Quality of life in children with hydrocephalus treated with endoscopic third ventriculostomy

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OBJECTIVE The objectives of this study were to determine the quality of life of a pediatric cohort with hydrocephalus treated by endoscopic third ventriculostomy (ETV), using the Hydrocephalus Outcome Questionnaire–Spanish version (HOQ-Sv), and study the clinical and radiological factors associated with a better or worse functional status.

METHODS This cross-sectional study was undertaken between September 2018 and December 2019. It comprised a series of 40 patients ranging from 5 to 18 years old with hydrocephalus treated by ETV. ETV was considered to be successful if there was no need for surgery for the treatment of hydrocephalus after a minimum follow-up of 6 months. The clinical variables included gender, age at hydrocephalus diagnosis, age at the time of ETV, age at completion of the questionnaire, etiology and type of hydrocephalus (communicating or not), prior shunt, repeat ETV, number of neurosurgical procedures, number of epileptic seizures, presenting signs, and follow-up duration until last office revision. The radiological variables were the Evans Index and the pre- and posttreatment frontooccipital horn ratio. An analysis was conducted of the association between all these variables and the various dimensions on the HOQ-Sv, completed by the parents of the patients via telephone or in the outpatient offices.

RESULTS The mean age of the children at ETV was 7 years (range 7–194 months), and on completing the questionnaire was 12 years (range 60–216 months). The mean HOQ scores were as follows: overall 0.82, physical domain 0.86, social-emotional (SE) domain 0.84, cognitive domain 0.75, and utility score 0.90. A history of epileptic crises was a predictive factor for a worse score overall and in the SE and cognitive domains. Factors related to a worse score in the physical domain were a previous shunt, the number of procedures, and the etiology and type of hydrocephalus. The mean follow-up duration from ETV to the last office visit was 5 years (64.5 months). No association was found between the degree of ventricular reduction and the quality of life.

CONCLUSIONS The factors related to a worse score in the different dimensions of the HOQ were a history of epileptic seizures, the number of procedures, communicating hydrocephalus, and having had a previous valve. No association was found between the reduction in ventricular size and the quality of life as measured on the HOQ-Sv.

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KEYWORDS endoscopic third ventriculostomy; ETV; quality of life; health outcome; hydrocephalus
psychometric properties have proven useful to measure the health status of these patients. A high correlation has been found between the cognitive domain of the HOQ and the use of neuropsychological tests in patients with chronic hydrocephalus. In 2017, Iglesias et al. validated the Spanish version of this questionnaire (HOQ–Spanish version [HOQ–Sv]) to quantify the health status of a typical population of children with hydrocephalus treated with a shunt in our hospital. However, few studies have used this instrument in patients with hydrocephalus treated via neuroendoscopy. Following the line of research in hydrocephalus at our hospital, we designed a parallel study in patients treated successfully with endoscopic third ventriculostomy (ETV).

The aims of this study were to determine the quality of life (using the HOQ-Sv) of a cohort of children with hydrocephalus treated by ETV, and analyze the clinical and radiological features associated with a better or worse functional status.

Methods
Study Cohort
We undertook this cross-sectional study between September 2018 and December 2019. The parents of 40 school-aged children (5–18 years old) treated with ETV at the Regional University Hospital in Málaga, Spain, completed the HOQ-Sv. Ten patients had previously been treated with a shunt (secondary ETV). Four patients had a prior history of ETV failure (repeat ETV), 3 of them treated with a shunt previously.

The patients included in the study were clinically stable after ETV at the time of completing the questionnaire. None had received any hospital treatment elsewhere. A successful ETV was defined as no need for surgery (shunt or ETV revision) for the treatment of hydrocephalus after a minimum follow-up of 6 months.

Data Collection
The clinical variables recorded included gender, age at treatment of hydrocephalus, prior valve history (secondary ETV), history of repeat ETV, age at latest ETV, number of neurosurgical procedures (1 or > 1), and age at completing the HOQ. The etiology of the hydrocephalus was classified as associated with spina bifida, aqueductal stenosis (AS) due to gliosis or tectal tumor, non-tectal tumor hydrocephalus, secondary to arachnoid cyst, communicating primary hydrocephalus, and other secondary causes. This last group comprised only patients with heterogeneous causes of hydrocephalus, such as posthemorrhagic hydrocephalus of prematurity; postinfectious, spontaneous hemorrhage not during the neonatal period; vascular; and malformative or other dysgenetic malformations. Chiari type I malformation and Dandy-Walker malformation were also included in secondary causes. The type of hydrocephalus was classified according to its pathophysiology as communicating or noncommunicating. Data were also recorded concerning a history of prior failed ETV (repeat ETV) and epilepsy, considered to be seizures with neurophysiological confirmation that had required anti-convulsant drugs at some time during their course.

Symptoms prior to the ETV were divided according to symptoms of “intracranial hypertension” (headache, vomiting, papilledema, or lethargy) and chronic or “long-standing,” such as insidious gait alteration, cognitive impairment, behavioral changes, macrocephaly, incontinence, or clinically nonspecific. Pathological intracranial pressure monitoring was undertaken in doubtful cases prior to treatment. The hydrocephalus health questionnaire, comprising 51 questions in the Spanish version (HOQ–Sv), was completed by the parents (mother or father) of the patients, who all agreed to participate in this study through informed consent, either at the outpatient office or over the telephone. Institutional ethics approval was obtained. The utility score was calculated to make comparisons with the general population. The follow-up duration (in months) from the successful ETV to the latest outpatient visit was also recorded.

The radiological variables calculated in the pre- and posttreatment cranial MRI (after at least 6 months) included the Evans Index (EI) and the frontooccipital horn ratio (FOHR). Change after the endoscopic therapy was considered to be significant if the reduction in the index used was > 10%. A normal value for the EI was set at < 0.3, and for the FOHR at 0.37. In patients who underwent ETV with no previous history of a shunt, the presurgical assessment was considered. In the event that the patient had a history of a shunt and the secondary ETV was performed in the context of valve failure, the pre-ETV MRI study showing an increase in the ventricular size despite the shunt (due to inherent failure) was considered. But if the secondary ETV was performed as part of a withdrawal protocol in the context of overdrainage, the imaging test prior to any treatment (before shunt insertion) was considered.

Statistical Analysis
The descriptive analysis is presented as percentages for the qualitative variables and measures of centralization and dispersion for the quantitative variables. Analysis between qualitative variables was conducted using contingency tables and the chi-square test or Fisher’s exact test. The association of scores on the HOQ–Sv (physical, SE, and cognitive domains and overall) and the independent variables was analyzed using parametric tests, analysis of variance (ANOVA and/or Student t-test), or nonparametric tests (Kruskal-Wallis and/or Mann-Whitney U-test), depending on the number of factor levels and the condition of normality. The linear relation between quantitative variables was studied with the Pearson or Spearman correlation. In all the inferential analyses, significance was set at p < 0.05. The statistical analysis was performed with R (version 3.2.1) and SPSS (version 25, IBM Corp.).

Results
Table 1 shows the clinical characteristics of the series, 70% of whom were male (28/40). The mean age at ETV was 7 ± 4 years (range 7–194 months), and at the time of completing the questionnaire it was 12 ± 4 years (range 60–216 months). The mean follow-up duration was 64.5
months (i.e., 5.4 years) ± 3.8 months (range 7–156 months). Table 2 shows the mean scores of the various dimensions on the HOQ-Sv, and Fig. 1 shows their distribution. Eleven patients received more than 1 neurosurgical procedure, including a second ETV (previous shunt) in 10. Three required repeat ETV. Another patient with a failure of the first ETV was treated with repeat ETV.

Factors Associated With Scores on the HOQ-Sv

Table 3 shows the association among the different variables and the scores on the questionnaire. The score for the physical domain was significantly associated with the etiology of the hydrocephalus (p = 0.004); the patients with AS and arachnoid cysts had the best scores (0.95 and 0.96, respectively), while the worst scores were found in patients with communicating primary hydrocephalus (0.76) and secondary causes (0.71). The type of hydrocephalus was also significantly (p = 0.027) associated with the scores on the physical domain, with noncommunicating hydrocephalus having a better score (0.89) than communicating hydrocephalus (0.75). A history of a prior shunt was associated with a worse HOQ-Sv score in the physical domain (p = 0.007). The score for the physical domain was also significantly associated with the number of neurosurgical procedures: patients who underwent more than 1 operation had worse scores (0.73) compared to those who had just 1 procedure (0.90). A history of epileptic seizures was predictive of a worse HOQ-Sv score in the SE and cognitive domains and overall. Figures 2 and 3 show the box plots related to the etiology of the hydrocephalus and a history of epilepsy, respectively. No correlation was found between the scores for the different HOQ domains and such variables as age at treatment of hydrocephalus, age at ETV, age at completion of the questionnaire, and overall follow-up duration of the patients (in months).

Association Between Ventricular Size After ETV and HOQ Scores

After treatment, a significant reduction in the ventricular size was noted in both ventricular indices: the pre- and posttreatment scores were 0.48 ± 0.08 and 0.42 ± 0.07 for the FOHR, and 0.40 ± 0.09 and 0.34 ± 0.08 for the EI (p < 0.001). The degree of reduction of the ventricular size after ETV was not associated with a better or worse score in the different HOQ domains (EI and FOHR). Table 3 also shows the association between the HOQ score and whether or not there was any significant change (> 10%) in the EI and FOHR after treatment with ETV (“change in EI” and “change in FOHR”).

Discussion

Comparisons of Health Status

The use of the HOQ and its adaptation to the Spanish version (HOQ-Sv scale) have been shown to be valid to quantify and determine which factors affect the quality of life in children with hydrocephalus,1 as previously reported by Platenkamp et al.6 using the Dutch version. Internal consistency obtained using the Cronbach alpha coefficient in our original report was similar to that previously reported by Kulkarni et al.,4 with values between 0.767 and 0.929 for all dimensions of quality of life. The incorporation of the HOQ as an instrument to measure the functional status of these patients in different centers improves its external validity and enables comparison with the scores obtained in other populations.1,4,6 At the same time, periodic follow-up of these patients (every 6 months or annually) provides very valuable information about their state of health and evolution, allowing identification of areas that need greater attention through targeted therapies. The HOQ has resulted in numerous studies assessing whether the state of health differs depending on the treatment, with either ETV or a valve. Our study is unique in its adaptation of the HOQ-Sv to determine quality of life in children with hydrocephalus treated with ETV. Comparison
between groups is hindered by the great heterogeneity of these patients. Early retrospective studies that included patients with hydrocephalus of diverse etiology found no better scores for ETV. However, the authors stressed the need for prospective studies to confirm these differences. Studies comprising more homogenous groups with similar characteristics concerning the etiology of the hydrocephalus and age at treatment failed to find significant differences between the two groups. Nevertheless, a negative correlation was found between the ventricular size and a worse score in the physical domain of the HOQ and the Health Utilities Index Mark 3 utility score. The recent prospective, multicenter study by Kulkarni et al. compared the health status and the FOHR in patients with AS treated during the first 2 years of life with either ETV or a valve and found no differences after 5 years of follow-up. These results, however, cannot be extrapolated to other groups of patients with hydrocephalus of different etiologies. Comparison of the HOQ scores for patients with a shunt and the scores obtained in our series of patients with ETV in the area of Málaga shows very important differences, and the two groups are not really comparable. However, the number of procedures in both groups was associated with worse results in the physical domain of the HOQ. Quality of life is conditioned by multiple factors that reflect the intrinsic heterogeneity of these groups of patients with hydrocephalus diagnosed at different ages, with diverse etiologies, treatments, and complications. ETV is generally reserved for older patients with more favorable etiologies who tend to fare better independent of the type of treatment. What does appear to be a clear predictive factor for a worse score, in both patients with a shunt and those with ETV, is a history of epileptic seizures, according to other studies. Our results were based on a small number of patients with a history of epilepsy (4 cases) and a diverse etiology of the hydrocephalus. Table 4 shows the results for the different groups of children with hydrocephalus treated by ETV published in the literature. The various series differ in their selection of the study patients. The HOQ scores do not, however, differ significantly between groups and are quite similar to those of our study and the prospective study on patients with purely obstructive hydrocephalus, with a similar follow-up period (5.4 and 5.2 years, respectively). However, in this
study, the ETV was undertaken earlier and the failure rate during the follow-up was 35.5%. In our study, in which the patients were shunt free at the end of the follow-up period, the etiology data showed that patients with hydrocephalus due to arachnoid cyst, AS, and spina bifida all had better overall scores. The worse results were noted in the patients with secondary etiologies. It is important to note, however, that these results were found in groups with a small number of patients. The group of “secondary etiologies” comprising very heterogeneous causes of hydrocephalus cannot be representative. Studies with a greater number of patients are recommended.

ETV in Communicating Hydrocephalus

Current thinking concerning the pathophysiology of hydrocephalus has led to ETV becoming another treatment option for both obstructive hydrocephalus and communicating hydrocephalus of diverse etiologies, with the success rate for this latter group being approximately 61%. In this type of chronic hydrocephalus, clinical and radiological assessment of therapeutic success can be made more difficult by insidious symptoms and the ventricular size may not be reduced after ETV. This was, in fact, seen in our study, in which ventricular size was reduced by 9% in communicating hydrocephalus and 15.3% in noncommunicating hydrocephalus (p = 0.043). In agreement with findings in other studies, the stability of the ventricular size after treatment was not associated with worse scores on the HOQ. Normalization of the

TABLE 3. Association between the clinical-radiological variables and the HOQ-Sv domains

<table>
<thead>
<tr>
<th>Variable</th>
<th>HOQ-Sv Domain Scores (p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Physical</td>
</tr>
<tr>
<td>Hydrocephalus etiology</td>
<td>0.004</td>
</tr>
<tr>
<td>Type of hydrocephalus</td>
<td>0.027</td>
</tr>
<tr>
<td>Prior valve</td>
<td>0.007</td>
</tr>
<tr>
<td>Re-ETV</td>
<td>0.768</td>
</tr>
<tr>
<td>No. of surgical procedures</td>
<td>0.033</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>0.060</td>
</tr>
<tr>
<td>Symptoms</td>
<td>0.855</td>
</tr>
<tr>
<td>Age at treatment</td>
<td>0.076</td>
</tr>
<tr>
<td>Age at ETV</td>
<td>0.962</td>
</tr>
<tr>
<td>Age at HOQ-Sv</td>
<td>0.339</td>
</tr>
<tr>
<td>Follow-up</td>
<td>0.254</td>
</tr>
<tr>
<td>EI</td>
<td>0.512</td>
</tr>
<tr>
<td>FOHR</td>
<td>0.186</td>
</tr>
<tr>
<td>Change in EI</td>
<td>0.680</td>
</tr>
<tr>
<td>Change in FOHR</td>
<td>0.374</td>
</tr>
</tbody>
</table>

Re-ETV = repeat ETV. Boldface type indicates statistical significance.

FIG. 2. Box plots showing the relation between the etiology of hydrocephalus and the scores on the different domains. Each box shows the median, the quartiles, and the extreme values for each category. Open circles refer to atypical values, and stars represent extreme outliers. The numbers next to these symbols represent the patient number of that individual patient. C primary = communicating primary hydrocephalus. Figure is available in color online only.
ventricular size, therefore, should not be the main aim of treatment, with a successful ETV compatible with a residual ventriculomegaly.\(^{17}\)

The method of assessing a successful ETV is not simple. Moreover, in patients with a previous shunt placement, if we just base the results on the ventricular size as the main criterion after ETV surgery, we must note that the ventricles may enlarge after shunt withdrawal, although this has no relation with neuroendoscopic failure. In our experience, the patient’s symptoms and the intracranial pressure record assume a fundamental role to confirm failure of ETV treatment.

Other radiological criteria, such as flow artifact, enlarged subarachnoid space, resolution of transependymal edema, or reduction of the third ventricle, can be considered favorable markers of a successful ETV.\(^{26–28}\) Nevertheless, in a few patients with chronic communicating hydrocephalus, a compensatory state could give rise to a less predictable evolution over the medium to long term and thus require a closer follow-up. Better HOQ scores have been reported in noncommunicating hydrocephalus,\(^{11,12}\) as seen in our study for the physical domain. Characteristics such as the integrity of the white matter, the brain volume, and the diffusion tensor imaging parameters could be more predictive of the neurocognitive results than the information about changes in the ventricular size.\(^{12,17}\)

**Limitations and Special Considerations**

This study was retrospective and the postsurgical MRI ventricular indices in some patients were measured from the 6th month after ETV, which may be too soon after the treatment. The classification of the etiology of the hydrocephalus was reduced due to the small sample size, which could result in an increased group heterogeneity and an underestimation of our results.
TABLE 4. Comparison of the HOQ scores for ETV treatment in different studies

<table>
<thead>
<tr>
<th>Variable</th>
<th>Kulkarni et al., 2010(^1)</th>
<th>Kulkarni et al., 2010(^1)</th>
<th>Kulkarni et al., 2018(^2)</th>
<th>Present Study, 2021</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study location</td>
<td>Multicenter</td>
<td>Toronto</td>
<td>Prospective multicenter</td>
<td>Málaga</td>
</tr>
<tr>
<td>Population</td>
<td>Diverse etiology</td>
<td>Hydrocephalus AS</td>
<td>Hydrocephalus AS</td>
<td>Diverse etiology</td>
</tr>
<tr>
<td>No. of patients</td>
<td>58</td>
<td>24</td>
<td>61</td>
<td>40</td>
</tr>
<tr>
<td>Age at treatment (mos)</td>
<td>66.9 ± 57.1</td>
<td>57.3 ± 57.7</td>
<td>5.6 ± 5.2</td>
<td>84 ± 48</td>
</tr>
<tr>
<td>Age at HOQ (yrs)</td>
<td>10.4 ± 3.5</td>
<td>12.3 ± 4</td>
<td>5.2 ± 0.5</td>
<td>12 ± 4</td>
</tr>
<tr>
<td>FOHR post ETV</td>
<td>0.46 ± 0.08</td>
<td>0.48 ± 0.10</td>
<td>0.43 ± 0.11</td>
<td>0.42 ± 0.07</td>
</tr>
<tr>
<td>HOQ physical domain</td>
<td>0.79 ± 0.19</td>
<td>0.88 ± 0.16</td>
<td>0.84 ± 0.19</td>
<td>0.86 ± 0.17</td>
</tr>
<tr>
<td>HOQ SE domain</td>
<td>0.73 ± 0.21</td>
<td>0.79 ± 0.21</td>
<td>0.84 ± 0.12</td>
<td>0.84 ± 0.17</td>
</tr>
<tr>
<td>HOQ cognitive domain</td>
<td>0.58 ± 0.30</td>
<td>0.72 ± 0.26</td>
<td>0.76 ± 0.22</td>
<td>0.75 ± 0.26</td>
</tr>
<tr>
<td>HOQ overall</td>
<td>0.70 ± 0.22</td>
<td>0.81 ± 0.19</td>
<td>0.82 ± 0.15</td>
<td>0.82 ± 0.14</td>
</tr>
<tr>
<td>Utility score</td>
<td>0.79</td>
<td>0.89</td>
<td>0.90</td>
<td>0.90</td>
</tr>
</tbody>
</table>

Data given as mean ± SD unless otherwise indicated.

Conclusions

The HOQ-Sv scale is valid to quantify the quality of life in children with hydrocephalus treated by ETV, and to determine which factors affect quality of life. In addition, the results enable comparison with the scores obtained in other populations. Epilepsy was a factor with a poor prognosis in the SE and cognitive domains and overall. A history of a prior valve, the number of surgical procedures, communicating hydrocephalus, and secondary etiology are predictive of a worse course in the physical domain. In patients who undergo a successful ETV, the posttreatment stability in the ventricular size is not associated with a worse quality of life.

References


Disclosures
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions
Conception and design: Ros-Sanjuán. Acquisition of data: Ros-Sanjuán, Iglesias-Moroño, Ros-López, Delgado-Babiano. Analysis and interpretation of data: Ros-Sanjuán, Rius-Díaz. Drafting the article: Ros-Sanjuán. Critically revising the article: Ros-Sanjuán, Iglesias-Moroño, Ros-López. Reviewed submitted version of manuscript: Ros-Sanjuán. Approved the final version of the manuscript on behalf of all authors: Ros-Sanjuán. Statistical analysis: Ros-Sanjuán, Rius-Díaz. Administrative/technical/material support: Iglesias-Moroño, Arráez-Sánchez. Study supervision: Iglesias-Moroño, Ros-López, Arráez-Sánchez.

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