The extended treatment of children with myelomeningocele (MMC) has been at the center of ethical debate because of the expected quality of life, related to the severity of the associated outcomes in both early and later life. In the 1970s, this led to the development of the Lorber criteria to distinguish between severe and less severe cases of MMC. If cases were considered too severe for active treatment, namely closure of the defect and in the vast majority subsequent shunt insertion, palliative care or active termination of life could be offered as an alternative to prevent unnecessary prolongation of suffering. In the Netherlands, every case of termination of life in newborns is assessed using guidelines from the Groningen Protocol. Its foundation is based on the concept of unbearable suffering, which is described for infants as "... not dependent on intensive medical treatment but for whom a very poor quality of life, associated with sustained suffering, is predicted."

**ABBRVIATIONS**
- CFCS = Communication Function Classification System
- HROQL = health-related quality of life
- MMC = myelomeningocele
- NRS = numeric rating scale
- PEDI-CAT = Pediatric Evaluation of Disability Inventory

**ACCOMPANYING EDITORIAL**
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Since the routine 20-week anomaly ultrasound scan during pregnancy was implemented in the Netherlands, MMC has mostly been detected before the time limit of legal termination of pregnancy. This warrants patient-centered counseling with a shared decision-making approach between the future parents and doctors regarding whether to continue or terminate a pregnancy. This decision greatly relies on adequate predictions of the child’s quality of life, mobility, severity of pain, ability to communicate, and number of surgeries needed throughout life.

Predicting the future quality of life in MMC patients is extremely difficult and becomes more important with the introduction of fetal surgery. When choosing to continue a pregnancy, future parents are faced with the choice between fetal surgery, which shows clear benefits for the patient but comes with well-established maternal risks, and postnatal surgery, which has no maternal risks.

We previously reported on the short-term conditions of newborns with MMC in our Rotterdam study on discomfort and pain in newborns with MMC. Our findings showed that, in all cases, there were low levels of discomfort and pain. Adequate comfort levels could be achieved with a routine pain protocol (consisting of painkillers and physical therapy) in all newborns with MMC independent of the severity of the disease. Our current study assesses the long-term conditions of the same group of MMC patients based on their quality of life, functioning, and extent of pain and fatigue.

Methods

Patient Selection and Data Extraction

This study is a retrospective, single-institution, cohort study. We obtained approval from the Erasmus Medical Center Medical Ethical Review Board. The parents of the 28 included patients in our former study were sent a letter detailing the purpose and procedures of this research project. Parents and patients who agreed to participate were invited for an interview at our outpatient clinic or were visited at home after the collection of written informed consent. The duration of the full interview session ranged from 2 to 3 hours. The order in which all questionnaires were administered was the same for all participants.

Patient Characteristics

For patient characteristics, we collected data on age, sex, education level, and MMC severity. We distinguished between primary, special primary, secondary, and special secondary education. MMC severity was based on the Lorber criteria, which include thoracolumbar lesions, severe paraplegia, gross enlargement of the head, kyphosis and other severe congenital defects, or birth injuries as adverse prognostic criteria.

Health-Related Quality of Life and Functional Outcome

The primary outcome was health-related quality of life (HRQOL) measured with the Dutch version of the KIDSCREEN-27 questionnaire. This questionnaire consists of several questions among 5 domains: physical well-being, psychological well-being, parent relations and autonomy, social support and peers, and school environment. Questions are answered on a 5-point scale (total score range 0–100) considering a time frame of 1 week and assess the frequency of behavior and feelings. Higher total scores indicate higher quality of life.

We used the Pediatric Evaluation of Disability Inventory (PEDI-CAT) to measure functional outcome. The PEDI-CAT provides normative data on the child’s functioning relative to that of his or her peers. The normative standardization sample was based on an extensive online panel. The domains tested are daily activities, mobility, social/cognitive items, and responsibility.

Ambulation and Communication

Ambulation was scored using the Hoffer ambulation scale. The level of communication was scored by parents using the Communication Function Classification System (CFCS). The CFCS was initially designed to classify the daily communication of patients with cerebral palsy and consists of a 5-point scoring scale, looking at all forms of communication, verbal and nonverbal.

Pain and Fatigue

Pain and fatigue were scored based on the week prior to the interview using the numeric rating scale (NRS), in which pain and fatigue are represented on a scale where a score of 0 represents absolutely no pain and fatigue and a score of 10 represents the worst imaginable pain and fatigue (see Bolton and Gladman et al. for validation).

Non-MMC Group Data

To compare functioning and quality of life between MMC children and a healthy population, we created a healthy population comparison group (non-MMC group) based on the means of reference data from the KIDSCREEN-27 and its manual. We paired every child in our population with a healthy child of their age (based on obtaining a normal score).

Statistical Analysis

We did not assess distribution for nominal or ordinal data. Statistical differences in age, sex, and education between severe (i.e., Lorber) and less severe (i.e., non-Lorber) MMC groups were determined using the Mann-Whitney U-test, Fisher exact test, and Fisher-Freeman-Halton exact test. A Shapiro-Wilk test was used to evaluate the distribution of all nonnormal group data. A box plot and Mahalanobis distance were checked to determine univariate or multivariate outliers. Assumptions of linearity were assessed using a scatterplot. Box’s M-test was used to determine the homogeneity of variance-covariance matrices. Hotelling’s $T^2$ was run to determine the effect of MMC and Lorber versus non-Lorber patients on KIDSCREEN-27 and PEDI-CAT scores. Subgroup analysis of KIDSCREEN-27 and PEDI-CAT domains was done using an independent t-test or Well’s t-test when the assumption of equal variance could be met. A Bonferroni adjusted $\alpha$ level of 0.05 with a simultaneous 95% confidence level was used. A $p$ value $\leq 0.05$ was considered.
significant, and all analyses were performed using SPSS version 22.0 software (IBM Corp.).

Results

Patient Characteristics

Twenty-two subjects entered this follow-up study. The mean age on the interview day was 11.0 years (95% CI 10.4–11.6), ranging from 8.0 to 12.9 years. Our patient population consisted of Lorber (n = 6) and non-Lorber (n = 16) subjects. Sex, age, and level of education showed no significant differences between both groups (Table 1). The reasons for not participating were lack of interest (n = 2), anxiety issues (n = 1), major surgery scheduled (n = 1), family-related circumstances (n = 1), and no response (n = 1).

HRQOL of Children Born With MMC

Five quality-of-life measures were assessed via the KIDSCREEN-27 questionnaire: physical well-being, psychological well-being, parent relations and autonomy, social support and peers, and school environment. Patients with MMC versus the non-MMC group had a significantly lower mean score in all subdomains, as shown in Table 2. The differences between the non-MMC group and the MMC group on the overall KIDSCREEN-27 scores were statistically significant (F[5, 38] = 41.049, p < 0.001; Wilks’ Λ = 0.156; partial η² = 0.844), with the scores in the MMC group being lower. Similar differences were seen between the non-Lorber and Lorber groups (F[4, 17] = 7.182, p < 0.001; Wilks’ Λ = 0.372; partial η² = 0.628). The mean mobility scores were 15.3 points (95% CI 11.5–19.0; p < 0.01) higher in the non-MMC group than in the MMC group and 12.6 points (95% CI 7.0–18.1; p = 0.573) higher in the non-Lorber group than in the Lorber group. The MMC group also scored significantly lower regarding daily activity, cognitive, and responsibility scores than the non-MMC group. However, there was no significant difference between the Lorber and non-Lorber groups in these domains (Table 3).

Mobility

Nearly half of the patients (45.5%) are household or community ambulators, and the remaining patients are wheelchair-bound. The household/community ambulator group consists entirely of non-Lorber patients.

Communication

All patients reached level I (n = 18) or II (n = 4) on the CFCS, which means that they were able to communicate effectively, albeit slowly in 4 patients. There was no statistical difference between Lorber and non-Lorber patients regarding CFCS (p > 0.05). The 4 patients with CFCS level II did report self-evaluated slower communication compared with peers.

Pain and Fatigue

Almost three-quarters of the patients experienced some degree of pain in the week prior to the interview. Whereas most children (n = 12) reported low levels of pain

<table>
<thead>
<tr>
<th>TABLE 1. Patient characteristics</th>
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<tr>
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<tr>
<td>Sex</td>
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<td>Male</td>
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<tr>
<td>Female</td>
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<td>Mean age, yrs (SD)</td>
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<tr>
<td>Education</td>
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<tr>
<td>Primary school</td>
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<td>Secondary school</td>
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<td>Special primary school</td>
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<td>Special secondary school</td>
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<td>Values are given as the number of patients (%) unless otherwise indicated.</td>
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<th>TABLE 2. KIDSCREEN-27 subscores evaluated between the cohort versus the normal group and the non-Lorber versus the Lorber group</th>
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<tr>
<td><strong>Difference</strong></td>
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<td>Physical well-being</td>
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<tr>
<td>Psychological well-being</td>
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<tr>
<td>Parent relations &amp; autonomy</td>
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<tr>
<td>Social support &amp; peers</td>
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<td>School environment</td>
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* Equal variance is not assumed.
(NRS scores of 1.0–3.0), 4 children reported moderate levels (NRS scores of 4.0–6.0). In total, 6 patients (27.3%) reported no pain in the week prior to the interview. Pain could be effectively treated with pain medication in all patients.

Four children (18.2%) reported no fatigue in the week prior to the interview. Eighteen children experienced some degree of fatigue on average, ranging from moderate fatigue (8 patients; NRS scores of 4.0–6.0) to severe fatigue (10 patients; NRS scores of 7.0–9.0).

There were no significant differences in pain or fatigue between Lorber (mean 1.8 ± 0.7) and non-Lorber (mean 1.9 ± 0.5) patients (95% CI −1.85 to 1.99; t(20) = 0.079; p = 0.913).

### Number of Surgeries

Overall, patients had a mean number of 18 ± 5 (range 6–30) surgeries consisting of 1.2 ± 0.6 (range 0–14) neurosurgical procedures, 11.8 ± 0.6 (range 6–23) orthopedic procedures, and 11.8 ± 0.6 (range 6–23) urological procedures. The number of surgeries was the highest in the 1st year after birth (mean 1.3 ± 0.4). The Lorber group (16.7 ± 5.2) did not differ significantly from the non-Lorber group (16.4 ± 6.0) (95% CI 5.45–6.03; t(11) = 0.112; p = 0.913).

### Discussion

Among the many factors affecting the quality of life and function in spina bifida patients, the level of mobility, sensory deficits, cognitive impairments, and incontinence seem to be major contributing factors. This study shows that MMC patients score considerably lower regarding functioning and quality of life when compared with their peers without MMC, but this did not directly translate into a worse perception of physical well-being. Comparing Lorber and non-Lorber MMC patients, we found a significant difference only regarding perceived quality of life in the school environment and not in the other domains. Considering the effects of MMC on the quality of life and the number of surgeries, we conclude that MMC is a severe but manageable condition.

The primary motivation for conducting this study was to offer new insights into the long-term follow-up of MMC patients. No study before has reported on the same group of patients 10 years after the initial evaluation of discomfort and pain. This study does not offer a direct cross-sectional comparison with our previous work on the same cohort 10 years ago. Changes in age are reflected in different and often more complex parameters of quality of life. Hence, a direct comparison would not be sufficient.

In the Netherlands, the active ending of life for newborns with severe MMC has been at the center of debate for many years. This resulted in a broader discussion about the option of active termination of life for newborns with severe untreatable diseases in general. Eventually, the Groningen Protocol was developed in 2004 to aid clinicians when making these difficult decisions. Its unique perspective has sparked an international debate over the past 2 decades. The protocol contains a specific set of criteria that are essential in evaluating clinical decisions. This process warrants careful discussions considering different viewpoints, but the active ending of a newborn’s life is legal under Dutch law when the criteria are met. Infants born with a severe MMC will often have profound disabilities with a significant impact on their daily lives and hence could be considered to suffer unbearably and hopelessly according to the criteria mentioned in the Groningen Protocol. Active termination of life was reported in 22 cases of severe MMC between 1997 and 2004 using the criteria set within the Groningen Protocol.

In their cohort, Verhagen et al. included 22 newborns with severe MMC. Their lives were terminated because it was concluded that unbearable and hopeless suffering was present and that their future quality of life would be severely affected. This included potential hospital dependency, lifelong and untreatable discomfort and pain, an inability to communicate, and low self-sufficiency. Despite the undeniable severe impact on quality of life, we argue that the prediction of future unbearable suffering in this group of patients remains challenging. We observed relatively low levels of pain, apart from 4 patients with moderate levels of pain in the week before the interview. More importantly, this pain could be adequately managed for all patients using low-impact analgesics. Fatigue ranged from moderate to severe. These scores are lower than self-reported pain and fatigue ratings in children with, for instance, chronic arthritis or cerebral palsy. We understand the differences in methodological use between these studies and ours, but we think it is acceptable to state that these MMC children do not suffer unbearably. Also, this suffering also does not continue throughout their youth, which is regarded as another argument for eligibility according to the Groningen Protocol.

Because of their physical and cognitive impairments, MMC patients are thought to experience a significant dependency on parents and caretakers. Dependency on the

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**TABLE 3. PEDI-CAT subscores evaluated between the cohort versus the normal group and the non-Lorber versus the Lorber group**

<table>
<thead>
<tr>
<th>Subscore</th>
<th>Mean Difference</th>
<th>95% CI</th>
<th>p Value</th>
<th>df*</th>
<th>t</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily activity score</td>
<td>−6.19</td>
<td>−9.26</td>
<td>23</td>
<td>−4.16</td>
<td>&lt;0.001</td>
<td>20</td>
</tr>
<tr>
<td>Mobility score</td>
<td>−15.29</td>
<td>−19.01</td>
<td>21</td>
<td>−5.84</td>
<td>&lt;0.001</td>
<td>11</td>
</tr>
<tr>
<td>Cognitive score</td>
<td>−3.88</td>
<td>−5.58</td>
<td>25</td>
<td>−4.69</td>
<td>&lt;0.001</td>
<td>12.58</td>
</tr>
<tr>
<td>Responsibility score</td>
<td>−4.81</td>
<td>−7.3</td>
<td>25</td>
<td>−3.99</td>
<td>0.001</td>
<td>9.35</td>
</tr>
</tbody>
</table>

* Equal variance is not assumed.
medical circuit, which involves frequent hospital visits and surgeries, is seen as a factor that affects patients’ quality of life. In our cohort, children had indeed undergone a considerable number of surgeries in the first 10 years of their lives. Even though our results show a significant difference between PEDI-CAT (limitations in activity level) and KIDSCREEN-27 (HRQOL) scores between the MMC population and the non-MMC group, this difference was not significant in terms of physical and psychological well-being. Additionally, our findings also show that all children can communicate effectively, although some were considered slow.

This study has several limitations because of its retrospective nature and sample size, especially when comparing the Lorber group to the non-Lorber group. The sample size was dictated by reporting on the same cohort as 10 years ago. In the future, we recommend that a prospective cohort study with a larger sample size be conducted to overcome these limitations.

Conclusions

Our study shows that MMC is a severe lifelong condition that affects patients’ lives in many domains and that all our patients are capable of effective communication, irrespective of the severity of MMC.

Overall, our data show that in newborn MMC patients, future unbearable suffering with respect to pain, mobility, cognition, and communication is hard to predict and may not always occur. The difficulty of defining and predicting unbearable suffering after birth as well as in future life underlines the extreme importance of adequate counseling based on the available literature for future parents confronted with a spina bifida pregnancy.

References


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: de Jong, Eelkman Rooda. Acquisition of data: Eelkman Rooda, Kik. Analysis and interpretation of data: Spoor, Kik. Drafting the article: Spoor. Critically revising the article: all authors. Approved the final version of the manuscript on behalf of all authors: de Jong. Statistical analysis: Kik.

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