

ENDOSCOPIC THIRD VENTRICULOSTOMY IN PEDIATRIC PATIENTS: THE CANADIAN EXPERIENCE

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(see appendix)

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OBJECTIVE: Reports from relatively small series of pediatric patients predominantly from single centers have hampered accurate analysis of outcome from endoscopic third ventriculostomy. We combined patients from nine pediatric neurosurgery centers across Canada to obtain a better estimate of outcome and identify factors affecting success of the procedure.

METHODS: Databases were recoded for uniformity. Failure of the procedure was defined as any subsequent operation or death resulting from hydrocephalus. Time to failure was analyzed by Kaplan-Meier estimate and Cox proportional hazard analysis.

RESULTS: During a 15-year period (1989–2004), 368 patients underwent the procedure. The average age was 6.5 years, and 57% were male. Aqueduct stenosis and tumors were the most common etiology, comprising 34 and 29%, respectively. Twenty-two percent of the patients had been previously shunted. The 1- and 5-year success rates were 65 and 52%, respectively. Factors included in the Cox model were age, sex, etiology of hydrocephalus, previous surgery, center volume, and surgeon volume. By multivariate analysis, only age had a significant effect on outcome, with younger patients failing at higher rates, particularly neonates and infants.

CONCLUSION: Based on data from multiple Canadian centers, age seems to be the primary determinant of outcome in endoscopic third ventriculostomy in pediatric patients. Failure rates are particularly high in neonates and young infants; thus, the role of this procedure in this age group should be carefully considered.

KEY WORDS: Endoscopic third ventriculostomy, Hydrocephalus, Outcome, Pediatric

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Endoscopic third ventriculostomy (ETV) has been advocated as a treatment for pediatric patients with obstructive hydrocephalus (12, 20). Common etiologies treated include aqueduct stenosis and tumors such as tectal glioma, although a large variety of conditions, including myelomeningocele, have also been addressed (11, 17). The most controversial issue in the application of ETV in children is whether or not there is a lower age limit at which the treatment is ineffective, or particular etiologies in which the failure rate is so high that the procedure seems unwarranted (15, 16). There are reports that support the conflicting notions that outcome after ETV is a function of age (13, 14, 21), that outcome is independent of age (4, 9), and that the outcome is primarily determined by the etiology (1, 7, 8).

Most of the reported series are from single centers with relatively small numbers of patients, which may explain the conflicting results. We formed the Canadian Pediatric Neurosurgery Study Group in (Appendix) February 2000 to conduct collaborative studies to answer questions such as the important determinants of outcome after ETV by pooling patients from a num-

ber of centers. Our findings suggest that age is the primary determinant of outcome in pediatric patients undergoing ETV.

PATIENTS AND METHODS

After acceptance of a study proposal, the 22 identified Canadian pediatric neurosurgeons from nine centers were asked to submit their ETV cases during the period from January 1989 to December 2004. A standard data form was circulated, although many of the centers had maintained their own individual and, in many cases, prospective databases. These databases were recoded for uniformity, and additional information, if available, was solicited.

Information recorded included patient demographics; etiology (divided into aqueduct stenosis, tumor, intraventricular hemorrhage, myelomeningocele, postinfectious hydrocephalus, intracranial cyst, and other); any previous operations, including ventriculoperitoneal (VP) shunts; surgeon; surgical procedure; operative complications; subsequent operations; and date of the last follow-up examination. Failure of ETV was defined as

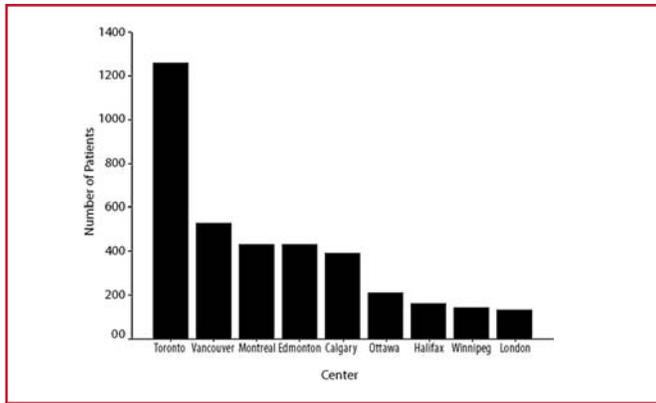


FIGURE 1. Bar graph showing the number of patients contributed by center.

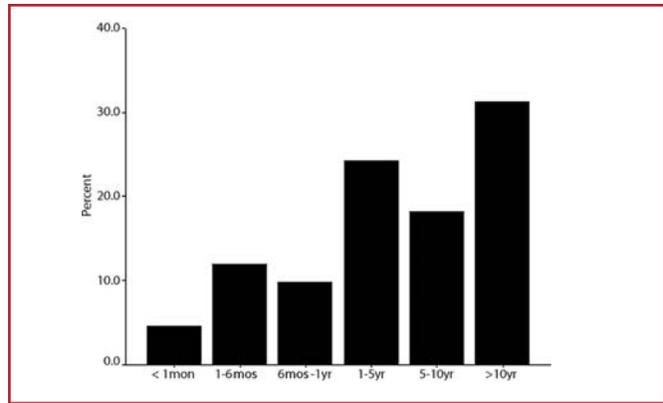


FIGURE 2. Bar graph showing distribution by age group category.

any subsequent surgical procedure for cerebrospinal fluid (CSF) diversion, as determined by the operating surgeon, or death related to hydrocephalus management. Patient follow-up was measured as either time to ETV failure or the last follow-up visit. Surgeons and centers were divided into low and high volume based on less than, greater than, or equal to 20 procedures. Age categories were subdivided into younger than 1 month, 1 to 6 months, 6 months to 1 year, 1 to 5 years, 5 to 10 years, and older than 10 years, along what seemed to be reasonable physiological divisions.

Statistical analysis was performed using SPSS (version 11; SPSS, Inc., Chicago, IL). Overall Kaplan-Meier estimates of success, including estimates for different age groups, and etiology were generated. Univariate analysis was conducted using Cox Regression, with age as a continuous variable. Factors in which the significance level was less than 0.2 were entered into a multivariate analysis also using Cox Regression. *P* values were adjusted for multiple comparisons.

RESULTS

Seventeen surgeons from nine centers contributed data from a total of 368 patients to the study. The number of patients contributed per center ranged from 13 to 126, with an average of 41 patients per center (Fig. 1). The number of cases per surgeon ranged between one and 91. Six centers and six surgeons performed 20 or more procedures each. The age of the patients at the time of surgery ranged from 1 day to 20 years (average age, 6.5 yr; median age, 4.8 yr). Figure 2 shows the distribution of the patients by age group. Male patients comprised 57% of the patients. Brain tumors and aqueduct stenosis were the most common etiologies of hydrocephalus, representing 34 and 29% of the patients, respectively (Fig. 3). The most common tumor type was tectal glioma (40%), followed by third ventricular tumors (26%). Previous shunt surgery was performed in 22% of the patients; an additional 15% of the patients had a previous intracranial procedure. Complications occurred in 14% of the patients, with the most common complications being CSF leak or meningitis (Table 1). The follow-up period, which was measured as time to ETV failure or the last follow-up visit, ranged from 0 days to 12.8 years (average, 2.0 yr). Using the definition of failure, 149 (40%) of the patients failed the operation. By Kaplan Meier estimates, the 1- and 5-year ETV success rates were 65 and 52%, respectively (Fig. 4).

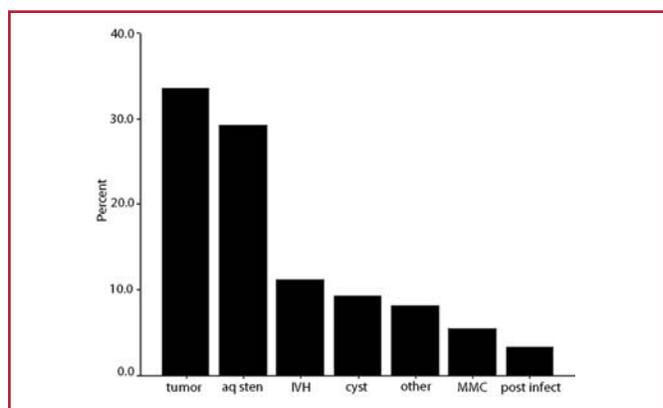


FIGURE 3. Bar graph showing the etiology of hydrocephalus. aq sten, aqueduct stenosis; IVH, intraventricular hemorrhage; MMC, myelomeningocele; post infect, postinfectious.

TABLE 1. Complications

Complication	Percentage of patients
Cerebrospinal fluid leak	3.6%
Meningitis	2.8%
Hemorrhage	1.4%
Hypothalamic injury	1.4%
Cranial nerve injury	1.4%
Seizure	1.4%
Other ^a	1.4%
Total	13.6%

^a Two cases of rapid delayed deterioration and death 2 years and 3.5 years after endoscopic third ventriculostomy (10).

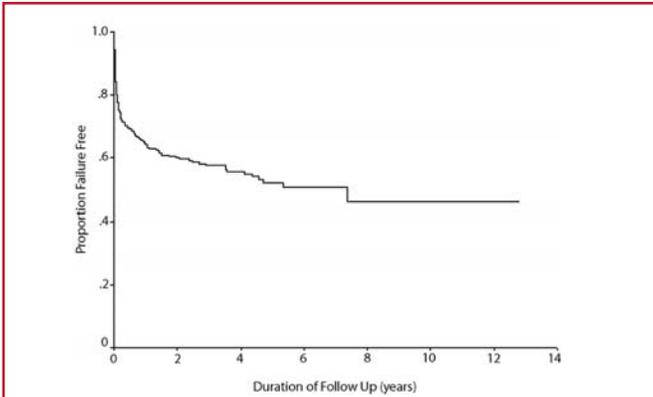


FIGURE 4. Line graph showing the overall failure rate of ETV in the entire population of patients.

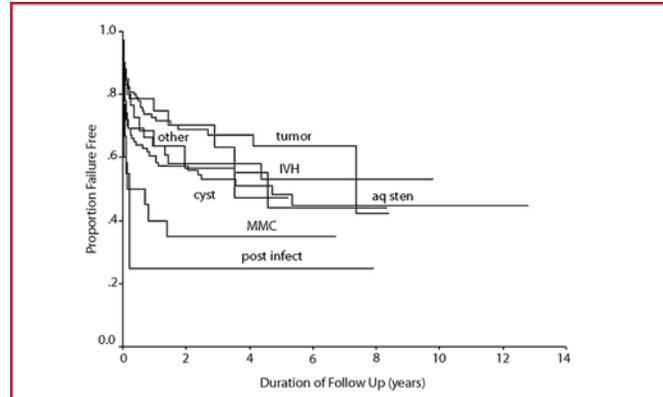


FIGURE 6. Line graph showing a comparison of the success rate according to the etiology of hydrocephalus. There is no obvious difference in outcome. Aq sten, aqueduct stenosis; IVH, intraventricular hemorrhage; MMC, myelomeningocele; post infect, postinfectious.

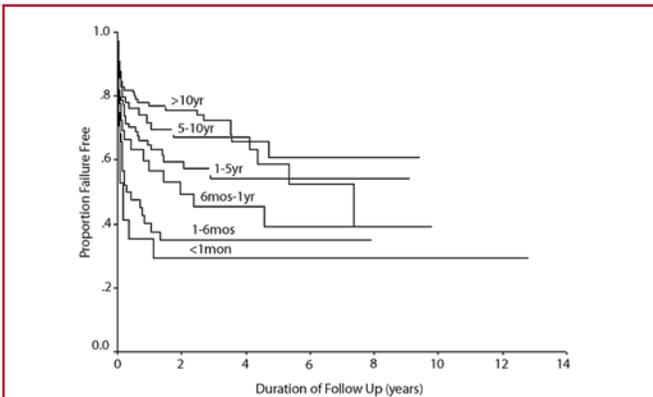


FIGURE 5. Line graph showing a comparison of the success rate according to age group. Outcome improves with increasing age.

Comparison of ETV success by age category, as plotted in Figure 5, showed a progressive increase in success rate with increasing age. The five-year success rate in patients younger than 1 month old was 28%, compared with 68% in patients older than 10 years. Comparison of ETV success by etiology showed clustering of the different etiologies (Fig. 6). Those etiologies with the lowest success rate, myelomeningocele and postinfectious etiology, had relatively small numbers of patients (18 and 11, respectively). By univariate analysis, age ($P < 0.0001$) and etiology ($P = 0.014$) were both significant, with center volume, surgeon volume, previous operation, and patient sex having no effect. By multivariate analysis, only age ($P = 0.0001$) was significant, with etiology being nonsignificant with the P values adjusted for multiple comparisons.

DISCUSSION

Many neurosurgeons think, and many previous reports have suggested, that younger patients have a significantly lower

ETV success rate than older patients. Although this is not universal, some have suggested an age threshold of 1 or 2 years for performing the operation (13, 14, 21). Some fairly large series have found no age effect and, therefore, have suggested that age not be a limiting consideration (2). Accounting for these differences in surgical experience has been difficult, and the question regarding the effect of small numbers of patients from single centers has always been present. This study was an attempt to move beyond these limitations by collecting a large number of patients from multiple centers, albeit from a single country.

The patients in this study seemed to represent the typical pediatric patients to which this procedure is typically proposed: those with obstructive hydrocephalus, usually at the level of the aqueduct. Their ages, on average, are considerably older than those who receive VP shunts, indicating that they do represent a different patient population (6). More than 26% of these patients had undergone previous surgery, usually a VP shunt and other surgery, typically for a brain tumor or intracranial cyst. Complications occurred in 13.6% of the patients, which is not an insignificant number. Fortunately, serious neurological injury or hypothalamic or cranial nerve injury was rare. Two patients experienced rapid delayed deterioration, with death 2 and 3.5 years after ETV, both of which have been reported previously (10). The average follow-up period of 1.85 years may seem short for a study covering a 15-year period. However, follow-up was halted at the time of failure, which occurred in 39% of the patients; most were within 6 months of the operation.

The overall estimates of 1- and 5-year success rates of 65 and 52% are lower than some other reports (4, 13). These estimates are clearly a function of the definition of success and of the age of the patients in the study. We used a fairly strict definition of successful outcome: no further CSF diversion procedures. Others have allowed subsequent temporary CSF drainage procedures or repeat early ETV to be included under the original surgical procedure (2). This is not unreasonable from the patient's point of

view but makes comparison difficult with other procedures such as a VP shunt, in which the same definition of failure that we used in this study is usually invoked (18). The advantage of having contributions from multiple centers and surgeons with widely varying levels of experience is that the estimates cited in this report are fairly realistic of what might be expected in the general community and, thus, more generalizable.

Univariate analysis found no effect of the aforementioned surgical experience of the surgeon or center as defined by a high volume level of 20 cases. This is counterintuitive because ETV is recognized to be a difficult surgical procedure with a steep learning curve, and other endoscopic procedures have identified a significant learning effect. It is possible that most inexperienced colleagues obtained the assistance of a more experienced colleague, masking this learning effect, or that the level of 20 cases is not an accurate threshold of experience. Despite this finding, most would advocate that surgeons embarking on this procedure receive proper training and the help of an experienced colleague because the complications can be significant and lethal. Previous operation also had no apparent effect on outcome. Similarly good success rates in patients with previous shunts have been reported (2, 3, 5).

Age and etiology were both significant in determining outcome by univariate analysis, but only age remained significant by multivariate analysis. This suggests that age is the primary determinant of outcome and should be considered seriously in evaluating patients, particularly very young patients. There is recent support for this finding. In a single-center review of 203 pediatric and adult patients followed for longer than 20 years, Kadrian et al. (13) found a similar improvement in outcome with increasing age by multivariate analysis. Their success rate in children younger than 1 month of age was less than 20%. The physiological explanation for this age effect is not clear. Possible explanations are that the infant brain, meninges, and cranium cannot tolerate the persistent elevated increased intracranial pressure that occurs after this procedure or that their absorptive system is immature. Young age is also a risk for CSF shunt failure (18, 19); therefore, young age may be a risk factor for any CSF diversion procedure.

That etiology did not have a significant effect is also somewhat surprising because one might anticipate failure in patients with disrupted absorption pathways, such as postinfectious hydrocephalus or posthemorrhagic hydrocephalus, and because failure has been previously reported to occur in these patients. This result probably speaks more to the limited extent to which the pathogenesis of hydrocephalus is understood. Nevertheless, it suggests that patients with hydrocephalus of any etiology can be considered for this operation.

The implications of the effect of age on outcome are several. Surgeons considering patients younger than the age of 1 month in whom one can anticipate a failure rate approaching 75% need to include the increased risk of a significant complication of ETV over a CSF shunt in their decision making. Many surgeons would consider their patients better off without any implanted hardware. However, if implanted hardware is sure to follow in many of them, with an interceding failed operation

of increased risk, it may not be such a bad option. Because an implanted shunt is not a clear risk for failure of the procedure at a later age, one could always propose "staging" the ETV procedure with a CSF shunt first and considering an ETV at the time of failure. When evaluating surgical series, it is very important to account for the age distribution of the patients because this can have a profound effect on outcome.

There are several limitations to this study. A portion of the patients' data was accrued retrospectively. It was not possible to verify much of the data, including the imaging, and the data were recoded after the fact for conformity. Patient selection, operative technique, and further surgery for complications or ETV failure were determined by the individual surgeons. Despite the attempt to attain a large group of patients, there may be smaller groups of patients with particular etiologies in whom small numbers of patients may mask important outcome effects.

CONCLUSIONS

Age seems to be the primary determinant of outcome in pediatric patients undergoing an ETV, with younger patients having a poorer success rate. Particular etiologies and the coexistence of a previous shunt do not seem to be contraindications to the procedure. Although surgical experience did not seem to affect outcome, complications from this procedure are considerable and surgeons should be adequately trained or assisted by an experienced surgeon.

APPENDIX

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COMMENTS

The ongoing debate regarding the role of age as an independent predictor of endoscopic third ventriculostomy (ETV) success is nearly put to rest with this multi-institutional cooperative study by Dr. Drake and the Canadian Neurosurgery Study Group. Aside from the obvious worth of this article, the authors have successfully taken on the daunting task of coordinating a cooperative investigation to study an important clinical question. Their conclusion that age is the only statistically significant variable in infants that influences ETV outcome is convincing. The major limit of this study is the unavoidable subjectivity in defining etiology (secondary aqueductal occlusion), clinical outcome (decision to shunt), and postoperative magnetic resonance image interpretation (ventricular size).

In addition to clarifying this very important issue surrounding ETV success in young children, other interesting and unexpected conclusions were drawn. Specifically, the finding that surgeon experience had no influence on success rates was of interest, given the clear documentation from other experienced endoscopic surgeons that morbidity is reduced with increasing technical experience. I was also surprised that the 1- and 5-year success rates were only 65% and 52%, respectively. These figures may be influenced by the relatively young age of the patients in this series compared with most other publications.

As much as I admire this work and the design of the study, I am uncertain that the results will alter my practice. The low morbidity associated with ETV balanced by the lifetime risk of ventriculoperitoneal shunting remains a convincing argument in favor of a trial of ETV in patients younger than 1 year of age. However, the results do offer a very good basis from which accurate rates of success and morbidity can be introduced into the informed consent process.

Mark M. Souweidane
New York, New York

This is a collaborative analysis of ETVs in children, performed by a large group of Canadian neurosurgeons from several centers. It is concluded that the success rate at 5 years is approximately 52%, and that late failures may occur, sometimes with fatal consequences. Etiology of hydrocephalus was not a strong predictor of success. I think that this is partially explained by the fact that most of the patients who underwent the procedure had the standard indications, namely, aqueductal stenosis and tectal glioma. The most important factor predicting failure of the procedure was a young age, which has been noted by others. The complication rate was generally low, and no instances of basilar artery damage were reported.

This large series confirms the observations of others. It is more in keeping with the experience of many of us, and is more realistic than some overly optimistic, single-institution series that have been published.

Leslie N. Sutton
Philadelphia, Pennsylvania

This is an important report analyzing the variables that affect outcome after ETV. The authors have reported data from a multicenter analysis of 368 patients in the pediatric population who underwent ETV for treatment of hydrocephalus. Age was found to be the main determinant of outcome, independent of etiology; failure rates were highest in neonates and young children. This finding should be an important consideration for any neurosurgeon contemplating this procedure.

ETV has traditionally been used to treat hydrocephalus related to obstructive etiologies. As the authors point out, the lack of etiology as

