The incidence and effect of tethered cord release for tethered cord syndrome in patients with myelomeningocele: a population-based study

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OBJECTIVE The goal of this study was to establish an incidence and assess the effect of tethered cord release for tethered cord syndrome in patients with myelomeningocele.

METHODS The study population was based on the Western Denmark Myelomeningocele Database, which contains all patients born with myelomeningocele in western Denmark since 1970. The study population was cross-referenced in 2015 with a database for surgical procedures containing all surgical procedures performed in the central Denmark region since 1996. Patients alive between 1996 and 2015 were identified. Incidences were calculated and presented for year of age. File reviews were conducted for all patients who underwent the procedure. Follow-up was divided into short-term and long-term follow-up.

RESULTS One hundred sixty-six patients were alive during various time periods between 1996 and 2015. Of these, 45 patients underwent the procedure. Seven underwent reoperation. The median age for the procedure was 12 years and the highest incidence was found at 15 years of age. Incidence was bimodal with highest incidence in children and adolescents. The most common indications were progressive spine deformity (40%), deteriorating ambulation (38%), and deteriorating neurogenic bladder and/or bowel dysfunction (32%). The mean short-term follow-up was 4.7 months and the mean long-term follow-up was 72.6 months. Postoperatively, the majority had improved (27%) or stabilized (27%) at short-term follow-up. At long-term follow-up, most patients were stable (27%) or had deteriorated (24%). For both follow-up terms there was a loss of approximately one-third of all patients. Complications occurred in 17% of the procedures.

CONCLUSIONS In this population-based study, tethered cord release has the highest incidence in children and adolescents. The beneficial effect of the procedure seems to be short term. Due to the uncertainty of a long-term effect of the procedure in patients with myelomeningocele and the registered complications, the authors suggest that this surgical indication should be reserved for well-selected patients.

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KEYWORDS myelomeningocele; spina bifida; incidence; tethered cord syndrome; tethered cord release; spine

MYELOMENINGOCELE is a congenital malformation of the spine due to a faulty closure of the neural tube in the embryonic spine.¹ It is a rare condition in Denmark due to a high rate of termination of pregnancy after prenatal diagnostics, with the incidence of live-born patients being 0.8 per 10,000 births.² The functional consequences of myelomeningocele depend on the level of the lesion,³ and range from difficult-to-detect symptoms, to loss of muscle control of the lower extremities and bladder and bowel dysfunction. All patients born with myelomeningocele in western Denmark have the spinal malformation closed during the first few days after birth.

At some point throughout life, patients with myelomeningocele may develop tethered cord syndrome. This presents with a broad variety of progressive symptoms including deteriorating ambulation, sensory changes and/or spasticity in the lower extremities, back and/or leg pain, scoliosis, neurogenic bladder and bowel dysfunction, syringomyelia, and/or Chiari malformation.^{4–12} The pathophysiology is not known. However, it is likely that traction of the spinal cord impairs oxidative metabolism in the spinal cord.¹³ The tethering in patients born with myelomeningocele is thought to be caused by an arachnoid membrane and fibrous tissue developing around the spi-

ABBREVIATIONS TCR = tethered cord release.

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nal cord after the repair of the spinal malformation.¹³ Accurate diagnosis is challenging. The symptomatology of patients with myelomeningocele is complex and we lack data on the natural history of functional deterioration. The vast majority of patients will have at least one competing diagnosis with similar symptoms (shunt dysfunction, Chiari II malformation) and, finally, we lack paraclinical tools that are able to detect tethered cord syndrome—almost all patients with myelomeningocele have radiological signs of tethering.

The treatment is surgical, with the aim to release the spinal cord by untethering through scar tissue removal around the spinal cord/cauda equina. There are many studies concerning the effect of the treatment; however, some of the cohorts studied include different congenital malformations,^{14,15} giving them a very different baseline physical status,^{16–18} and very few are population-based.

With this study, we aim to report a population-based incidence of tethered cord release (TCR) for tethered cord syndrome in patients born with myelomeningocele, and give data on surgical indication as well as short- and long-term effect of TCR.

Methods

This study was based on a population extracted from the population-based Western Denmark Myelomeningocele Database. All patients who have undergone surgery or been hospitalized at the Department of Neurosurgery at Aarhus University Hospital for myelomeningocele since January 1, 1970, have been registered. Surgical treatment for myelomeningocele in western Denmark, which is a well-defined geographical area with approximately 1.8 million inhabitants (as of 2008),¹⁹ is exclusively done at our institution.

A cross-reference was performed with our study population and data on TCR surgery from data registered at our institution. Data include all procedures carried out within the central Denmark region since January 1, 1996. Only patients who were alive between January 1, 1996, and June 19, 2015, were included. Age at procedure, number at risk per year of age, and incidences were calculated.

The following data were derived through file review: admission length, indication for surgery, perioperative and postoperative complications, and neurological status, as well as data on neurogenic bladder and bowel dysfunction. Follow-up was divided into 2 categories: the first was short term, defined as follow-up within 1 year (if multiple, the follow-up visit closest to surgery was chosen). The second category was long term, defined as follow-up after 1 year (if more, the latest one was chosen). For both follow-up terms, status was compared with the preoperative symptoms and deemed by the operating surgeon as improved, stable, or deteriorated. Chiari malformation and syringomyelia were deemed by a specialist in neuroradiology as improved, stable, or deteriorated on MRI, comparing the pre- and postoperative images. Patients who underwent reoperation with TCR were registered as lost at long-term follow-up with respect to the first surgery. The majority of data are delivered as descriptive data, due to low numbers in several categories.

Prior to initiation of the study, the Danish Health and Medicines Authority and the Danish Data Protection Agency gave permission to collect the required data.

Results

One hundred eighty-seven patients were available in the database (Fig. 1). Six patients were excluded due to misdiagnosis. Of the remaining patients, 166 were alive during various time periods between January 1, 1996, and June 19, 2015 (Table 1). Forty-five patients underwent TCR procedures, of which group 7 also underwent reoperation. Only primary TCR was used to calculate incidence. Both primary TCR and reoperations were used in studying indications and outcome ($n = 52$). Three patient files containing 5 procedures were lost, leaving 47 procedures for review (Fig. 1).

Baseline data can be seen in Table 1. Data are given for patients who underwent TCR and for those who did not undergo TCR. No difference was noted on myelomeningocele level. One of the patients who underwent TCR died (2%), compared to 9 of those who did not undergo TCR (7%). However, there was no statistical difference in mortality between these groups ($p = 0.29$).

The incidence of TCR can be seen in Fig. 2, which shows a bimodal age pattern with increased incidence between 5 and 12 years of age, and between 14 and 21 years of age. The median age for the procedure was 12 years of age, and the highest incidence was found at 15 years of age.

All procedures were indicated by a neurosurgical consultant with a subspecialty in pediatric spine neurosurgery. Several indications for TCR were found in our study. Spine deformity, deteriorating ambulation, and bladder and/or bowel dysfunction were the most frequent. For further details, see Table 2. Spine deformity, followed by contractures of the lower extremities, were the most frequent indications in patients undergoing reoperation. A dedicated team of 2 surgeons performed all surgeries, to ensure the highest level of expertise. Intraoperative neurophysiological monitoring was not available at the time in our institution.

Perioperative complications occurred in 1 of 47 operations (2%); this was a neurotmesis. Due to the poor preoperative neurological status of the patient, no major neurological worsening was observed. Postoperative complications occurred in 7 procedures (15%). Of these, 2 were CSF leakage, 2 were suspected meningitis (both treated before CSF was cultured), 1 was a wound infection, 1 was a fistula, and 1 was fecal incontinence. This results in a total complication rate of 17%. One procedure (2%) was discontinued prematurely due to high risk of neurological deterioration in a complete TCR procedure. The median number of days admitted was 6 days (range 1–12 days).

Short-term follow-up was on average 4.7 months (range 1.2–10.5 months) and long-term follow-up was on average 72.6 months (range 22.8–153.5 months). The number of patients who improved was halved between short- and long-term follow-up, whereas the number of patients who deteriorated increased more than 4 times. The percentage of patients who stabilized is approximately the same at

FIG. 1. Flow chart showing inclusion criteria for patients with myelomeningocele.

TABLE 1. Baseline data in 166 patients with myelomeningocele

Variable	Entire Cohort	Pts Who Did Not Undergo TCR	Pts Who Underwent TCR	p Value*
No. of pts	166	121	45	NA
Lesion level				
Cervical	2	2	0	1.00
Thoracic	16	11	5	0.77
Lumbar	134	97	37	0.83
Sacral	14	11	3	0.76
Median age in yrs (range)	25 (0–46)	30 (0–46)	21 (12–40)	NA
No. of males (%)	82 (49)	60 (50)	22 (49)	NA

NA = not applicable; pts = patients.

* The p value was calculated for difference in lesion level constructions between the 2 groups, and was determined using Fisher's exact test.

FIG. 2. Graph showing incidence per year of age, with number of procedures (y-axis) and year of age at procedure (x-axis). Number of patients alive at a specific year of age during the study period is stated as the number at risk (NAR). The percentages denote the proportion of patients who underwent operation at that year of age. Reoperations were excluded in this chart.

short- and long-term follow-up (Table 2). Loss to follow-up was approximately one-third in both short- and long-term follow-up groups.

Discussion

We found the highest incidences of TCR in our population-based study to be at 15 years of age. We found some effect of the procedure at short-term follow-up; however the beneficial effect seems to decline for the vast majority at long-term follow-up. No data were lost before calculating the incidence, giving us a reliable population-based incidence of TCR for tethered cord syndrome in patients with myelomeningocele. We found a prevalence of 27%. This was comparable to other studies.^{6,20,21}

The age distribution is consistent with the ages of the first and second growth spurts in humans. An earlier study provided a similar graph of a cohort of patients with myelomeningoceles who underwent TCR procedures.⁴ These authors' retrospective data demonstrated that most patients were between 2 and 8 years of age; however, the number at risk per year of age was not reported.

Another retrospective article from 1997¹⁶ reports similar results, with most patients undergoing surgery before 12 years of age. These authors found an incidence per year of age between 1% and 8%, at 8 years of age and 2 years of age, respectively. The results of a study from 1998 are comparable to ours, with the majority of the procedures occurring at the ages of 2–10 and 12–14 years.²²

The most common indication for surgery in our study was spine deformity, followed by deteriorating ambulation and neurogenic bladder and/or bowel dysfunction. This was consistent with other studies.^{4,6,7,14,21}

The results from our study suggest a beneficial effect of the procedure at short-term follow-up, where patients improved or stabilized in their symptoms. However, this trend declined at long-term follow-up, where more patients continued deteriorating. This is also consistent with previous reports.^{4,6,7,14,21,23,24} Perhaps TCR does not alter the long-term natural history of myelomeningocele. Whether intraoperative neurophysiological monitoring may have changed outcome by enabling a more aggressive and sufficient surgical release is uncertain.^{25–27} Nevertheless, axial pain in the back and pain in lower extremities seem to

TABLE 2. Indications for surgery and findings on short- and long-term follow-up for 47 procedures in patients with said indication

Indication*	No. of Pts (%)	Findings on Postop Follow-Up							
		Short Term				Long Term			
		Improved	Stabilized	Deteriorated	Lost	Improved	Stabilized	Deteriorated	Lost
Spine deformity	19 (40)	6	7	1	5	0	1	11	7
Deteriorating ambulation	18 (38)	5	8	1	4	2	6	4	6
Neurogenic bladder &/or bowel dysfunction	15 (32)	5	4	1	5	2	6	1	6
Syringomyelia	12 (26)	1	1	0	10	3	3	0	6
Lower-extremity spasticity	6 (13)	2	2	1	1	0	1	3	2
Contractures	6 (13)	1	0	1	4	1	1	3	1
Axial pain in back & lower extremities	6 (13)	4	1	0	1	4	1	0	1
Chiari II malformation	5 (11)	0	2	0	3	0	3	0	2
Sensory symptoms	4 (9)	1	0	0	3	1	3	0	0
Total no. (%)	91 (194)	25 (27)	25 (27)	5 (5)	36 (40)	13 (14)	25 (27)	22 (24)	31 (34)

* Ranked by frequency of occurrence, in descending order.

continue to benefit from the procedure, with most patients still improving at long-term follow-up. Pain is arguably a solid indication with good outcome for TCR in patients with myelomeningocele.²⁸

The peri- and postoperative complication rate found in this purely myelomeningocele-based study was 17%, comparable to reports of other studies, with complication rates between 7% and 33%.^{4,6,7,21,29} However, these studies are performed in either a case mix or institution-based cohorts. Overall, mixed-diagnosis cases could be argued to have a better baseline morbidity, and therefore experience fewer complications.

We did not find any mortality related to TCR surgery. This is in agreement with other studies.^{4,6,14} Our own findings report a mortality rate of 2% in the group who underwent the procedure and 7% in the group who did not undergo the procedure; however, this was not significant. Patients offered surgery may be considered to be generally in better health than the average patient, which may be the explanation for difference in mortality.

A major strength of this study is that it is based on the Western Denmark Myelomeningocele Database, which consists exclusively of patients born with myelomeningocele. Therefore, this study does not comprise patients with different congenital malformations. Furthermore, the database is population-based, because socialized health-care in Denmark ensures that all patients born with this malformation in western Denmark are brought to the Department of Neurosurgery at Aarhus University Hospital. The database of surgical procedures maintained by the hospital administrative unit is population based, and identifications in both databases are made by the same unique personal identification number, reducing the risk of missing information.

The study consists of retrospective data. Data collection is not complete for many patients, with a notable loss to follow-up in both the short and the long term. Bias is possible; however, the impact is less clear. Using the procedure to evaluate incidence according to age might underestimate the incidence of tethered cord syndrome. There might also be an observational bias due to previous knowledge that tethered cord syndrome has the highest incidence in childhood and adolescence. Our inclusion cutoff was 1970. Patients born before that date may have undergone detethering during our study period. However, this is not expected to be a large number, because the incidence seems highest for children and adolescents in our and other studies.

Conclusions

Tethered cord syndrome in patients with myelomeningocele has the highest incidence in children and adolescents. The highest incidence is at 15 years of age. There seems to be a beneficial effect of TCR in patients with myelomeningocele at short-term follow-up; however, the effect seems to fade away over time. Due to the uncertainty of a long-term effect and the registered possible complications attributed to TCR for tethered cord syndrome in patients with myelomeningocele, this surgical indication should be reserved for well-selected patients.

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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: Borgstedt-Bakke, Gudmundsdottir, Rasmussen. Acquisition of data: Borgstedt-Bakke. Analysis and interpretation of data: Borgstedt-Bakke, Wichmann, Rasmussen. Drafting the article: Borgstedt-Bakke, Wichmann, Rasmussen. 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: Borgstedt-Bakke. Statistical analysis: Borgstedt-Bakke, Wichmann. Administrative/technical/material support: Gudmundsdottir, Rasmussen. Study supervision: Gudmundsdottir, Rasmussen.

Supplemental Information

Previous Presentations

A previous version of this work has been published in abstract form at the Society for Research into Hydrocephalus and Spina Bifida (SRBSH) annual meeting and presented orally in the Guthkelch Finalists Presentation at said meeting at Washington University School of Medicine, St. Louis, Missouri, held on June 21–24, 2017. The name of the presentation was “The incidence and effect of tethered cord release for tethered cord syndrome in myelomeningocele patients—a population-based study.”

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