Predicting who will benefit from endoscopic third ventriculostomy compared with shunt insertion in childhood hydrocephalus using the ETV Success Score

Clinical article

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Object. The authors recently developed and internally validated the ETV Success Score (ETVSS)—a simplified means of predicting the 6-month success rate of endoscopic third ventriculostomy (ETV) for a child with hydrocephalus, based on age, etiology of hydrocephalus, and presence of a previous shunt. A high ETVSS predicts a high chance of early ETV success. In this paper, they assess the clinical utility of the ETVSS by determining whether long-term survival outcomes for ETV versus shunt insertion are different within strata of ETVSS (low, moderate, and high scores).

Methods. A multicenter, international cohort of children (≤ 19 years old) with newly diagnosed hydrocephalus treated with either ETV (489 patients) or shunt insertion (720 patients) was analyzed. The ETVSS was calculated for all patients. Survival analyses with time-dependent modeling of the hazard ratios were performed.

Results. For the High-ETVSS Group (255 ETV-treated patients, 117 shunt-treated patients), ETV appeared to have a lower risk of failure right from the early postoperative phase and became more favorable with time. For the Moderate-ETVSS Group (172 ETV-treated patients, 245 shunt-treated patients), ETV appeared to have a higher initial failure rate, but after about 3 months the instantaneous risk of ETV failure became slightly lower than shunt failure (that is, the hazard ratio became < 1). For the Low-ETVSS Group (62 ETV-treated patients, 358 shunt-treated patients), the early risk of ETV failure was much higher than the risk of shunt failure, but the instantaneous risk of ETV failure became lower than the risk of shunt failure at about 6 months following surgery (the hazard ratio became < 1).

Conclusions. Across all ETVSS strata, the risk of ETV failure becomes progressively lower compared with the risk of shunt failure with increasing time from the surgery. In the best ETV candidates (ETVSS ≥ 80), however, the risk of ETV failure is lower than the risk of shunt failure very soon after surgery, while for less-than-ideal ETV candidates (ETVSS ≤ 70), the risk of ETV failure is initially higher than the risk of shunt failure and only becomes lower after 3–6 months from surgery. These results need to be confirmed by larger, prospective, and preferably randomized studies. (DOI: 10.3171/2010.8.PEDS103)

Key Words • endoscopy • hydrocephalus • pediatric neurosurgery • endoscopic third ventriculostomy • shunt

Abbreviations used in this paper: ETV = endoscopic third ventriculostomy; ETVSS = ETV Success Score.

The debate over ETV versus CSF shunting for the treatment of childhood hydrocephalus remains largely unresolved.1,2,4,6,7,9,11,16,18,20 Recently, we used confounder-adjustment techniques (propensity score modeling) to compare the failure rate of ETV versus shunt placement.13 We found that, once adjusted for confounders, ETV is associated with a higher initial failure rate, but, over time, the failure rate becomes lower than that associated with shunt placement. In a separate publication, we used logistic regression techniques to develop and internally validate a prediction score that would, with good accuracy, predict the 6 month success rate of ETV, taking into account the patient’s age and the etiology of their hydrocephalus.14 The end product of this was the development of the ETV Success Score (ETVSS) (Table 1)—a simple means to predict
Endoscopic third ventriculostomy versus shunt insertion

TABLE 1: Calculation of the ETVSS*

<table>
<thead>
<tr>
<th>Score</th>
<th>Age</th>
<th>Etiology</th>
<th>Previous Shunt</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1 mo</td>
<td>postinfectious</td>
<td>previous shunt</td>
</tr>
<tr>
<td>10</td>
<td>1 mo to &lt;6 mos</td>
<td>myelomeningocele, IVH, non-tectal brain tumor</td>
<td>no previous shunt</td>
</tr>
<tr>
<td>20</td>
<td>6 mos to &lt;1 yr</td>
<td>aqueductal stenosis, tectal tumor, other</td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>1 yr to &lt;10 yrs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>≥10 yrs</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* The ETVSS is calculated as Age Score + Etiology Score + Previous Shunt Score. Abbreviation: IVH = intraventricular hemorrhage.

ETV success with scores ranging from 0 (extremely poor chance of ETV success) to 90 (extremely high chance of ETV success). We suggested that the ETVSS could be used to meaningfully select good candidates for ETV.

There were 2 main limitations to our previous work, however. First, it left unanswered the question: how would patients with equivalent ETVSSs fare with a shunt instead of an ETV? The ETVSS predicts success based on age and etiology, both of which likely have prognostic significance for shunt-treated patients also. Therefore, it is possible that the ETVSS may simply select patients who will do very well with either ETV or a shunt, without a clear relative benefit of one over the other. Second, the ETVSS was designed to predict relatively short-term outcome only—that is, the chance of being failure-free at 6 months. How would these patients do after a longer period of follow-up, and would the ETVSS still be predictive of good outcome? The current analysis is our attempt to address these issues. In this report, we tested whether the success rate predicted by the ETVSS would specifically translate into different long-term outcomes for ETV compared with shunt placement.

Methods

Patient Population

The cohort for this study was accrued from 3 main sources and has been described previously. All patients were 19 years old or younger; had newly diagnosed, previously untreated, high-pressure hydrocephalus; and were treated by pediatric neurosurgeons at specialized centers. The ETV cohort was collected from 12 centers in Canada, Israel, and the United Kingdom, and the patients were treated between 1989 and 2006. The shunt cohort was collected from the Shunt Design Trial (patient recruitment 1993–1995 from Canada, France, the Netherlands, and the US) and the Endoscopic Shunt Insertion Trial (patient recruitment 1996–1999 from Canada, the Netherlands, the United Kingdom, and the US). Permission was granted from each trial’s principal investigators for analysis of data. Since these trials demonstrated no difference in outcome in the treatment arms, data from all patients were analyzed collectively for this study. All data were anonymized and data collection adhered to local research ethics protocols.

We defined the failure of treatment as any subsequent surgical procedure for definitive CSF diversion (either shunting or ETV) or death related to hydrocephalus management.

Statistical Analysis

For each patient in the cohort we calculated the ETVSS (Table 1), regardless of whether the patient was actually treated by ETV or shunt insertion. The ETVSS is based on the patient’s age, hydrocephalus etiology, and presence of a previous shunt. Since all patients in our cohort had newly diagnosed hydrocephalus, no patient had a previous shunt. The ETVSS ranges from 0 to 90, and the number itself roughly approximates the percentage chance that an ETV will be successful at 6 months. For example, an 8-month-old with aqueductal stenosis and no previous shunt would have an ETVSS of (30 + 30 + 10) = 70, or a roughly 70% chance of having a successful ETV without failure at 6 months postprocedure. We have previously demonstrated the internal validity of the ETVSS. We stratified the sample into patients with a high ETVSS (≥80), those with a moderate ETVSS (50–70), and those with a low ETVSS (≤40). Within each of these stratified groups we performed comparative survival analyses, using the time to treatment failure as the outcome of interest. We used Kaplan-Meier methods to construct survival curves. We performed survival analyses using Cox proportional hazards models to compare ETV failure relative to shunt failure. This provides a hazard ratio, which is the instantaneous risk of ETV failure compared with shunt failure, at a given moment in time following surgery (values greater than 1 indicate a higher chance of ETV failure than shunt failure). We discovered, however, that the assumption of proportional hazards was violated, based on visual inspection of the treatment survival curves (the curves crossed each other) and significance of the interaction of time and treatment (p < 0.001). This meant, therefore, that the risk of ETV failure compared with shunt failure was not constant after surgery. Rather, it changed as a function of time after surgery. Because of this, we used a Cox regression model that would allow the hazard ratio to change over time following surgery. We performed survival analyses using Cox proportional hazards models to compare ETV failure relative to shunt failure. This provides a hazard ratio, which is the instantaneous risk of ETV failure compared with shunt failure, at a given moment in time following surgery (values greater than 1 indicate a higher chance of ETV failure than shunt failure). We discovered, however, that the assumption of proportional hazards was violated, based on visual inspection of the treatment survival curves (the curves crossed each other) and significance of the interaction of time and treatment (p < 0.001). This meant, therefore, that the risk of ETV failure compared with shunt failure was not constant after surgery. Rather, it changed as a function of time after surgery. Because of this, we used a Cox regression model that would allow the hazard ratio to change over time following surgery (values greater than 1 indicate a higher chance of ETV failure than shunt failure). We discovered, however, that the assumption of proportional hazards was violated, based on visual inspection of the treatment survival curves (the curves crossed each other) and significance of the interaction of time and treatment (p < 0.001).
logarithmic curves in Fig. 3. These curves are presented to 48 months after surgery, after which the number of patients left in the analysis was very small.

For the High-ETVSS Group, ETV appeared to have a lower risk of failure right from the early postoperative phase onwards (Fig. 3). There was a reasonable separation of the survival curves at 3 years that appeared to diverge further with time (Fig. 2A), but the number of shunt-treated patients in this analysis was limited.

For the Moderate-ETVSS Group, ETV appeared to have a higher initial failure rate, but it became slowly and progressively more favorable over time. After about 3 months from surgery, the instantaneous risk of ETV failure became slightly lower than the risk of shunt failure (the point at which the hazard ratio curve in Fig. 3 crosses below 1) and the survival curves crossed at about 30 months (Fig. 2B).

For the Low-ETVSS Group, the early risk of ETV failure was very high, as expected, but among those who survived this early phase, their risk of ETV failure became lower than the risk of shunt failure at about 6 months following surgery. Although the survival curves appeared to cross at about 42 months, the number of ETV patients left in the analysis was too small for strong conclusions (Fig. 2C).

**Discussion**

Although the role of ETV appears to be expanding, the major unanswered challenge has been to better define the outcome of ETV, especially in comparison with standard shunting. The development of the ETVSS was our attempt to more strictly predict successful outcome from ETV and thereby formally quantify the effect of the known patient prognostic factors of age and etiology. The current analysis suggests that the ETVSS can be useful in guiding clinical decision making. First, we have shown that the ETVSS predicts not just short-term ETV outcome (as it was designed to do), but also longer-term outcome. The 3-year success rates for the High- and Moderate-ETVSS groups were 72% and 52%, respectively, suggesting that early ETV success leads to a high chance of longer-term success, as well. The corollary of this is that ETV appears to have a low delayed failure rate in comparison with shunt placement, although late ETV failures certainly do occur. Interestingly, a lower delayed ETV failure rate compared with shunt placement (that is, a hazard ratio of < 1) was seen across all strata of ETVSS after 6 months following surgery (Fig. 3). Second, we have shown that the success of ETV and CSF shunting are different within strata of ETVSS. In patients with ETVSS ≥ 50 (the High-ETVSS and Moderate-ETVSS groups), there was little difference among the shunt-treated patients, who all had a 3-year survival rate of approximately 50%. In contrast, there is a stark difference among the shunt-treated patients, who all had a 3-year survival rate of approximately 50%. In contrast, there is a stark difference in ETV outcome for those with a high ETVSS versus those with a moderate ETVSS: the 3-year success rates were 72% and 52%, respectively. Within the Low-ETVSS Group, shunt insertion appears to have superior success for at least the first 2 years after treatment, although the longer-term failure rate still appears to favor ETV. Therefore, the ETVSS does not simply indiscriminately predict overall hydrocephalus treatment success, but, rather, it specifically differentiates the expected survival outcome of shunt insertion versus ETV.

It is important to recognize the limitations of our analysis. Our data are not randomized nor was outcome blinded. While for the shunt-treated cohort all outcome data were collected prospectively and subject to independent adjudication, this was not the case for the ETV-treated cohort, for whom failure was determined by the treating surgeon. Although our sample is the largest of

**TABLE 2: Summary of patients’ characteristics**

<table>
<thead>
<tr>
<th>Variable</th>
<th>ETV (489 patients)</th>
<th>Shunt (720 patients)</th>
<th>Overall (1209 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>age at treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 mo</td>
<td>36 (7.4)</td>
<td>234 (32.5)</td>
<td>270 (22.3)</td>
</tr>
<tr>
<td>1 to &lt;6 mos</td>
<td>78 (16.0)</td>
<td>240 (33.3)</td>
<td>318 (26.3)</td>
</tr>
<tr>
<td>6 to &lt;12 mos</td>
<td>35 (7.2)</td>
<td>83 (11.5)</td>
<td>118 (9.8)</td>
</tr>
<tr>
<td>1 to &lt;10 yrs</td>
<td>206 (42.1)</td>
<td>122 (16.9)</td>
<td>328 (27.1)</td>
</tr>
<tr>
<td>≥10 yrs</td>
<td>134 (27.4)</td>
<td>41 (5.7)</td>
<td>175 (14.5)</td>
</tr>
<tr>
<td>etiology of hydrocephalus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>stenosis of cerebral aqueduct</td>
<td>168 (34.4)</td>
<td>53 (7.4)</td>
<td>221 (18.3)</td>
</tr>
<tr>
<td>tectal tumor</td>
<td>61 (12.5)</td>
<td>0</td>
<td>61 (5.0)</td>
</tr>
<tr>
<td>other brain tumor</td>
<td>114 (23.3)</td>
<td>48 (6.7)</td>
<td>162 (13.4)</td>
</tr>
<tr>
<td>post-IVH</td>
<td>53 (10.8)</td>
<td>161 (22.4)</td>
<td>214 (17.7)</td>
</tr>
<tr>
<td>myelomeningocele</td>
<td>10 (2.0)</td>
<td>178 (24.7)</td>
<td>188 (15.6)</td>
</tr>
<tr>
<td>other</td>
<td>83 (17.0)</td>
<td>280 (38.9)</td>
<td>363 (30.0)</td>
</tr>
<tr>
<td>mean ETVSS (± SD)</td>
<td>71 ± 16</td>
<td>51 ± 19</td>
<td>59 ± 20</td>
</tr>
</tbody>
</table>

* Values represent number of patients (%) unless otherwise indicated.
this nature ever analyzed, our individual stratified analyses suffered from limited numbers of patients, particularly within the High- and Low-ETVSS groups (lacking shunt-treated and ETV-treated patients, respectively). Our use of a logarithmic time-dependent hazard function is complex and does not lend itself to intuitive interpretation. It was important, however, to use this to faithfully model the true interaction of treatment failure for these 2 interventions. Our data only allowed for meaningful analysis up to 48 months posttreatment. Given the nature of the survival curves, it seems that the true benefit from ETV would be incurred with longer follow-up. Once beyond the early steep failures seen within the first 3–6 months, all indications are that the failure rate for ETV

![Fig. 2. The Kaplan-Meier survival curves for each strata of ETVSS, with ETV survival shown as dotted lines and shunt survival as solid lines. A: High-ETVSS Group (score ≥ 80). B: Moderate-ETVSS Group (score 50–70). C: Low-ETVSS Group (score ≤ 40).]

### TABLE 3: Treatment success stratified by ETVSS*

<table>
<thead>
<tr>
<th>Variable</th>
<th>High ETVSS (≥80)</th>
<th>Moderate ETVSS (50–70)</th>
<th>Low ETVSS (≤40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>no. of patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ETV</td>
<td>255</td>
<td>172</td>
<td>62</td>
</tr>
<tr>
<td>shunt</td>
<td>117</td>
<td>245</td>
<td>358</td>
</tr>
<tr>
<td>cumulative treatment survival at 36 mos (95% CI)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ETV</td>
<td>0.72 (0.65–0.78)</td>
<td>0.52 (0.44–0.60)</td>
<td>0.37 (0.24–0.49)</td>
</tr>
<tr>
<td>shunt</td>
<td>0.54 (0.39–0.68)</td>
<td>0.49 (0.41–0.57)</td>
<td>0.38 (0.31–0.44)</td>
</tr>
</tbody>
</table>

* Survival figures obtained via Kaplan-Meier survival methods.
is ultimately lower than that for shunt placement. Therefore, longer-term follow-up might reveal further benefit from ETV that is not evident in our report. Our analysis only examined time to first treatment failure and ignored the many other important aspects of treatment success, including the morbidity associated with the treatment and complications of shunt or ETV failure. As well, we did not examine the effects of repeated failures and other long-term complications, such as slit ventricles. Previous work has suggested that these factors can impact the most important outcome, quality of life.12,15 Future studies will need to examine this aspect in further detail. We also recognize that the current version of the ETVSS has not been externally validated and its predictive accuracy might be improved in the future with the inclusion of other predictive features, including preoperative imaging features and intraoperative findings.8,19 It is our goal to continually refine the ETVSS as our understanding of ETV success evolves over the coming years.

Given these inherent limitations, our results have to be interpreted cautiously. Specifically, we do not present these as a replacement for randomized data or even contemporaneously collected prospective data. Our analysis is, by no means, definitive. Rather, we feel that this represents, for the time being, one of the most methodologically and statistically rigorous comparisons of ETV versus shunt placement, but much further work is required.

The High-ETVSS Group, with scores ≥ 80, represents a select group of patients: all are over 1 year of age and the vast majority will have aqueductal stenosis or tectal tumors. These represent the classic indications for ETV, for which there is likely widespread consensus. Ours is one of very few analyses, however, to provide a true direct comparison of this group of patients to similar patients with shunts.17 An early and lasting survival benefit with ETV is suggested by examination of the survival curves (Fig. 2A) and the hazard ratio curves (Fig. 3). In less-favorable ETV candidates, however, the survival benefit is either equivocal (for the Moderate-ETVSS Group) or virtually nil (for the Low-ETVSS Group), at least until 4 years after surgery. An optimistic interpretation of the hazard ratio curves in Fig. 3 is that with longer follow-up, ETV might eventually be shown to be beneficial. This would require that a patient survive with the ETV for at least 4 years, after which the risk of long-term failure would be lower than would be seen with a shunt placement. In a sense, this then becomes a question of whether to “front-load” the risk with an ETV (which has a higher early failure rate) for possible long-term benefit or “back-load” the risk with a shunt (which has better early success, but perhaps worse long-term risks). Since individual tolerance for risk varies, sharing this information with families can provide extra guidance for treatment decisions.

Conclusions

We have shown that the ETVSS can be used to differentiate expected survival outcomes for patients treated with ETV compared with CSF shunting. In all ETVSS strata the risk of ETV failure becomes progressively lower compared with the risk of shunt failure with increasing time from the surgery. In the best ETV candidates (those with ETVSS ≥ 80), however, the risk of ETV failure is lower than that of shunt insertion right after surgery, while for less than ideal ETV candidates (ETVSS ≤ 70), the risk of ETV failure is initially higher than that of shunt insertion and only becomes lower after 3–6 months from surgery. Our results will need to be confirmed with further prospective and, preferably, randomized studies.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper. No external funds were received for this study.

Author contributions to the study and manuscript preparation include the following: Conception and design: all authors. Acquisition of data: all authors. Analysis and interpretation of data: Kulkarni, Kestle. Drafting the article: Kulkarni. Critically revising the article: all authors. Reviewed final version of the manuscript and approved it for submission: all authors. Statistical analysis: Kulkarni. Study supervision: Kulkarni.

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