study whether adding other characteristics to the ETVSS for the selection for re-ETV patients will lead to better success rates. For this purpose, a prospective study is needed. Still, a more fundamental question is whether (some) patients will fare better with a shunt or with a re-ETV.

Then there is the matter of definitions. What constitutes successful treatment? Is it solely the absence of subsequent treatment for hydrocephalus? Or should we focus on neurocognitive functioning and/or quality of life? Like many other authors, we used the former definition; this was one of the many limitations of a retrospective study. It seems appropriate to use measures of outcomes that matter to patients.⁶

As has been stressed before, prospective studies are mandatory. However, the issue of gathering larger (prospective) cohorts of patients might prove problematic. We used the retrospective data of all treated pediatric patients over the course of many years from almost all academic centers in the Netherlands, and still the cohort leaves us

a relatively small number of cases for analysis. For larger data sets, international collaboration is needed, but the duration of the enrollment period for the International Infant Hydrocephalus Study has proven that achieving sufficient inclusion rates in an international multicenter collaborative study is tough even when the study is well designed.²

Gerben E. Breimer, MD, PhD

Academic Medical Center, Amsterdam, The Netherlands

Eelco W. Hoving, MD, PhD

University Medical Center, Utrecht, The Netherlands

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