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ORIGINAL PAPER

Trends in incidence and long-term outcomes of myelomeningocele in British Columbia

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Abstract

Purpose Myelomeningocele is typically a disabling condition that results in neurologic, orthopedic, and urologic morbidity. The aim of this study was to examine the trends over time in both incidence and outcomes of myelomeningocele (MMC) in British Columbia (BC).

Methods A retrospective chart review was performed of all children with MMC followed in the British Columbia Children's Hospital (BCCH) Spinal Cord Clinic between 1971 and 2016. The incidence of new MMC cases and the long-term outcomes of MMC were compared between two 10-year cohorts. The first cohort comprised children born with MMC between 1971 and 1981, and the second cohort comprised children born with MMC between 1996 and 2006.

Results A total of 309 children with MMC were followed in the BCCH Spinal Cord Clinic between 1971 and 2016. There were 101 and 46 children with MMC in the two-time cohorts, respectively. Between the earlier and later cohorts, there was a significant difference in the following: MMC incidence [2.5/10,000 births vs 1.1/10,000 births, respectively ($p = 0.0002$)], mortality [18 vs 0% ($p = 0.0009$)], and the proportion of cases repaired in under 48 h [56 vs 98% ($p < 0.0001$)]. For surviving children, the proportion of children attending special classes was significantly different between the earlier and later cohorts [16 vs 46%, respectively ($p = 0.0002$)], whereas all other outcome measures, including the proportion with hydrocephalus, kyphoscoliosis, Chiari II surgery, bowel and bladder continence, recreation participation, obesity, and ambulation, were not significantly different.

Conclusions In BC, the incidence of new cases of MMC has decreased between 1971 and 2016, while the probability of survival for these patients has increased. Despite earlier and more universal post-natal repair, long-term outcomes have not improved significantly over time. Future research should focus on developing ways of reducing disability and improving quality of life for MMC patients and their families.

Keywords Myelomeningocele · Spina bifida · Long-term outcome · Quality of life · Multidisciplinary clinic

Introduction

Myelomeningocele (MMC) is the most common open neural tube defect, with an incidence of approximately 0.20–0.40/1000 births/year in Canada and the USA [1–3]. It is typically a disabling condition that results in neurologic, orthopedic, and/or urologic morbidity, as well as a reduction in health-related quality of life compared with the general population without MMC [4, 5]. Children with MMC are usually followed and managed through a multidisciplinary clinic to help coordinate their physical and psychosocial medical care efficiently and effectively [6, 7]. In British Columbia (BC), which currently has a population of 4.7 million people, all patients with MMC have been and are still followed in a multidisciplinary clinic at BC Children's Hospital (BCCH), originally called the Spina Bifida Clinic, but renamed the Spinal Cord Clinic (SCC). Though both short- and long-term outcomes of MMC have been studied, there has been little research into how these outcomes have evolved over time [4, 8, 9]. We

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aimed to study the trends over time in both incidence and outcomes of MMC through retrospective analysis of the patient population of children with MMC who were followed in the SCC at BCCH over the past 40 years. Both cohorts received the same multidisciplinary comprehensive care from the SCC at BCCH. Specifically, we compared an earlier and a more recent 10-year cohort of children born with MMC and followed for a minimum follow-up of 10 years.

Methods

Ethics approval was obtained from the University of British Columbia Children's and Women's Research Ethics Board. A retrospective chart review was performed of all children with MMC followed in the BCCH Spinal Cord Clinic between 1971 and 2016. The number of new diagnoses of MMC per year was identified by searching the SCC database as well as the BCCH neurosurgery division's surgical database for patients with either a diagnosis of MMC or closure of MMC. BCCH is the only pediatric neurosurgery center in the province of BC and therefore, it is likely that all live-born children with MMCs in BC were included in our analysis. We compared the number of new diagnoses per year to the number of live births in BC for that same year to calculate the annual live birth MMC incidence from 1971 to 2016 [10].

The incidence of new MMC cases and the long-term outcomes of MMC were compared between two 10-year cohorts. The first cohort (C1) comprised children born with MMC between 1971 and 1981 and followed for 8.6–19.6 years, for whom charts had been reviewed and outcomes reported previously by Steinbok et al. in 1992. The second cohort (C2) comprised children born with MMC in the most recent 10-year period that allowed for a similar minimum follow-up, namely children born between 1996 and 2006. The goal was to create two cohorts that were as similar as possible except for the dates of birth. We reviewed the charts of C2 in detail and then compared their outcomes to the previously published results of C1 [4]. The charts of C1 were not reviewed and the original data used in the previously reported study of C1 (Steinbok et al. 1992) were no longer available, so that information about C1 was only what was available in the published report.

For charts that were reviewed, MMC lesions were defined by location as follows: thoracolumbar L1 or above, midlumbar L2-L4, and lumbosacral L5-sacrum. If a lesion spanned two regions, it was classified under the more superior of the two. The following data were extracted from the health records: time to myelomeningocele repair, mortality and time to mortality, hydrocephalus diagnosis, treatment with a shunt, time to shunt revision(s), number of shunt revisions, number of shunt infections, kyphoscoliosis diagnosis, any other neurosurgical procedures, locomotion and mobility aids, orthopedic operations, urologic operations, obesity, recreational activity, school performance, and bowel and bladder continence. Social continence of bladder and bowel was defined as "being dry most of the time without the use of a diaper" [4]. Bladder continence was further subdivided into those who achieved continence using intermittent catheterization (IC) and if they did, whether it was performed by the patient or somebody else. For patients who were continent of bowel, their method of continence was also recorded. Community ambulation was defined as "the ability to get around without the use of a wheelchair" [4]. Ambulation was further subdivided into children who were community ambulators at some point in their lives (with or without aids), children who were community ambulators at their most recent follow-up (with or without aids), children who were community ambulators without aids, and children who were mobile only with a wheelchair.

Variables were compared between C1 and C2 using chi-square/Fisher exact test for categorical outcome variables and student *t* test for continuous variables with a statistical significance threshold set at $p = 0.05$. The Bonferroni correction was applied to reduce the chances of obtaining false-positive results due to multiple comparisons. We divided our initial critical p value of $p = 0.05$ by 33 which was the number of comparisons where we calculated a p value to result in a new significance threshold set at $p = 0.002$.

Results

Incidence

A total of 309 children with MMC were followed at BCCH between 1971 and 2016. A comparison of 5-year intervals during this time period shows a trend of decreasing incidence of MMC between 1971 and 2000, followed by a relatively steady period until the last available data in 2016 (Fig. 1). In C1, the mean incidence was 2.5 births per 10,000, compared with 1.1 births per 10,000 in C2 which was a statistically significant difference ($p = 0.0002$). These incidence measures reflect live births and do not include pregnancy terminations following prenatal diagnosis.

Demographic data for cohort 2

There were 51 children followed at BCCH who were born with a MMC between 1996 and 2006. Five children were excluded because they did not meet the minimum duration of follow-up at the BCCH clinic: all had moved out of the province of BC and were 1 to 7 years old at the last available follow-up. The 46 remaining children were 10.5 to 20.3 years old (mean of 15.7 years old) at the time of their last available follow-up (Table 1) and comprised the eligible C2. Of these, 46 children 28 (61%) were male and 18 (39%) were female.

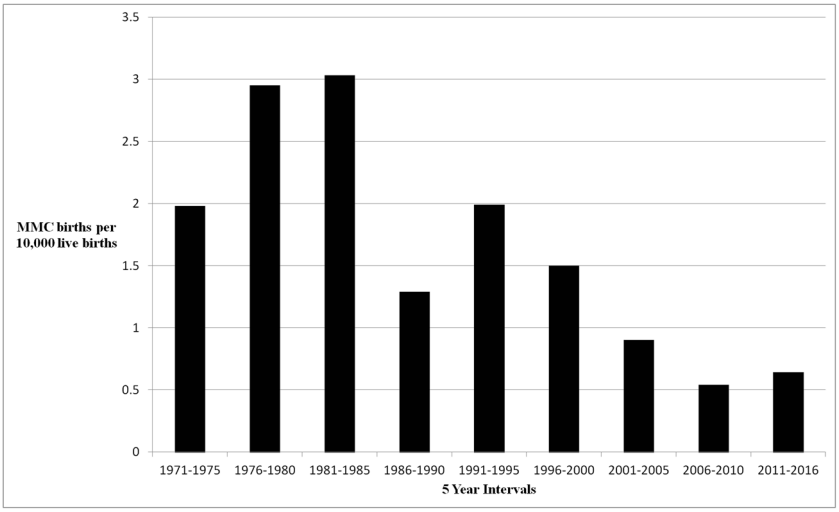

Fig. 1 A comparison of eight mean incidences over 5-year ranges of MMC births per 10,000 live births and one mean incidence over a 6-year range

The lesion levels were as follows: thoracolumbar 8 (17%), mid-lumbar 23 (50%), and lumbosacral 15 (33%). One child did not have mode of delivery information available: of the 45 remaining children, 23 (51%) were born by caesarean section and 22 (49%) by spontaneous vaginal delivery. These results are compared to the demographic data for C1 in Table 1.

Hydrocephalus, scoliosis, and Chiari II malformations

Surgical information for C2 such as the proportion of children with hydrocephalus, shunt insertions/revisions, shunt infections, kyphoscoliosis, and Chiari II surgery was recorded and compared to C1 (Table 2). There was no statistically significant difference in any of these surgical variables between the 2 cohorts. Forty-two (91%) of the 46 children in C2 were documented as having hydrocephalus: 35 (76%) had shunts inserted and one had an endoscopic third ventriculostomy (ETV) for management of their hydrocephalus. Thirteen (37%) of the 35 children with shunts in C2 needed a revision to their shunt in the first year of life. Twenty-two (63%) of the 35 children in C2 with shunts needed 1–3 revisions over the follow-up period, 7 (20%) needed no revisions, and 6 (17%) needed more than 3 revisions. Twenty-three (50%) of the 46 children in C2 were documented as having some form of kyphoscoliosis. Of the 23 children with kyphoscoliosis in C2, 7 (30%) had orthopedic instrumentation for correction. Five children (11%) in C2 had surgery performed for Chiari II malformation.

Functional outcomes

Rates of bowel and bladder continence as well as methods of achieving continence were recorded and compared between C1 and C2 (Table 2). The rates of bowel or bladder continence were statistically no different between the 2 cohorts. Thirty-one (67%) of the 46 children in C2 achieved social continence of urine, with 29/31 (94%) achieving continence by using intermittent catheterization; 22 performed by themselves and 7 by another person. In C1, by comparison, 62 of 83 (75%) were socially continent, with 51 of the 62 (82%) achieving this by IC, self-performed in 38 and by another person in 11. Thirty-six (78%) of the 46 children in C2 achieved social continence of stool with both C2 and C1 using a similar variety of methods to achieve continence including enemas, suppositories, cecostomy tubes, digital sweeps, oral medication, diet control, and nothing special.

Locomotion, recreation, and body composition

Twenty-nine (63%) of the 46 children in C2 were community ambulators at some time in their lives, with 25 (54%) of those children remaining community ambulators until the last available follow-up. All 29 children who were community ambulators at some time had intact quadriceps. Five (11%) of the 46 children were community ambulators without aids while 17/46 (37%) were mobile only with a wheelchair. Forty (87%) of the 46 children in C2 used some kind of orthotic vs 63/83 (76%) in C1. In C2, the most common orthotic reported was ankle-foot orthosis (AFOs). Most children in C2 participated in some kind of recreational activity with 20/46 (43%) participating in regular activity, 20/46 (43%) participating in intermittent activity, and 6/46 (13%) participating in no activity. There was a large variety of activities reported from children in C2. Some examples include walking, horseback riding, sledge hockey, wheelchair basketball, weight lifting, hiking, and karate. The most commonly reported recreational activity was swimming. Five (11%) of the 46 children in C2 were classified as obese, based on a comment in the medical record, not on BMI. Most children who were obese were not community ambulators in both C1 and C2 with four of the five

Table 1 Comparison of demographic, repair, and lesion location information between the C1 and C2 cohorts. The data for C1 is from Steinbok et al. [4]

Variable	1971–1981 (C1)	1996–2006 (C2)	*p* value
Population			
N	101	51	
Mortality	18% (18/101)	0% (0/46)	0.0009*
Average gestational age (weeks) [a]		37.8	
Mode of delivery[a, b]			
Caesarean section		51% (23/45)	
Spontaneous vaginal delivery		49% (22/45)	
Time to repair			
Average time to MMC repair (days)[a]		0.58	
Repaired in ≤ 48 h	56% (57/101)	98% (45/46)	< 0.0001*
Repaired in > 48 h–≤ 1 week[c]	10% (10/101)	0% (0/46)	
Repaired in > 1 week ≤ 1 month[c]	3% (3/101)	0% (0/46)	
Repaired in > 1 month[c]	10% (10/101)	0% (0/46)	
Not repaired[c]	21% (21/101)	2% (1/46)	
Sex			
Male	45% (45/101)	61% (28/46)	0.073
Female	55% (56/101)	39% (18/46)	
Lesion site			
Thoracolumbar	27% (27/101)	17% (8/46)	0.201
Mid-lumbar	34% (34/101)	50% (23/46)	0.059
Lumbosacral	40% (40/101)	33% (15/46)	0.445
Follow up group			
N[d]	83	46	
Mean age at follow-up (years)[e]	13.4	15.7	
Range of age at follow-up (years)	8.6–19.6	10.5–20.3	

*Significant at $p < 0.002$

[a] Data not available for the 1971–1981 cohort

[b] One child did not have mode of delivery information available in their chart

[c] Due to small numbers could not statistically analyze

[d] Change in *N* is due to mortality in C1 and removing children who did not have sufficient follow-up in C2

[e] Full data not available for the 1971–1981 cohort to perform *t* test

obese children in C2 primarily using a wheelchair for locomotion even though they had the functional ability to ambulate. None of the measures for locomotion, recreation, or rates of obesity were significantly different between C1 and C2.

School performance

School performance was assessed as a measure of intellectual function and compared to C1 (Table 2). The only school performance outcome that was statistically significantly different in C2 vs C1 was the proportion of children attending special class. Twenty-one (46%) of the 46 children in C2 were attending special class, which ranged from programs teaching basic life skills to grade appropriate programs with modified curriculum in the form of an individualized education plan (IEP) (Table 2), compared to 13/83 (16%) in C1 ($p = 0.0002$). Ten of the 21 children that were categorized as being in the special class category had an IEP but were actually in grade-appropriate classes. Sixteen (35%) of the 46 children in C2 were attending normal grade-appropriate classes without an IEP. The remainder of the C2 children were either home schooled 5/46 (11%) or attended normal class, but not grade appropriate 4/46 (9%). The most common learning problem reported for both C1 and C2 was challenges learning math, requiring additional support.

Table 2 Surgical information and quality of life outcome comparisons between the two cohorts. The data for C1 is from Steinbok et al. [4]

Outcome	1971–1981 (C1)	1996–2006 (C2)	*p* value
Hydrocephalus			
Number with hydrocephalus	92% (93/101)	91% (42/46)	0.839
Number shunted	84% (85/101)	76% (35/46)	0.248
- Shunt revision in first year of life	51% (43/85)	37% (13/35)	0.164
- 1–3 revisions	54% (46/85)	63% (22/35)	0.368
- > 3 revisions	32% (27/85)	17% (6/35)	0.096
- No revisions	14% (12/85)	20% (7/35)	0.414
Shunt infection rate per shunt surgery	5%	4.6%	1.0
Kyphoscoliosis			
Total number	42% (42/101)	50% (23/46)	0.367
Number having instrumentation	38% (16/42)	30% (7/23)	0.521
Chiari II surgery	7% (7/101)	11% (5/46)	0.415
Continence			
Socially continent of urine	75% (62/83)	67% (31/46)	0.333
Socially continent of stool	86% (71/83)	78% (36/46)	0.247
Ambulation			
Ambulatory at some point in their lives (with or without aids)	58% (48/83)	63% (29/46)	0.580
Ambulatory at last follow up (with or without aids)	54% (45/83)	54% (25/46)	1.0
Ambulatory without aids	24% (20/83)	11% (5/46)	0.075
Mobile only with wheelchair	42% (35/83)	37% (17/46)	0.580
School			
Normal class, grade appropriate	58% (48/83)	35% (16/46)	0.012
Normal class, not grade appropriate	24% (20/83)	9% (4/46)	0.037
Home school	2% (2/83)	11% (5/46)	0.028
Special class[a]	16% (13/83)	46% (21/46)	0.0002*
-IEP, grade appropriate [b]		22% (10/46)	
-IEP or life skills program, not grade appropriate[b]		24% (11/46)	
Recreation			
Regular sports or PE	46% (38/83)	43% (20/46)	0.743
Intermittent activity	43% (36/83)	43% (20/46)	1.0
No activity	11% (9/83)	13% (6/46)	0.736
Body composition			
Obesity	15% (12/83)	11% (5/46)	0.526

*Significant at $p < 0.002$

[a] Special class was classified as anything outside of normal unmodified school curriculum

[b] Data not available for the 1971–1981 cohort

Discussion

Incidence

In this review, the incidence of MMC followed at the SCC decreased over time. This decreased incidence of live-born infants with MMC is consistent with other reports and may reflect a combination of improved maternal folate status and increased pregnancy terminations following prenatal diagnosis, as has been previously suggested [1, 2, 11, 12]. Folic acid fortification was introduced in Canada in 1997 [11–13]. The mean incidence of MMC followed at BCCH between 1971 and 1996 before folic acid fortification was 2.25 births per 10,000. After folic acid fortification was introduced, from 1997 to 2016, the mean incidence of MMC followed at BCCH was 0.82 births per 10,000, which was a statistically significant decrease ($p < 0.0001$). To

further support the association of folic acid fortification on incidence of MMC live births, Fig. 1 shows a pattern of decreasing MMC incidence from 1971 to 2000 followed by a relatively stable incidence from 2001 to 2016. A decrease in incidence after 2000 is consistent with results from De Wals et al. who looked at the incidence of MMC in multiple Canadian provinces that included live births, still births, and pregnancy terminations [1]. The results from De Wals et al. looking at MMC incidence showed "a stable rate from 1993 through 1997, followed by a decrease from 1998 to 2000 and stabilization thereafter" [1]. Children in their study were not considered to be born in the post-fortification period until after March 31st, 2000 [1]. This is due to results that suggest red blood cell (RBC) folate levels did not plateau until late 1999 [13], even though folic acid fortification began as early as 1997 [14–16]. Therefore, in Fig. 1, the incidence displayed before 1995 reflects a pre-fortification period, 1996–2000 reflects a partial-fortification period, and 2001 onwards reflects a full-fortification period. Figure 1 shows that there was a large reduction in incidence once folic acid was introduced (1991–1995 vs 1996–2000), followed by another reduction then stabilization of the incidence once RBC folate levels are suggested to have plateaued (1996–2000 vs 2001–2016) [13]. Our results from the population followed at BCCH therefore may also suggest that folic acid fortification played a role in reducing MMC incidence, but may not have had its full effect until RBC folate levels plateaued years following its introduction. Interestingly, there was also one 5-year period in the pre-fortification period from 1986 to 1990 that had a large reduction in incidence before returning to higher levels in the period immediately after. We are not sure why the isolated reduction occurred over this time period.

Our calculated incidence of MMC was based on children who were seen at the Spinal Cord Clinic at BCCH. Therefore, unlike De Wals et al., it does not include children with MMC who were stillbirths or whose pregnancies were terminated, which has been reported to be up to 46% [1]. This means that our incidence data does not fully capture all the diagnoses of MMC in BC, but it does reflect the dramatic reduction in live birth MMC cases followed at BCCH from 1971 to 2016 and more specifically after the suggested plateau of RBC folate levels in 1999 [13].

Survival

The C1 cohort had a survival of 82% after 8.6 to 19.6 years of follow-up. This is similar to results from other studies that looked at MMC patients born between 1975 and 2003, where a survival of approximately 75% after 20–25 years of follow-up was described [8, 17]. Of the 18 children who died in C1, two children died from a CNS infection, one from complications of a Chiari malformation, one from increased intracranial pressure, one from septicemia, one from renal failure, one from hemolytic uremia syndrome, and in 11 children, the cause of death was unclear or not reported [4]. Our more recent cohort (C2) had 100% survival after a follow-up of 10.5 to 20.3 years old which is consistent with other studies that report that survival during infancy and preschool years for children born with MMC has continued to improve over the last few decades [8]. One key factor that may partly explain the different survival rates between C1 and C2 is the fact that during the time of the C1 cohort, some children were treated with closure of the MMC and shunting for hydrocephalus, while others were not offered such treatment in the perinatal period if it was expected that they may not survive [4]. Patients in C1 where repair was performed after 1 month or not at all were selected to receive nonaggressive treatment initially, and in this group, the survival was the lowest at 55% (17/31) [4]. On the other hand, survival for C1 patients who had a time to repair of less than 48 h was 97% (55/57), which is comparable to the survival rate from C2. This suggests that a transition towards more aggressive and earlier treatment for all newborns with MMC seems to have improved survival into early adulthood.

School performance

There were significantly more children in C2 than in C1 that were attending special class. School performance may be considered a marker for intellectual function, but the differences observed may reflect a shift in special needs education support in BC, rather than a difference in the cognitive capacity of the children in C2 vs C1. Many of the children who were recorded as being in the "Special Class" category of our study were enrolled in an IEP at school. An IEP is for students that range from needing more than minor adaptations to educational materials, instruction, or assessment methods to students who are working on regular curriculum outcomes but need an additional classroom teacher for educational support [18]. IEPs were brought into BC in 1996 [19]. Thus, it is probable that some of the children in C1 who were held back to a lower grade or who had difficulties in grade-appropriate classes for their age, in more recent years, would have had an IEP in school and placed in the Special Class category. For example, in C2, 10 of the 21 children in the Special Class category were in grade-appropriate class but had an IEP. If these children went to school when IEPs were not available, they likely would have been placed in a grade-appropriate class or held back to a lower grade without other accommodations, therefore not meeting our criteria for the Special Class category. Our results in C2 for the proportion of MMC children who require some or all special education classes is similar to what was reported by Bowman et al. [8]. Recent studies suggest that in patients with spina bifida, there is a dose-dependent relationship where the higher the level of education achieved, the less likely the individuals are to rate themselves as being permanently disabled [20]. Given education may be an important predictive factor for disability, it would be interesting to know whether programs such as IEPs in British Columbia are facilitating higher education achievement in patients with spina bifida.

Other outcome measures

Except for the proportion of children in special classes, all of our other outcome measures between C1 and C2, including proportion with hydrocephalus, kyphoscoliosis, Chiari II surgery, bowel and bladder continence, recreation participation, obesity, and ambulation, were not significantly different. Even with an improved understanding of MMC, it seems that children followed with MMC today do not have a significantly different prognosis for many measures than they did approximately 2 decades earlier. Since the BCCH Spinal Cord Clinic was established in 1969, all patients in C1 and C2 received comprehensive, multidisciplinary follow-up until they graduated from the clinic at the start of adulthood [6]. For MMC patients, adequate follow-up with a team of specialists is important for preventing significant morbidity and mortality, but it seems that the effect of these multidisciplinary clinics on many outcome measures has not significantly evolved over time [7]. As with achieving higher levels of education, there is a suggested dose-dependent relationship between the frequency of bowel incontinence and perceived permanent disability in patients with spina bifida [20]. Results from our study suggest bowel continence measures have not evolved over time and given its suggested importance for predicting permanent disability, future work should investigate how to improve the bowel management programs for these patients.

Limitations

There were a few limitations to our study that should be discussed. We no longer had access to the original data that was analyzed by Steinbok et al. due to how long ago it was collected [4]. This meant that we could not compare many of our continuous variables between the cohorts such as "average gestational age" and "average time to repair." Additionally, results from this study may not be generalizable to other centers due to different specialists and treatment protocols [21]. Furthermore, as this was a retrospective chart review, the data being collected was limited to what was found in the patient's chart, varying in detail depending on the reporting physician and patient and family's recall ability.

Conclusion

In British Columbia, the incidence of new cases of MMC has significantly decreased over time between 1971 and 2016 while the chance of survival for these patients has significantly increased to now close to 100%. The drop in incidence may be due to a combination of food folate fortification in 1997 and increased MMC pregnancy terminations, while survival may have improved due to earlier and more universal post-natal repair. Despite earlier and more universal post-natal repair, most of the long-term outcomes, such as ambulation and bowel/bladder continence, have not changed significantly over time for MMC patients followed at BCCH. There appears to be better educational support for these children, with the institution of IEPs in the education system in BC in 1996. Future research should focus on developing ways of reducing disability and improving quality of life for MMC patients and their families.

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Compliance with ethical standards

Ethics approval The study was approved by the Children's and Women's Health Centre of British Columbia Research Ethics Boards, approval number: H17-00277.

Disclosure The authors have nothing to disclose.

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

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