The long-term success of ETV in the treatment of primary aqueductal stenosis in pediatric patients has been widely discussed in the literature.2 On the other hand, the long-term outcome of obstructive hydrocephalus in patients with a history of IVH or infection or in those with hydrocephalus associated with tumors of the posterior fossa or of the quadrigeminal and pineal regions, myelomeningocele and Chiari malformation Type II, or Dandy-Walker syndrome, has been the object of few articles concerning patients under 16 years of age.23,24 Late closure of the stoma in patients with these kinds of hydrocephalus can be manifested by signs of sudden-onset intracranial hypertension and can have potentially disastrous consequences.3,11,18 The aim of this article is to assess the capacity of cine phase-contrast MR imaging to identify late failure in asymptomatic pediatric patients treated with ETV for hydrocephalus.

Methods. This study was a retrospective evaluation of cases involving patients who underwent ETV between January 1, 1999, and December 31, 2008, at the pediatric neurological surgery service of the University of Padua. Before 2004, patients were routinely followed up with cine MR imaging at 3, 6, and 12 months after ETV. In 2004, a protocol of annual cine MR follow-up was instituted as a result of a case of fatal late failure. The authors evaluated all cases of late failure identified through cine MR imaging and performed a statistical analysis to investigate the relationship between ETV failure and several variables, including the cause of hydrocephalus for which ETV was originally indicated.

Results. In a series of 84 patients (age range 6 days–16 years), 17 patients had early ETV failure. Of the remaining 67 patients, 5 (7%) were found to have no CSF flow through the fenestration and recurrent ventriculomegaly when assessed with cine MR imaging at 1, 2, 3, 4, and 7 years after ETV. The patient in whom ETV failure was identified 1 year postoperatively had Dandy-Walker malformation. The patients in whom ETV failure was identified 2, 3, and 4 years postoperatively all had undergone ETV for treatment of postinfective hydrocephalus. The patient in whom ETV failure was identified 7 years postoperatively had a cystic arachnopathy in the fourth ventricle after cerebellar astrocytoma removal.

Conclusions. Patients who undergo ETV for infective hydrocephalus and Dandy-Walker malformation should receive long-term follow-up, because late closure of the stoma may occur progressively and slowly. Intraoperative observation of thickened arachnoid membranes at the level of the interpeduncular cisterns at the first ETV and a progressive decreasing of CSF flow through the stoma on routine cine MR imaging should be considered unfavorable elements entailing a significant risk of deterioration. (DOI: 10.3171/2011.1.FOCUS10303)

Key Words • endoscopic third ventriculostomy • pediatric hydrocephalus • cine phase-contrast MR imaging

Abbreviations used in this paper: ETV = endoscopic third ventriculostomy; IVH = intraventricular hemorrhage.
Methods

This study was prompted by a fatal outcome of a case in 2004. The child died 1320 days after undergoing ETV for hydrocephalus linked to Dandy-Walker syndrome; she had signs of fatal intracranial hypertension and an occluded stoma demonstrated by cine MR imaging. This patient had not been followed up with radiological evaluation beyond 1 year after ETV because she did not show any signs or appear to experience any symptoms of intracranial hypertension.

The study consisted of a retrospective analysis of 84 cases involving patients ranging in age from 6 days to 16 years at the time of ETV. These patients had originally been selected for a first ETV after MR imaging confirmed enlargement of the lateral and third ventricles with absence or reduction of systolic/diastolic flow void through the sylvian aqueduct and the fourth ventricle outlet. The ETVs were performed at a single institution (University of Padua) by the same neurosurgeon (R.F.) between January 1, 1999, and December 31, 2008. A correct technical execution of ETV requires an adequate diameter of the stoma in the floor of the third ventricle and the perforation of the arachnoid membranes in the interpeduncular cistern, using a flexible endoscope, a monopolar wire, and balloon catheter.10

In 52 of these 84 patients, ETV was performed as a primary procedure and in 32 it was performed after shunt malfunction.

The follow-up assessments included an analysis of neurological evaluations and cine MR imaging at 3, 6, and 12 months after the procedure to identify early failure of ETV. Before the death of the child described above, cine MR imaging was not routinely performed beyond 12 months postoperatively. In 2004, however, the protocol was changed, and follow-up was continued on an annual basis. In cases in which more than a year had elapsed since radiological examination, the patients were re-examined with cine MR imaging and followed up annually thereafter with additional cine MR imaging.

The MR imaging examinations were performed using a 1.5 T scanner (Achieva; Philips Medical Systems) with a phased-array head coil and with patients placed supine. Cine phase-contrast axial and sagittal MR images were obtained using retrospective cardiac gating to evaluate CSF flow. The qualitative flow parameters were acquired in a plane perpendicular to the long axis of the aqueduct, passing through its midportion (TR 23 msec, TE 14 msec, flip angle 15°, field of view 80 x 80, pixel size 0.38 x 0.55 mm, matrix 208 x 145). The flow-velocity sensitivity (velocity encoding) was set at 15 cm/second. The scanning time varied from 7 to 9 minutes depending on the heart rate. On midsagittal MR images, cranial flow was seen as a bright signal and caudal flow as a dark signal.17

Statistical Analysis

Plots showing ETV failure as identified by cine MR imaging were calculated using the Kaplan-Meier method, and differences in the occurrence of ETV failure in patients who had postinfective hydrocephalus and those with hydrocephalus due to other causes were evaluated with the log-rank test. Student t-tests were used for normally distributed variables, while for non-normally distributed variables, the Mann-Whitney U-test or the Kruskal-Wallis test was performed. For nominal variables, the chi-square or Fisher exact test was used. Significance was set at p < 0.05.

The day of the surgery for shunt placement was considered the end point in cases of failure. The etiology of hydrocephalus, patient age at initial ETV, and shunt malfunction as a reason for ETV were analyzed.

Results

Population

Cases involving 84 children (51 boys and 33 girls) were reviewed for this study. The children’s mean age (± SD) at the time of ETV was 5.4 ± 4.9 years (median 4.6, range 6 days–16 years). There was no significant difference in mean ages between the male and the female patients. The cause of hydrocephalus was related to infection (postinfective hydrocephalus) in 9 cases, aqueductal stenosis in 22, spina bifida in 14, expansive tumor with posterior fossa involvement in 16, hemorrhage in 18, and Dandy-Walker malformation in 5 (Table 1). In 32 cases, the ETV was performed after a shunt malfunction. The mean duration of the shunt treatment was 8.2 ± 3.9 years (median 8.4 years, range 1–15.9 years).

Hemorrhagic/Infective Hydrocephalus

Of 27 patients with posthemorrhagic or postinfective hydrocephalus, 9 (6 post-IVH and 3 postmeningitic) presented with an early failure between 2 and 76 days after ETV (median 27 days). Cine phase-contrast MR imaging in the remaining 18 asymptomatic patients (13 with post-IVH hydrocephalus and 5 with postinfective hydrocephalus) documented an obstruction of the stoma with an increase in ventricular size, without any neurological signs or symptoms in 3 cases of postmeningitic hydrocephalus: in 2 patients, 2 and 6 years after ETV was performed for shunt malfunction, and in 1 case, 4 years after ETV was performed for newly diagnosed hydrocephalus (when the patient was 4 years old).

TABLE 1: Incidence of early failure of ETV stratified by cause of hydrocephalus*

<table>
<thead>
<tr>
<th>Cause of Hydrocephalus</th>
<th>Total No. of Cases</th>
<th>Early ETV Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>infection</td>
<td>9 (10.7)</td>
<td>6 (66.7)</td>
</tr>
<tr>
<td>aqueductal stenosis</td>
<td>22 (26.2)</td>
<td>18 (81.8)</td>
</tr>
<tr>
<td>spina bifida</td>
<td>14 (16.7)</td>
<td>11 (78.6)</td>
</tr>
<tr>
<td>tumor</td>
<td>16 (19)</td>
<td>15 (93.7)</td>
</tr>
<tr>
<td>hemorrhage</td>
<td>18 (21.4)</td>
<td>12 (66.7)</td>
</tr>
<tr>
<td>DWM</td>
<td>5 (6)</td>
<td>5 (100)</td>
</tr>
<tr>
<td>all causes</td>
<td>84 (100)</td>
<td>67 (79.7)</td>
</tr>
</tbody>
</table>

* Values represent numbers of cases (%). Abbreviation: DWM = Dandy-Walker malformation.
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Hydrocephalus Due to Aqueductal Stenosis

Of 22 patients who underwent ETV for secondary hydrocephalus due to aqueductal stenosis, 4 (18%) experienced ETV failure between 7 and 16 days postoperatively. In the remaining 18 patients, stoma patency was monitored with cine phase-contrast MR imaging for a median of 75 months (range 14–128 months) after treatment.

Tumor-Related Hydrocephalus

Ten patients were treated for hydrocephalus related to a posterior fossa tumor (cerebellar pilocytic astrocytoma in 6 cases, medulloblastoma in 3, ependymoma in 1). In all but one of these patients, cine MR imaging performed between 50 and 122 months (median 90 months) after ETV showed restoration of CSF flow from the third ventricle through the sylvian aqueduct to the fourth ventricle. All these patients studied with cine MR imaging showed reduced ventricle size, presence of flow through the aqueduct, and closure of the stoma (which was no longer necessary after tumor resection). Patients with tumor-related hydrocephalus had a greater reduction in ventricle size than patients with other kinds of hydrocephalus.

The only patient with tumor-related hydrocephalus in whom we identified late failure had originally undergone ETV at 2 years of age, before resection of a cerebellar astrocytoma. Cine MR imaging performed 7 years later showed obstruction of the stoma with enlargement of the ventricles; shunt placement was necessary to treat the ventriculomegaly.

Of 6 patients treated with ETV for hydrocephalus related to neoplasms of the quadrigeminal and pineal region, 1 was treated with a shunt for an obstruction of the stoma 3 months after the resection of a pineal teratoma. A patient with a tectal plate glioma underwent a repeat ETV, 11 months after the first one, for closure of the stoma by gliotic tissue of the third ventricular floor.

Myelomeningocele-Related Hydrocephalus

Fourteen patients underwent ETV for treatment of hydrocephalus associated with Chiari malformation Type II. In 7 of these patients, ETV was performed as an initial procedure for the treatment of hydrocephalus; in 3 of these patients, who were all under 1 month of age at the time of ETV, the procedure failed, whereas in the other 4, who were all over 2 months of age at surgery, the procedure was successful. In the remaining 7 patients, ETV was performed because of shunt malfunction, and none of these patients experienced ETV failure. (Published studies of ETV in patients with myelomeningocele have shown that the outcome is better in patients who have previously been treated with shunt placement than in those who undergo ETV in their first months of life as the initial treatment for hydrocephalus.)

HydrocephalusAssociated with Dandy-Walker Malformation

The 5 patients with Dandy-Walker malformation had significant enlargement of the ventricles and aqueductal patency on preoperative cine MR imaging—even the 2 patients undergoing ETV due to a shunt malfunction. The endoscopic procedure was used not only to perform the third ventriculostomy, but also for a transaqueductal inspection, and to confirm the membranous obstruction of the foramina of Luschka and Magendie, which are very difficult to evaluate with MR imaging. Cine MR imaging 14–97 months after ETV demonstrated an occluded stoma and increased ventricle size in 1 of these 5 patients (14 months after ETV) and a reduction of cyst and ventricle size in only 1 patient.

Comparison of Early and Late Failure Cohorts

A statistical analysis was performed to compare the early ETV failure and late ETV failure cohorts with respect to hydrocephalus etiology, patient age at ETV, and shunt malfunction as the reason for ETV.

Early ETV failure occurred in 17 cases at a mean ± SD of 57 ± 44 days postoperatively (median 57 days, range 2–179 days; Fig. 1). There was no significant difference in the percentage of failures with respect to hydrocephalus etiology (chi-square test, p = 0.30; Table 1). Nevertheless, it can be noted that the highest rates of early ETV failure occurred in patients with postinfective hydrocephalus (33.3%), posthemorrhagic hydrocephalus (33.3%), and spina bifida (21.4%). Among the patients with posterior fossa tumors, only 1 experienced early ETV failure (a rate of approximately 6%). There was no case of early ETV failure among the patients with Dandy-Walker malformation (although this was a smaller group with only 5 patients).

There was no significant difference in the length of period between the ETV and early failure with respect to causes of hydrocephalus (Kruskal-Wallis ANOVA, p = 1). There was no significant difference in rate of early ETV failure with respect to shunt malfunction as the reason for ETV (18% early ETV failure rate in patients with shunt failure vs 21% in those who did not have previous shunt placement; chi-square test, p = 0.8). The mean age at ETV placement was lower in the group with early ETV failure (3.6 ± 4.8 years, in contrast with 5.9 ± 4.9 years in those who did not experience early failure; p = 0.08).

In the remaining 67 cases (excluding the 17 early failures), the children were asymptomatic. Cine MR imaging, however, showed an obstruction of the stoma in 5 of these patients. Notably, ETV failure occurred in 50% (3 of 6)
of the cases of postinfective hydrocephalus (Table 2). The incidence of late failure was significantly higher in children with postinfective hydrocephalus than in those with hydrocephalus of other causes (bilateral Fisher exact test, \( p = 0.004 \)). Three of the 5 children with late failure identified by cine MR imaging had undergone ETV for shunt failure, but there was no statistically significant association between previous shunt placement and late ETV failure (\( p = 0.31 \)). Similarly in this group of 32 children who had shunt malfunction, there was no significant association between pathology and obstruction of CSF flow (\( p = 0.34 \)). Cine MR imaging showed a failure of the ETV in these 5 children after a mean period of 4 ± 2.5 years (median 4 years, range 1.2–7.1 years). In the 3 cases of postinfective hydrocephalus, the period between the ETV procedure and failure was 2, 4, and 6 years; in the patient with the posterior fossa tumor the period was 7 years, and for the patient with Dandy-Walker malformation it was a little more than 1 year.

The mean age at ETV was lower in the patients who experienced early failure than in those who experienced late failure (3.3 ± 1.9 years vs 6.1 ± 5 years). However, this difference was not significant (Mann-Whitney U-test, \( p = 0.38 \)).

In the 67 patients who did not experience early ETV failure, the overall mean duration of follow-up was 6 ± 2.8 years (median 6.5, range 0.8–10.5 years). Figure 2 presents the Kaplan-Meier plots showing the failure of the ETV, comparing the group with postinfective hydrocephalus with those with hydrocephalus due to other causes; log-rank testing showed a statistically significant difference (\( p = 0.00004 \)). The median of the plot related to the infective pathology is at 5.8 years (95% CI 3.2–8.5 years).

In 12 patients (18% of the group of 67), who had no signs or symptoms of intracranial hypertension, MR imaging showed ventricular size reduction and no flow through the ventriculostomy. Nine of these patients, who had been treated for posterior fossa tumors, had prolonged follow-up ranging from 16 to 118 months.

Revision ETV was performed for occlusion of the stoma on the basis of MR imaging in only 4 patients (2 with myelomeningocele, 1 with aqueductal stenosis, and 1 with tectal plate gliomas). The procedure was successful in all 4 cases, and no other patients required any additional procedures for issues related to CSF flow.

### TABLE 2: Incidence of "no flow" findings on cine MR imaging (late failure) stratified by cause of hydrocephalus

<table>
<thead>
<tr>
<th>Cause of Hydrocephalus</th>
<th>Total No. of Cases</th>
<th>Late ETV Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No</td>
</tr>
<tr>
<td>infection</td>
<td>6 (9)</td>
<td>3 (50)</td>
</tr>
<tr>
<td>aqueductal stenosis</td>
<td>18 (26.9)</td>
<td>18 (100)</td>
</tr>
<tr>
<td>spina bifida</td>
<td>11 (16.4)</td>
<td>11 (100)</td>
</tr>
<tr>
<td>tumor</td>
<td>15 (22.4)</td>
<td>14 (93.3)</td>
</tr>
<tr>
<td>hemorrhage</td>
<td>12 (17.9)</td>
<td>12 (100)</td>
</tr>
<tr>
<td>DWM</td>
<td>5 (7.4)</td>
<td>4 (80)</td>
</tr>
<tr>
<td>all causes</td>
<td>67 (100)</td>
<td>62 (92.5)</td>
</tr>
</tbody>
</table>

* Values represent number of cases (%).

### Discussion

Cases with prolonged follow-up and late failure of ETV were described by Cinalli et al.\(^2\) (range of follow-up 1 month–6 years), Siomin et al.\(^23\) (8 days–6 years), Wagner and Koch\(^26\) (2 weeks–6 years), and Mohanty et al.\(^25\) (8 weeks–2 years). In an article published in 2007, Lipina et al.\(^18\) reported the case of an 11-year-old girl who died of late ETV failure. In reviewing the literature, they identified 13 other reported cases, including the total of reported cases, including their own, to 14 (8 with obstructive hydrocephalus associated with aqueductal stenosis, 4 with congenital hydrocephalus, and 2 with tumors of the quadrigeminal region). Analyzing these cases, they found that the time from ETV to death ranged from 1 month to 7 years, and that 8 of the 14 patients had undergone ETV after a shunt malfunction. In these series cine MR imaging was only performed later than 1 year after ETV when there were symptoms of failure. Fukuhara and colleagues\(^18\) used cine MR images to confirm an obstruction of the stoma, but only considered a cine MR imaging finding of obstruction diagnostic when the patients presented with signs of intracranial hypertension.

Reviewing the literature about delayed failures in pediatric patients with secondary obstructive hydrocephalus or hydrocephalus associated with Dandy-Walker syndrome,\(^18\) we were unable to find reports of routine radiological follow-up after the first few years following endoscopic treatment.

The prolonged postoperative cine MR imaging follow-up (6 ± 2.8 years) in 67 patients with different hydrocephalic pathologies, without signs or symptoms at the time of imaging, is what makes our study unique. Obviously, in some of these patients the repeated imaging was “unnecessary,” but our aim was to identify particular etiological types of hydrocephalus that require long-term follow-up with cine MR imaging.

In our pediatric series, in contrast to the article of Lipina et al.,\(^18\) there were no late ETV failures in patients with obstructive hydrocephalus associated with aqueductal stenosis. In these cases the obstruction of the stoma, as has been described, happens rapidly and is related to a
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defect in the CSF absorptive capacity. In our series, ETV was repeated 1 year after the first surgery for closure of the stoma by gliotic tissue in only 1 patient with tectal plate glioma.

Our cine MR imaging studies carried out between 2007 and 2008 demonstrated that, of 67 patients, 5 children had an obstruction of the stoma and an increase of the dimensions of the ventricle cavities, without neurological signs and symptoms 1, 2, 4, and 7 years after ETV, after at least 3 cine MR imaging studies showing patency of the stoma and unchanged ventriculomegaly. Three of these 5 patients had postinfective hydrocephalus, one had Dandy-Walker syndrome, and the last had a posterior fossa tumor. In the patients with postinfective hydrocephalus, thickened arachnoid membranes were observed at the level of the interpeduncular cisterns during the initial ETV, but there was a good flow through the stoma at the end of the procedure. In 2 cases of Dandy-Walker syndrome (including the one with a fatal outcome that prompted this study), the patients had a late closure of the stoma, without neurological signs of increased intracranial pressure. In the patient who had undergone resection of a cerebellar pilocytic astrocytoma (without tumor seeding or extension at the level of the prepontine cistern), cine phase-contrast MR imaging 3 years after ETV demonstrated flow through the stoma and cystic arachnopathy in the fourth ventricle. Reduction of the ventricle size had not been achieved after the radical removal of the tumor, and this can be considered as an anatomical predictive element of treatment failure in patients treated for a neoplasm of the posterior fossa. Nevertheless, nothing was observed during the original ETV procedure in any of the 5 cases that would suggest that these patients were at particular risk for long-term ETV failure. Furthermore, the possibility of disastrous consequences increases because neurological symptoms may also manifest some months after complete occlusion of the stoma, with exhaustion of physiological mechanisms of compensation.

The obstruction of the stoma demonstrated by the cine MR images was controlled with a new endoscopic procedure in all 5 children. In each case intraoperative diagnostic observation demonstrated that the closure of the stoma was caused by the gliotic tissue and by the formation of arachnoid membranes in the interpeduncular cistern. The analysis of these intraoperative observations suggested a high risk of failure of ETV, justifying shunt placement during the same operation. This approach, as described by Warf and Kulkarni, should also be applied at the time of the first ETV to avoid the risk of late failure. In this series, in contrast to that of Hader et al., there was no statistically significant difference in the rate of ETV failure when comparing patients who had or had not undergone previous shunt placement. It has been confirmed that infants with postinfective hydrocephalus, posthemorrhagic hydrocephalus, and hydrocephalus associated with spina bifida have a high risk of ETV failure when the procedure is performed before they reach 2 months of age. Kadrian et al. observed that ETV success is strongly dependent on patient age, with 41% of patients who underwent ETV at 1–6 months of age still presumed to have a functioning ETV 5 years postoperatively. These reported data and the fact that the formation of gliotic membrane in the stoma and the interpeduncular cistern is more common in infants than adults, suggest the need for close follow-up with cine MR imaging to reveal an early malfunction.

Conclusions

Cine phase-contrast MR imaging has a high capacity to detect a flow defect through a ventriculostomy, raising the suspicion of ETV failure. It remains to be established how long-term follow-up should be continued. In this retrospective study, 20 of 67 patients in whom follow-up cine MR imaging was performed were studied at least 7 years after ETV, and in these 20 patients, cine MR imaging showed no obstruction of the stoma. The number of patients in this study is still too small to allow definitive conclusions to be drawn, but we have attempted to define a population of patients (those with postinfective hydrocephalus or hydrocephalus associated with Dandy-Walker malformation) who may be at an increased risk for late ETV failure.

 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 funds were received in support of this work. No benefits in any form have been or will be received from a commercial party related directly or indirectly to the subject of this manuscript.

Author contributions to the study and manuscript preparation include the following. Conception and design: Faggin. Acquisition of data: Faggin, Denaro, Meneghini, Calderone. Critically revising the article: Faggin. Reviewed final version of the manuscript and approved it for submission: all authors. Statistical analysis: Faggin. Administrative/technical/material support: Calderone.

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