Clinical implications of medulloblastoma subgroups: incidence of CSF diversion surgery

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OBJECT While medulloblastoma was initially thought to comprise a single homogeneous entity, it is now accepted that it in fact comprises 4 discrete subgroups, each with its own distinct demographics, clinical presentation, transcriptomics, genetics, and outcome. Hydrocephalus is a common complication of medulloblastoma and not infrequently requires CSF diversion. The authors report the incidence of CSF diversion surgery in each of the subgroups of medulloblastoma (Wnt, Shh, Group 3, and Group 4).

METHODS The medical and imaging records for patients who underwent surgery for medulloblastoma at The Hospital for Sick Children were retrospectively reviewed. The primary outcome was the requirement for CSF diversion surgery either before or within 60 days of tumor resection. The modified Canadian Preoperative Prediction Rule for Hydrocephalus (mCPPRH) was compared among subgroups.

RESULTS Of 143 medulloblastoma patients, treated from 1991 to 2013, sufficient data were available for 130 patients (15 with Wnt, 30 with Shh, 30 with Group 3, and 55 with Group 4 medulloblastomas). Of these, 28 patients (22%) ultimately underwent CSF diversion surgery: 0% with Wnt, 29% with Shh, 29% with Group 3, and 43% with Group 4 tumors. Patients in the Wnt subgroup had a lower incidence of CSF diversion than all other patients combined (p = 0.04). Wnt patients had a lower mCPPRH score (lower risk of CSF diversion, p = 0.045), were older, had smaller ventricles at diagnosis, and had no leptomeningeal metastases.

CONCLUSIONS The overall rate of CSF diversion surgery for Shh, Group 3, and Group 4 medulloblastomas is around 30%, but no patients in the present series with a Wnt medulloblastoma required shunting. The low incidence of hydrocephalus in patients with Wnt medulloblastoma likely reflects both host factors (age) and disease factors (lack of metastases). The absence of hydrocephalus in patients with Wnt medulloblastomas likely contributes to their excellent rate of survival and may also contribute to a higher quality of life than for patients in other subgroups.

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KEY WORDS medulloblastoma; molecular subgroups; hydrocephalus; shunt; endoscopic third ventriculostomy; mCPPRH; pediatric; oncology; posterior fossa

MEDULLOBLASTOMA is the most common malignant pediatric brain tumor and is a common cause of morbidity and death among pediatric neurosurgery patients. Current therapy for medulloblastoma consists of maximal safe resection, craniospinal radiotherapy for children older than 3 years of age, and subsequent high-dose chemotherapy. 

Survivors are often left with significant sequelae of both the disease and its therapy, all of which can have a serious and negative impact on a patient’s quality of life. In the past, medulloblastoma was thought to consist of a heterogeneous small blue cell tumor of the cerebellum. More recently it has

ABBREVIATIONS ETV = endoscopic third ventriculostomy; FOR = frontal and occipital horn ratio; mCPPRH = modified Canadian Preoperative Prediction Rule for Hydrocephalus.


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become apparent and well accepted that in reality there are 4 distinct subgroups of medulloblastoma, each with its own specific demographics, clinical presentation, imaging features, basic biology, response to therapy, and outcome. These 4 subgroups, Wnt, Shh, Group 3, and Group 4 medulloblastoma, will likely be subdivided in future clinical trials of medulloblastoma and each will each require its own specific type of targeted therapy.

By definition, medulloblastomas arise within the posterior fossa, usually from the cerebellum. It is very common for medulloblastoma patients to present with noncommunicating hydrocephalus due to occlusion of the fourth ventricle or its outlets by the mass in the posterior fossa. It is also possible for medulloblastoma patients to present with communicating hydrocephalus, usually secondary to leptomeningeal metastases. Indeed, it is quite common for a medulloblastoma patient’s primary presentation to be as the result of the hydrocephalus rather than direct effects of the tumor mass itself.

The treatment of hydrocephalus in a child with a posterior fossa tumor varies by individual and by institution, depending on the clinical and radiological presentation. Options for treatment of hydrocephalus range from tumor resection alone, with or without temporary external CSF drainage, to endoscopic third ventriculostomy (ETV) or placement of a permanent CSF diversion device (usually a ventriculoperitoneal shunt). Shunt procedures can add significantly to a patient’s morbidity and mortality due to complications such as shunt infection, shunt blockage, and shunt overdrainage. In the past, there was also a worry that CSF diversion in a patient with leptomeningeal metastases might lead to systemic metastases of the medulloblastoma. The rate of CSF diversion surgery in medulloblastoma patients varies in the literature but likely hovers around 33%. Many other elements in the presentation and care of children with medulloblastoma vary by subgroup, so we decided to determine the subgroup specific incidence of CSF diversion surgery.

Methods

Subgrouping of Medulloblastoma Tissue

All tissue samples were subgrouped using nanoString limited gene expression profiling from either frozen or formalin-fixed paraffin-embedded–derived tissue as previously described.

Study Design and Data Collection

This is a retrospective cohort review of patients surgically treated for medulloblastoma at The Hospital for Sick Children in Toronto. Data on the molecular subgroup status of 143 medulloblastoma tissue samples were available, collected from June 1991 to March 2013. After obtaining permission for data review from the institutional Research Ethics Board, we identified 130 patients in whom clinical and hydrocephalus parameters were available in sufficient quality for analysis. Thirteen patients were excluded, 11 for missing preoperative imaging or missing data on hydrocephalus treatment, one because he died within 30 days after surgery, and one because he had previously undergone shunt placement for other reasons. Demographic data, information on tumor and CSF diversion surgeries, and data on metastatic disease status at diagnosis were reviewed in the patient chart. Data entry was performed using Microsoft Access 2013 and statistical analysis using IBM SPSS v22.

Hydrocephalus Parameters

To formally assess hydrocephalus and the probability of the need for CSF diversion surgery after tumor resection, we applied the modified Canadian Preoperative Prediction Rule for Hydrocephalus (mCPPRH). This scale was developed by Riva-Cambrin et al. in 2009 and validated by Foreman et al. in 2013. The validation study recommended the use of the parameter “transpendermal edema” instead of “papilledema” (as suggested in the original publication) to overcome the lack of clinical data for papilledema usually observed in the retrospective setting. We were facing this same issue and therefore used the modified version of the CPPRH—the mCPPRH. Demographic, clinical, and radiological parameters to calculate the mCPPRH score are summarized in Table 1. The score ranges from 0–10, with a score of 4 points or higher delineating a high risk for the need of CSF diversion surgery (50% of the patients or more) after tumor resection.

Calculation of the ventricular size was performed on the last preoperative CT or MRI scan before first tumor resection. As the term “moderate/severe” hydrocephalus in the mCPPRH scale appears to be somewhat arbitrary, we decided to calculate the “frontal and occipital horn ratio” (FOR) developed by Kulkarni et al. in 1999. The cutoff from “none/mild” to “moderate/severe” hydrocephalus was chosen at a FOR of 0.45, in accordance with the authors’ recommendation. As the FOR does not have an independent prognostic value for the need of CSF diversion surgery, this parameter was solely used to decide about assignment into the two subscore groups of “none/mild” and “moderate/severe” hydrocephalus. In cases in which preoperative imaging was missing, the variable for the degree of hydrocephalus was adopted from the radiology report, as suggested by the original publication.

Data Presentation and Statistical Analysis

After collection of the aforementioned data, the database was de-identified and the key to link demographics to

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt;2 yrs</td>
<td>3</td>
</tr>
<tr>
<td>Presence of transepndymal edema</td>
<td>1</td>
</tr>
<tr>
<td>Moderate/severe hydrocephalus</td>
<td>2</td>
</tr>
<tr>
<td>Cerebral metastases</td>
<td>3</td>
</tr>
<tr>
<td>Preop estimated tumor diagnosis</td>
<td></td>
</tr>
<tr>
<td>Medulloblastoma</td>
<td>1</td>
</tr>
<tr>
<td>Ependymoma</td>
<td>1</td>
</tr>
<tr>
<td>Dorsal exophytic brainstem glioma</td>
<td>1</td>
</tr>
<tr>
<td>Total possible</td>
<td>10</td>
</tr>
</tbody>
</table>

TABLE 1. The mCPPRH score in children with posterior fossa neoplasms
patient identifier stored on a separate encrypted drive. The de-identified database was then transferred to IBM SPSS v22 for statistical analysis.

For the comparison of molecular medulloblastoma subgroups, patients were first divided according to their subgroup status into a Wnt, Shh, Group 3, and Group 4 collective. Then p values were calculated across the subgroups using the 1-way ANOVA for continuous variables and the chi-square test for categorical variables. Additionally, each variable in every subgroup was compared pairwise with the remainder of the patients using the t-test for comparison of means for continuous variables and the Fisher exact test for categorical variables.

In addition to the stratification into molecular subgroups, the patients were also divided according to the requirement for CSF diversion surgery. Patients in the CSF diversion surgery group were defined as those who received a shunt or an ETV within 60 days of their first tumor resection surgery and excluded those who were treated 60 days after tumor resection surgery. We chose 60 days as the cutoff for the CSF diversion surgery group to exclude patients who were shunted at the end of life, when disseminated disease led to communicating (malsorption due to metastases), rather than obstructive (fourth ventricular outlet obstruction), hydrocephalus. The aforementioned statistical tests were similarly applied for these two groups.

Results

Of 130 patients, one-third (35%) were female, mean age at diagnosis was 86 months (7.2 years), and one-third had metastatic disease at diagnosis (31%). Fifteen patients (12%) were diagnosed with Wnt, 30 (23%) with Shh, 30 (23%) with a Group 3, and 55 (42%) with a Group 4 medulloblastoma. The mean follow-up time was 71 months (5.9 years). Thirty patients (23%) had died within that follow-up period with a mean survival time of 42 months (3.5 years). Twenty-eight (22%) individuals needed CSF diversion surgery within 60 days of resection. Two patients had a shunt placed before tumor resection. No ETVs were performed before the primary tumor resection, but 5 patients underwent ETV after tumor resection, and in 4 of these cases the ETV had to be converted to a ventriculoperitoneal shunt.

Demographics and Metastatic Status Across Molecular Subgroups

Table 2 provides an overview of demographic and metastatic status of all patients by subgroup. Sex, age at diagnosis, proportion of deceased patients, survival time, and metastatic status at diagnosis were significantly different in their distribution/mean value across the 4 subgroups. When comparing each subgroup individually to the remainder of the patients, Wnt patients were older (118 months), predominantly female (67%), less frequently had metastatic disease (7%), and were universally alive at follow-up. Patients in the Shh group were youngest (mean 69 months) and had the shortest survival time (mean 24 months) in the pairwise comparison. Group 3 patients were on the young side (mean 70 months) compared with the remainder of the individuals and had the highest rate (50%) of metastases at diagnosis. Patients with the longest mean survival time (mean 72 months) were found in Group 4. In the Wnt subgroup, no deaths occurred during the observational time. These subgroup-specific characteristics are consistent with the published literature.

“Infants” were regarded as those patients with medulloblastoma who were younger than the age of 3 years and were not subjected to craniospinal irradiation. In our series, Shh and Group 3 medulloblastomas showed a significantly higher proportion of very young children than Wnt and Group 4.

Hydrocephalus Parameters Across Molecular Subgroups

The parameters assessed to calculate the mCPPRH score are summarized in Table 3. An overall significant difference in distribution/mean value was found for the parameters age < 2 years, transepndymal edema, and mCPPRH score. Of note, the parameter age < 2 years is given by the authors of the mCPPRH scale and does not correspond to the age limit of 3 years used in the presentation of clinical parameters according to subgroups in Table 2. The latter was chosen because the age limit to administer radiotherapy was 3 years.

Because of missing data, we could not calculate the FOR for 25 patients (19%) or the mCPPRH score for 24 patients (18%). Wnt patients had a smaller FOR (0.39) in the pairwise comparison; the chi-square test p value across all subgroups, however, was greater than 5%. The mCPPRH score in the Wnt subgroup, though, was significantly smaller (1.92 points) with a significant p value for the chi-square test across all subgroups (p = 0.45). Group 4 patients had the highest rate of transepndymal edema (93%, p = 0.02).

Early CSF Diversion Surgery

Table 4 summarizes the data obtained in the patients who required CSF diversion surgery within 60 days compared with data acquired in those who did not. As mentioned above, a total of 28 patients (22%) ultimately needed surgical treatment for their hydrocephalus. Shunt-treated patients were significantly younger (59 vs 93 months, p = 0.0004) and, not surprisingly, had a higher mean mCPPRH score (4.09 versus 2.82 points, p = 0.002) than those not treated with a shunt. When looking at age distribution across the subgroups in the patients who underwent CSF diversion surgery, Shh patients were youngest (mean age 43 months, median age 26 months), although this difference was too small to be significant. Of the patients who did not undergo CSF diversion surgery, Wnt patients were significantly older (p = 0.02).

The observation that not a single patient in the Wnt subgroup needed CSF diversion surgery was also significant when compared with all non-Wnt patients (p = 0.04). The distribution across all subgroups, however, did not show a significant difference. In a binominal multivariate logistic regression analysis, only the mCPPRH score remained significant predictor for needing CSF diversion surgery. Being in the Wnt group alone was not independently predictive. The remaining variables (sex, proportion of de-
cessed patients, survival time, follow-up duration, and metastatic status) were not significantly different in the CSF diversion surgery groups. The incidence of metastatic disease at diagnosis, however, tended to be higher in the group needing CSF diversion surgery (43% vs 28%).

**Late CSF Diversion Surgery**

In addition to patients treated with CSF diversion acutely within 60 days of tumor resection, patients who needed CSF diversion after that time were additionally evaluated. Five patients were treated at a later point in time: none in the Wnt group, 1 of 30 in the Shh group (3%), 3 of 30 in Group 3 (10%), and 1 of 55 in Group 4 (2%). The p value across all subgroups was not significant; however, when comparing Group 3 patients who needed late CSF diversion surgery to the remainder of the patients, the p value was 0.46.

**Discussion**

The single entity formerly known as medulloblastoma is being rapidly replaced by the 4 accepted subgroups of medulloblastoma. In the next round of clinical trials, medulloblastoma patients will likely be divided according to the molecular subgroup of their lesion, and discussions of subgroup affiliation are currently part of the clinical consideration and treatment planning for patients with medulloblastoma in many first-world pediatric neurosurgical centers. Neurosurgeons are part of the team treating children with medulloblastoma and will therefore need to be familiar with the molecular subgroups of the disease to participate in these discussions and provide optimal care to their patients. In addition to tumor resection, initial and ongoing treatment of hydrocephalus is an important part of the neurosurgeon’s role in the care of medulloblastoma patients. The percentage of patients needing CSF diversion surgery in our cohort of patients (22%) seems acceptable and compares well with the literature. Our finding that no patients with Wnt medulloblastoma in our series required CSF diversion surgery likely relates to patient/host factors (older age at presentation, smaller ventricles at presentation, lower mCPPRH score, and lowest incidence of transependymal edema), as well as disease factors (near absence of leptomeningeal metastases), but might also relate to the specific biological characteristics of the Wnt subgroup. The absence of the need for CSF diversion surgery after 60 days also appears supportive of that observation, suggesting that all non-Wnt patients are prone to leptomeningeal spread at recurrence, leading to a higher rate of communicating hydrocephalus.

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**TABLE 2. Demographics and metastatic status across molecular subgroups**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (n = 130)</th>
<th>Wnt (n = 15)</th>
<th>Shh (n = 30)</th>
<th>Group 3 (n = 30)</th>
<th>Group 4 (n = 55)</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of females (%)</td>
<td>45 (34.6)</td>
<td>10 (66.7)†</td>
<td>14 (46.7)</td>
<td>6 (20.0)</td>
<td>15 (27.3)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Mean age at diagnosis in mos (median)</td>
<td>86 (80)</td>
<td>118 (101)†</td>
<td>69 (57)†</td>
<td>70 (59)†</td>
<td>95 (89)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>No. age &lt;3 yrs at diagnosis (%)</td>
<td>20 (15.4)</td>
<td>0 (0.0)</td>
<td>11 (36.7)†</td>
<td>9 (30.0)†</td>
<td>0 (0.0)†</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>No. deceased at last follow-up (%)</td>
<td>30 (23.1)</td>
<td>0 (0.0)†</td>
<td>11 (36.7)†</td>
<td>10 (33.3)</td>
<td>9 (16.4)</td>
<td>0.01</td>
</tr>
<tr>
<td>Mean survival of deceased in mos (median)</td>
<td>42 (34)</td>
<td>—</td>
<td>24 (14)†</td>
<td>34 (27)</td>
<td>72 (72)†</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Mean follow-up (median)</td>
<td>71 (62)</td>
<td>58 (47)</td>
<td>69 (61)</td>
<td>63 (54)</td>
<td>81 (76)</td>
<td>0.27</td>
</tr>
<tr>
<td>No. w/ metastasis at diagnosis (%)</td>
<td>40 (30.8)</td>
<td>1 (6.7)†</td>
<td>6 (20.0)</td>
<td>15 (50.0)†</td>
<td>18 (32.7)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

— = not applicable.
* Boldface indicates statistical significance.
† Significant difference when compared pairwise to remainder of patients.

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**TABLE 3. Hydrocephalus parameters across molecular subgroups**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (n = 130)</th>
<th>Wnt (n = 15)</th>
<th>Shh (n = 30)</th>
<th>Group 3 (n = 30)</th>
<th>Group 4 (n = 55)</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients age &lt;2 yrs (%)</td>
<td>8 (6.2)</td>
<td>0 (0.0)</td>
<td>4 (13.3)</td>
<td>4 (13.3)</td>
<td>0 (0.0)†</td>
<td>0.02</td>
</tr>
<tr>
<td>No. of patients w/ transependymal edema (%)†</td>
<td>86 (61.1)</td>
<td>8 (61.5)</td>
<td>16 (69.6)</td>
<td>21 (80.8)</td>
<td>41 (93.2)†</td>
<td>0.02</td>
</tr>
<tr>
<td>FOR§</td>
<td>0.43 (0.42)</td>
<td>0.40 (0.39)†</td>
<td>0.42 (0.40)</td>
<td>0.44 (0.43)</td>
<td>0.43 (0.43)</td>
<td>0.10</td>
</tr>
<tr>
<td>No. of patients w/ moderate/severe hydrocephalus (%)‡</td>
<td>37 (29.4)</td>
<td>2 (15.4)</td>
<td>7 (30.4)</td>
<td>10 (38.5)</td>
<td>18 (40.9)</td>
<td>0.36</td>
</tr>
<tr>
<td>No. of patients w/ cerebral metastases (%)</td>
<td>18 (13.8)</td>
<td>0 (0.0)</td>
<td>3 (10.0)</td>
<td>6 (20.0)</td>
<td>9 (16.4)</td>
<td>0.26</td>
</tr>
<tr>
<td>Mean mCPPRH score (median)‡</td>
<td>3.08 (2.00)</td>
<td>1.92 (2.00)†</td>
<td>2.83 (2.00)</td>
<td>3.38 (2.00)</td>
<td>3.36 (4.00)</td>
<td>0.045</td>
</tr>
</tbody>
</table>

* Boldface values indicate statistical significance.
† Significant difference when compared pairwise to remainder of patients.
‡ Information on 24 patients not available; percentages refer to total number with available information in each subgroup (Wnt = 13, Shh = 23, Group 3 = 26, and Group 4 = 44).
§ Information on 25 patients not available; percentages refer to total number with available information in each subgroup (Wnt = 12, Shh = 23, Group 3 = 26, and Group 4 = 44).
In summary, the most likely explanation for the Wnt patients not needing CSF diversion surgery is their lower mCPPRH score, meaning their risk profile is more favorable. In a binominal logistic regression analysis, being in the Wnt group did not independently influence the need for CSF diversion surgery.

We observed that ETV for the treatment of hydrocephalus in the acute setting had a high conversion rate to conventional shunt surgery of 80%. This is somewhat contradictory to reports citing a higher success rate for ETV but might be the result of the long observation period and the absence of the standard use of ETV to treat hydrocephalus due to posterior fossa tumors at our institution.

Our study does have limitations in that Wnt medulloblastomas are the least common (about 10%), data collection was retrospective, and the patients were accrued over a long period of time (22 years). The low incidence of Wnt medulloblastomas especially results in a small patient number when evaluating the Wnt subgroup separately. However, because CSF diversion can contribute serious morbidity and even occasionally lead to death, the lack of hydrocephalus in patients with Wnt medulloblastoma no doubt adds to the overwhelmingly favorable prognosis in this subgroup.

Furthermore, because a diagnosis of shunt-dependent hydrocephalus can decrease a patient’s quality of life, the freedom from hydrocephalus in Wnt medulloblastoma patients that we observed could contribute to a better quality of life than that experienced by children with other subtypes of medulloblastoma. In future studies, clinical data on larger numbers of Wnt medulloblastomas—the rarest subgroup of medulloblastomas—should be assessed in a multicenter fashion to confirm its association with a very low rate of CSF diversion surgery.

**Conclusions**

In a collective of 130 pediatric patients with medulloblastoma, the CSF diversion surgery rate was 22%. This rate was the same for the Shh, Group 3, and Group 4 molecular subgroup. In the Wnt subgroup, however, none of the patients needed CSF diversion surgery. The most likely explanation of this observation is the low risk profile of Wnt patients that is reflected in their lower mCPPRH score, suggesting again the relatively favorable clinical behavior of Wnt medulloblastomas.

**References**


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**TABLE 4. Data on CSF diversion surgery**

<table>
<thead>
<tr>
<th>Variable</th>
<th>CSF Diversion Required (n = 28)</th>
<th>Not Required (n = 102)</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. in subgroup (%)</td>
<td></td>
<td></td>
<td>0.17</td>
</tr>
<tr>
<td>Wnt</td>
<td>0 (0.0)†</td>
<td>15 (14.7)†</td>
<td></td>
</tr>
<tr>
<td>Shh</td>
<td>8 (28.6)</td>
<td>22 (21.6)</td>
<td></td>
</tr>
<tr>
<td>Group 3</td>
<td>8 (28.6)</td>
<td>22 (21.6)</td>
<td></td>
</tr>
<tr>
<td>Group 4</td>
<td>12 (42.9)</td>
<td>43 (42.2)</td>
<td></td>
</tr>
<tr>
<td>No. in Wnt subgroup (%)</td>
<td>0 (0.0)</td>
<td>15 (14.7)</td>
<td>0.04</td>
</tr>
<tr>
<td>No. female (%)</td>
<td>9 (32.1)</td>
<td>36 (35.3)</td>
<td>0.83</td>
</tr>
<tr>
<td>Mean age at diagnosis in mos (median)</td>
<td>59 (46)</td>
<td>93 (89)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Mean age in mos at diagnosis by subgroup (median)</td>
<td></td>
<td></td>
<td>0.10/0.02‡</td>
</tr>
<tr>
<td>Wnt</td>
<td>—</td>
<td>118 (101)†</td>
<td></td>
</tr>
<tr>
<td>Shh</td>
<td>43 (26)</td>
<td>78 (65)</td>
<td></td>
</tr>
<tr>
<td>Group 3</td>
<td>46 (34)</td>
<td>79 (66)</td>
<td></td>
</tr>
<tr>
<td>Group 4</td>
<td>79 (78)</td>
<td>99 (93)</td>
<td></td>
</tr>
<tr>
<td>No. dead at last follow-up (%)</td>
<td>7 (25.0)</td>
<td>23 (22.5)</td>
<td>0.80</td>
</tr>
<tr>
<td>Survival in mos of deceased (median)</td>
<td>43 (35)</td>
<td>42 (33)</td>
<td>0.93</td>
</tr>
<tr>
<td>Mean follow-up in mos (median)</td>
<td>77 (67)</td>
<td>70 (62)</td>
<td>0.50</td>
</tr>
<tr>
<td>No. w/ metastasis at diagnosis (%)</td>
<td>12 (42.9)</td>
<td>28 (27.5)</td>
<td>0.16</td>
</tr>
<tr>
<td>Mean mCPPRH score (median)§</td>
<td>4.09 (4.00)</td>
<td>2.80 (2.00)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

* Boldface indicates statistical significance.
† Significant difference when compared pairwise to remainder of patients.
‡ The p value on the left is for the CSF diversion group and that on the right is for the no-CSF diversion group.
§ Information on 24 patients not available.
39. Swartling FJ, Grimmmer MR, Hackett CS, Northcott PA, Fan...

**Author Contributions**
Conception and design: Schneider, Ramaswamy, Kulkarni, Bouffet, Taylor. Acquisition of data: Schneider, Ramaswamy, Bouffet. Analysis and interpretation of data: Schneider, Ramaswamy, Kulkarni, Taylor. Drafting the article: Schneider, Ramaswamy, Kulkarni, Bouffet, Taylor. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Schneider. Statistical analysis: Schneider, Ramaswamy, Kulkarni. Study supervision: Kulkarni, Bouffet, Taylor.

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