A validation study of the modified Canadian Preoperative Prediction Rule for Hydrocephalus in children with posterior fossa tumors

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OBJECTIVE Perioperative management of hydrocephalus in children with posterior fossa tumors (PFTs) remains challenging. The modified Canadian Preoperative Prediction Rule for Hydrocephalus (mCPPRH) has been previously described as a useful tool in predicting which children are at higher risk for permanent hydrocephalus following PFT resection and can be used in guiding treatment. The aim of this study was to externally validate this predictive model.

METHODS A retrospective review of the children treated in a single unit was conducted, recording all of the mCPPRH parameters (age, preoperative radiological diagnosis, presence of moderate/severe hydrocephalus, transependymal edema, and metastatic disease at the time of diagnosis), the need for a CSF diversion procedure at 6 months, time to surgery, and management of hydrocephalus. A receiver operating characteristic (ROC) curve was plotted using the mCPPRH, age, Evans index (EI), and frontooccipital horn ratio (FOHR), and an area under the curve (AUC) was calculated. A point-biserial correlation was run to determine the relationship between time to surgery, the insertion of an external ventricular drain (EVD), or initial EVD clamping and the development of postoperative persistent hydrocephalus.

RESULTS From a total of 75 patients (mean age 6.99 years, 62.7% male) who were included in the study, 8 (10.7%) required permanent CSF diversion following PFT resection. The AUC of the ROC curve was 0.618 for the mCPPRH (p = 0.18, SE 0.088, 95% CI 0.446–0.791), 0.633 for age (p = 0.26, SE 0.119, 95% CI 0.40.867), 0.604 for the EI (p = 0.34, SE 0.11, 95% CI 0.389–0.818), and 0.663 for the FOHR (p = 0.17, SE 0.121, 95% CI 0.427–0.9). A significant positive correlation between EVD insertion (r = 0.239, p = 0.03) and insertion of a ventriculoperitoneal shunt was found. A negative correlation between the postoperative clamping of the EVD (r = −0.158, p = 0.4) and the time to PFT surgery (r = −0.06, p = 0.6) did not reach statistical significance.

CONCLUSIONS The implementation of the mCPPRH score failed to reliably predict which children would require permanent CSF diversion following PFT resection when applied to this cohort. Clinical judgment remains the mainstay of choosing the perioperative treatment of hydrocephalus.

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ventriculostomy (ETV). \(^{19–22}\) prior to definitive resection. However, given that the majority of children with hydrocephalus at presentation will have no signs or symptoms of raised ICP following PFT resection, this management option remains controversial.

Riva-Cambrin et al. developed a predictive score based on a large Toronto (TOR) cohort \((n = 331)\) that could be reliably used to identify the patients at high risk of requiring treatment for persistent hydrocephalus after tumor resection \((\text{Canadian Preoperative Prediction Rule for Hydrocephalus [CPPRH]})^7\). An external cohort \((\text{Vancouver [VAN]})\) was used to successfully validate it. Foreman et al. \(^8\) subsequently described a modified version of the prediction model \((\text{mCPPRH})\) based on the Children’s Hospital of Alabama (CHA) cohort, replacing the presence of papilledema with radiological evidence of transependymal flow and using a total of five factors to predict the risk of developing hydrocephalus: age < 2 years, moderate/severe hydrocephalus, transependymal edema, preoperative tumor diagnosis, and presence of metastases. It has been suggested that this tool can be utilized to guide clinicians regarding the use of prophylactic CSF diversion and the optimal management of hydrocephalus perioperatively, with more aggressive measures deemed necessary in children categorized within the high-risk group.

To date there has been no external validation of the mCPPRH. The predictive model should ideally accurately predict the development of hydrocephalus when applied to all pediatric patients undergoing surgery for PFT resection. We aimed to externally validate the mCPPRH using our own cohort of patients. Secondary objectives were to assess for the presence of correlation between other perioperative variables \((\text{time to surgery, insertion of an external ventricular drain [EVD], and the initial clamping of it})\) and the development of persistent post–PFT resection hydrocephalus.

**Methods**

**Study Design and Participants**

We conducted a retrospective review of 75 patients with PFTs that were operated on in our unit \((\text{Department of Neurosurgery, Royal Victoria Infirmary})\) between 2005 and 2019, collecting data from paper and electronic records as well as pre- and postoperative MRI. Inclusion criteria were age < 18 years at the time of surgery, available preoperative MRI as well as imaging reports from a consultant neuroradiologist, and a minimum follow-up period of 6 months. Patients who underwent an ETV prior to or during the tumor resection were excluded. For patients with recurrent tumors and repeat operations, data were analyzed for the initial primary presentation and not the recurrences. If the initial presentation was before the time frame of our study, then such patients were excluded. The STROBE guidelines were used for the reporting of this study. \(^{23}\)

**Treatment**

All children were admitted under joint care with a pediatric neurooncologist following the initial diagnosis of a PFT. Patients were immediately started on corticosteroid treatment following the identification of a PFT, and definitive tumor resection was scheduled on the next available daytime \((\text{not emergency/off hours})\) operating list. Pretumor resection surgical treatment of the hydrocephalus was performed in the cases of impaired consciousness despite steroid treatment, and in the vast majority of those the insertion of an EVD was chosen, while few underwent an ETV. Following PFT resection, an EVD either remained clamped \((\text{based on the hypothesis that this would encourage the reestablishment of the normal CSF circulation})\) until there were clinical signs of raised ICP or was kept on continuous flow immediately postoperatively depending on the surgeon’s preference.

**Variables**

Radiological reports were used to record the most likely differential diagnosis of the tumor pathology as well as the presence of transependymal edema \((\text{increased T2 signal periventricularly on FLAIR MRI})\), the presence of moderate/severe hydrocephalus, and whether or not metastatic disease was evident. The presence of moderate/severe hydrocephalus was defined as Evans index \((\text{EI})\) > 0.3 or frontooccipital horn ratio \((\text{FOHR})\) > 0.37. The primary mCPPRH score calculation was based on the EI, but a secondary analysis was performed using the FOHR to assess for any differences in the accuracy of the predictive model. The time to surgery was defined as the time elapsed from original imaging \((\text{MRI})\) until definitive PFT resection. Management of perioperative hydrocephalus was recorded as 1) pretumor resection ETV, 2) insertion of an EVD, and 3) post–PFT resection insertion of a VPS or ETV, along with the time to definitive treatment in cases needing permanent CSF diversion. As per the original description of the predictive model, \(^7\) the need for permanent CSF diversion was recorded when it occurred within 6 months from PFT resection. The mCPPRH score was calculated based on the original study \((\text{range 0–10})\) and patients were classified into low \((0–4)\) and high \((5–10)\) risk.

**Ethical Compliance**

A Research Ethics Committee review was deemed unnecessary for this study, based on an evaluation using the relevant national research authority decision tool \((\text{Health Research Authority of the National Health System of the United Kingdom})\). Patient consent was not required as this was a retrospective analysis. Institutional approval for a service evaluation study was sought and obtained.

**Statistical Analysis**

A receiver operating characteristic \((\text{ROC})\) curve was produced for each possible numeric value of the mCPPRH score, as well as for each of the individual parametric variables of the score \((\text{age, EI, FOHR})\). The ability to accurately predict the development of hydrocephalus was assessed by calculating the area under the curve \((\text{AUC})\) for each one of the parameters. An AUC of 0.5 suggests no discrimination, 0.7–0.8 is considered acceptable, 0.8–0.9 is considered excellent, and more than 0.9 is considered outstanding. \(^{25}\) A point-biserial correlation was undertaken to determine the relationship between time to surgery, the
insertion of an EVD or the initial EVD clamping, and the development of postoperative persistent hydrocephalus requiring a CSF diversion procedure. Statistical analyses were performed using IBM SPSS Statistics (version 26; IBM Corp.).

Results
Participants and Descriptive Data
A total of 109 PFTs were operated on between 2005 and 2019 in our unit, and following application of the inclusion/exclusion criteria, a total of 75 patients were included in the analysis (Fig. 1). The mean age was 6.99 years (range 0.1–18 years) and there was a male predominance (62.7% male vs 37.3% female). A total of 8 patients (10.7%) required permanent CSF diversion, and of those, only 3 were considered as high risk per mCPPRH. A summary of demographics, clinical data, and outcome is presented in Table 1 and different modalities of treatment of hydrocephalus in this cohort are outlined in Fig. 2. Table 2 illustrates the mCPPRH scores for this cohort.

mCPPRH Validation
The AUC for the ROC curve of mCPPRH was 0.618 in our cohort (p = 0.18, SE 0.088, 95% CI 0.446–0.791), indicating a poor accuracy of the score to predict which children would eventually require CSF diversion. Similar accuracy was found when calculating the predictive ability for the development of hydrocephalus when assessing age (AUC = 0.633, p = 0.26, SE 0.119, 95% CI 0.4–0.867), EI (AUC = 0.604, p = 0.34, SE 0.11, 95% CI 0.389–0.818), and FOHR (AUC = 0.663, p = 0.17, SE 0.121, 95% CI 0.427–0.9) individually (Fig. 3). A secondary analysis was conducted based on the FOHR, as it is considered a more sensitive parameter to assess overall ventricular volume26,27 and has also been used by the original authors.7 Interestingly, this further reduced the accuracy of the suggested predictive model (AUC = 0.599, p = 0.25, SE 0.087, 95% CI 0.429–0.769).
Other Factors Associated With Persistent Postoperative Hydrocephalus

A point-biserial correlation revealed a significant positive correlation between EVD insertion ($r = 0.239$, $p = 0.03$) and insertion of a VPS. A negative correlation was observed between the postoperative clamping of the EVD ($r = -0.158$, $p = 0.4$) and the time to PFT surgery ($r = -0.06$, $p = 0.6$) with the development of postoperative hydrocephalus, but it did not reach statistical significance.

Discussion

We found that the mCPPRH model had poor accuracy in predicting which children in our cohort would require permanent CSF diversion following PFT resection. The size of our cohort ($n = 75$) was similar to the CHA cohort ($n = 76$) and slightly smaller than the VAN cohort ($n = 108$), while the original TOR cohort was significantly larger than all three ($n = 343$). However, this smaller sample size should ideally not eliminate the predictability of the score. We did not compare the characteristics (demographic and clinical) of our group with the groups that were used for the development of the CPPRH and mCPPRH in order to establish similarities of the characteristics, given that the purpose of an effective predictive model is its utility across a range of pediatric patients with PFTs. Our cohort had a lower rate of VPS insertion (10.7%).

TABLE 2. Summary of patient risk stratification according to mCPPRH and VPS insertion

<table>
<thead>
<tr>
<th>mCPPRH Risk Score</th>
<th>No Shunt (n = 67)</th>
<th>VPS (n = 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High risk (5–10)</td>
<td>20</td>
<td>3</td>
</tr>
<tr>
<td>Low risk (0–4)</td>
<td>47</td>
<td>5</td>
</tr>
</tbody>
</table>

1Values represent the number of patients.

FIG. 2. Summary of different treatments for hydrocephalus and outcomes.

FIG. 3. ROC curves for the mCPPRH, age, EI, and FOHR and the need for permanent CSF diversion: mCPPRH ($AUC = 0.618$, $p = 0.18$, SE 0.088, 95% CI 0.446–0.791), age ($AUC = 0.633$, $p = 0.26$, SE 0.119, 95% CI 0.4–0.867), EI ($AUC = 0.604$, $p = 0.34$, SE 0.11, 95% CI 0.389–0.818), and FOHR ($AUC = 0.663$, $p = 0.17$, SE 0.121, 95% CI 0.427–0.9). Figure is available in color online only.
compared to the CHA cohort, which had an 18% rate, even though our cohort had a significantly larger proportion of high-risk patients (30.7% vs 11%). This may reflect that factors other than those recordable in the preoperative phase, such as intraventricular blood content and volume of CSF drained, play a significant role in the development of persistent postoperative hydrocephalus or that some clinicians have a lower threshold in performing a permanent CSF diversion procedure in this population. Additionally, consistent with the mCPPRH, we observed the predictive accuracy of age, EI, and FOHR. This consistency suggests that these parameters are important when trying to predict which children are at high risk of permanent postoperative hydrocephalus. We found that combining age and EI or FOHR with the other three factors (radiological diagnosis, transependymal edema, and the presence of metastases) did not provide a significant additional predictive value for our cohort.

We identified a significant correlation between the insertion of an EVD and the insertion of a VP shunt. This correlation reflects that even though a predictive model was not used to identify high-risk patients to facilitate the decision-making in the management of perioperative hydrocephalus, clinical judgment was sufficient in identifying those children who were more at risk of developing significant hydrocephalus despite PFT resection. A negative correlation between the clamping of the EVD following PFT resection and VPS insertion is supportive of the theory that clamping encourages the early reestablishment of normal CSF flow and absorption when obstruction is removed. However, this correlation did not reach statistical significance. If such a correlation does exist in our cohort, it may be susceptible to selection bias as the surgeon would have chosen the patients that she or he deemed suitable for such management. Children who tolerated the clamping of the EVD may therefore have been those who did not have severe or long-term hydrocephalus, but rather obstructive hydrocephalus that resolved with tumor resection.

A negative correlation between the time to surgery and the need for VPS insertion likely reflects that children with clinical and radiological evidence of raised ICP, and thus more likely to need a post–tumor resection VPS, are more likely to undergo surgery sooner. We chose to use EI as a means of defining the presence of moderate/severe hydrocephalus given that this is an objective metric and thus more reliable. Utilizing a subjective measurement ideally should not change the accuracy of a model; otherwise, it is assumed that there is a difference between the radiologist’s subjectivity on defining the severity of hydrocephalus and the objective measurement, making the model subject to criticism. A secondary analysis using the FOHR reduced the accuracy of the model even further.

**Interpretation**

Here, we have provided a novel external validation study of the mCPPRH. Other studies have used the mCPPRH in retrospect to classify their patients. Schneider et al. have reported that it has proved to be a significant predictor for CSF diversion surgery. However, they did not calculate the score for a fifth of their patients, nor did they examine its accuracy as a predictive model.

The mechanism of persistent hydrocephalus following PFT resection in children has a multifactorial pathophysiology. Preoperative hydrocephalus is a result of direct obstruction as well as potential leptomeningeal disease impeding CSF absorption. However, perioperative factors are likely to be contributory in the development and persistence of abnormal CSF circulation following resective surgery. High protein and blood product content of the CSF following surgery may be a significant factor. Abraham et al. report that the presence of intraventricular blood on post–tumor resection brain imaging is a significant independent factor associated with persistent hydrocephalus. Furthermore, Srinivasan et al. reported that within their patient group that underwent prophylactic ETV, 8 were considered as high risk per mCPPRH, and from those, 3 patients required a VPS following tumor resection, all of whom had intraventricular blood on their post–tumor resection scan. Other factors such as type of dural closure and CNS infection have also been associated with the need for a permanent CSF diversion. It is therefore difficult to establish a predictive model for the development of postoperative hydrocephalus, based exclusively on preoperative factors given that intra- and postoperative factors are likely to significantly contribute to the risk as well. In our cohort, the use of an EVD correlated significantly with the need for a VPS, which is concordant with previously published data.

The authors describing the predictive models for hydrocephalus argue that the classification of patients can be used in favor of prophylactic ETV prior to PFT resection in the patients who are at high risk, even though this is actually rare in their practice. In our series, 20 patients were classified as high risk but did not require a permanent CSF diversion, indicating that these children might have undergone an additional unnecessary procedure (prophylactic ETV). Bognár et al. were against the use of prophylactic ETV, in light of the low postoperative frequency of hydrocephalus, which was 15% in their series. Moreover, Srinivasan et al., who retrospectively reviewed 95 children with PFTs, concluded that a pre-resection ETV did not reliably prevent the need for a CSF diversion procedure following tumor resection. In particular, children who theoretically stand to gain the most from pre-resection ETV (i.e., children who are at high risk of postresection hydrocephalus based on the mCPPRH score) do not actually see the intended benefit because ETV failure in the high-risk group was relatively high at 37.5%. Srinivasan et al. did associate a higher mCPPRH score with ETV failure.

Lin and Riva-Cambrin also described their experience of using the mCPPRH in their unit as an adjunctive tool for the perioperative management of hydrocephalus in this population. They suggest that all patients at high risk, as predicted by the mCPPRH score, and those at low risk but with moderate/severe hydrocephalus at presentation should have an intraoperative EVD insertion prior to tumor resection. In our cohort, there were 55 patients who had moderate/severe hydrocephalus at presentation and only 23 had an EVD inserted. Among those who required a VPS insertion, only 3 patients did not have an EVD inserted intraoperatively. This suggests that clinical judgment was appropriate in choosing the patients who would
require an EVD, and we inserted 32 fewer EVDs (42% less) than what would have been inserted if all patients at high risk according to the mCPPRH model had undergone insertion of an EVD.

Study Limitations
This is a retrospective series, and it is subject to reporting bias given that data had already been recorded for other than the purpose of this study. In addition, treatment decisions were made on an individual patient basis by the lead surgeon and so our observations are also subject to selection biases. However, age, EI, and radiological report at presentation (based on which the model is calculated) are all parameters that were reliably recorded and objectively assessed despite the study’s retrospective nature. This is also a small study population (n = 75) compared to the original study describing the CPPRH (n = 331), but it is nevertheless similar in size to the CHA cohort that was used to describe the mCPPRH (n = 76).

Conclusions
We have tested the mCPPRH in our 14-year cohort of 75 children operated on for PFTs and the model failed to accurately predict which children would develop persistent postoperative hydrocephalus requiring a permanent CSF diversion procedure. It is therefore unsuitable to be used as a means of selecting patients who would benefit from a prophylactic ETV. Clinical judgment remains the mainstay of choosing the perioperative treatment of hydrocephalus.

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: Cowie. Acquisition of data: Pitsika, Fletcher. Analysis and interpretation of data: Pitsika. Drafting the article: Pitsika. Critically revising the article: Pitsika, Coulter, Cowie. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Pitsika. Statistical analysis: Pitsika. Study supervision: Cowie.

Supplemental Information
Previous Presentations
Presented orally at the virtual European Society of Pediatric Neurosurgery Annual Meeting, April 28, 2021.

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