Congress of Neurological Surgeons Systematic Review and Evidence-Based Guidelines for Pediatric Myelomeningocele: Executive Summary

Catherine A. Mazzola, MD[*‡]
Nadege Assassi[§]
Lissa C. Baird, MD[¶]
David F. Bauer, MD[‖]
Alexandra D. Beier, DO[#]
Jeffrey P. Blount, MD[**]
Susan R. Durham, MD, MS[‡‡]
Ann Marie Flannery, MD[§§]
Paul Klimo, Jr, MD[¶¶‖‖##]
Catherine McClung-Smith, MD[***]
Dimitrios C. Nikas, MD[‡‡‡]
Patricia Rehring, MPH[§§§]
Mandeep S. Tamber, MD, PhD[¶¶¶]
Rachana Tyagi, MD[‖‖‖‖]

[*]Goryeb Children's Hospital, Morristown, New Jersey; [‡]Department of Neurological Surgery, Rutgers, Newark, New Jersey;
(Continued on next page)

Sponsored by: The Congress of Neurological Surgeons (CNS) and the Section on Pediatric Neurosurgery

Endorsed by: The Congress of Neurological Surgeons (CNS) and the American Association of Neurological Surgeons (AANS), the Spina Bifida Association (SBA)

Correspondence:
Catherine A. Mazzola, MD,
Rutgers New Jersey Medical School,
185 S Orange Ave, Newark, NJ 07103.
Email: catherine.mazzola@rutgers.edu

Received, March 25, 2019.
Accepted, May 11, 2019.
Published Online, August 16, 2019.

BACKGROUND: The incidence of spina bifida (SB) in the developing world is higher than in the United States because of malnutrition and folic acid deficiency during pregnancy. Advances in technology have made prenatal repair of myelomeningocele (MM) possible.
OBJECTIVE: The objective of the guidelines are, (1) To create clinical recommendations for best practices, based on a systematic review and analysis of available literature, (2) to obtain multi-disciplinary endorsement of these guidelines from relevant organizations, and (3) to disseminate the educational content to physicians to improve the care of infants with MM.
METHODS: The Guidelines Task Force developed search terms and strategies used to search PubMed and Embase for literature published between 1966 and September 2016. Strict inclusion/exclusion criteria were used to screen abstracts and to develop a list of relevant articles for full-text review.
RESULTS: Guidelines authors aimed to systematically review the literature and make evidence based recommendations about the timing of closure after birth, hydrocephalus, the impact of prenatal closure, and the effect of prenatal closure on ambulation ability and tethered spinal cord. Evidence concerning persistent ventriculomegaly and cognitive impairment was also evaluated. Hundreds of abstracts were identified and reviewed for each of the 5 topics. A total of 14 studies met stringent inclusion criteria.
CONCLUSION: Based on a comprehensive systematic review, a total of 5 clinical practice recommendations were developed, with 1 Level I, 2 Level II and 2 Level III recommendations.
The full guideline can be found at https://www.cns.org/guidelines/guidelines-spina-bifida-chapter-1.

KEY WORDS: Fetal, Guidelines, In utero, Myelomeningocele, Postnatal, Spina bifida, Tethered cord syndrome

Neurosurgery 85:299–301, 2019 DOI:10.1093/neuros/nyz261 www.neurosurgery-online.com

Spina bifida (SB) affects development and quality of life. Most infants with myelomeningocele (MM) have hydrocephalus (HC) and require surgical treatment. There are variations of clinical practice with regard to timing and type of closure, and antibiotic administration. While in utero closure of MM is an option for some women whose infants met certain criteria for diagnosis of SB as fetuses, globally, this option is not readily available. Some experts insert a ventriculoperitoneal shunt at birth, some advocate choroid plexus coagulation and endoscopic third ventriculostomies and others advocate conservative non-surgical management of HC and ventriculomegaly (VM).[1-3]

ABBREVIATIONS: AANS, American Association of Neurological Surgeons; **CNS,** Congress of Neurological Surgeons; **COI,** conflicts of interest; **HC,** hydrocephalus; **MM,** myelomeningocele; **MOMS,** Management of Myelomeningocele Study; **SB,** spina bifida; **VM,** ventriculomegaly

OBJECTIVES

Guidelines authors aimed to systematically review the literature and make evidence based recommendations about the timing of closure after birth, and to investigate the evidence concerning persistent VM and cognitive impairment.

METHODOLOGY

Process Overview

The Guideline Task Force members conducted a systematic review of the literature relevant to the management of MM in infants and children. Additional details of the systematic review are provided at https://www.cns.org/guidelines/guidelines-spina-bifida-chapter-1.

Selection of Clinical Topics

The goals of this effort were to discern the most effective strategies for a variety of MM-related problems, including timing of closure, antibiotics, and HC/ VM.

Literature Search

The search terms and strategies used to search The National Library of Medicine PubMed and Embase databases for relevant literature published between 1966 and September 2016 are available at https://www.cns.org/guidelines/guidelines-spina-bifida. Literature searches were supplemented with manual screenings of the bibliographies of all retrieved publications and other potentially relevant systematic reviews. All literature identified were subject to the article inclusion/exclusion criteria described at https://www.cns.org/guidelines/guidelines-spina-bifida-chapter-1.

Rating the Quality of Evidence

The quality of evidence was rated using an evidence hierarchy developed by the Joint AANS/CNS Guidelines Review Committee for 3 different study types including therapeutic effectiveness and diagnosis and prognosis (Appendix II). Additional information regarding the hierarchy classification of evidence can be located here: https://www.cns.org/guidelines/guideline-procedures-policies/guideline-development-methodology.

(Continued from previous page)

[§]Department of Surgery, Division of Neurosurgery, Robert Wood Johnson Medical School, New Brunswick, New Jersey; [¶]Department of Neurological Surgery, Oregon Health and Science University, Portland, Oregon; [‖]Department of Surgery, Division of Neurosurgery, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire; [#]Division of Pediatric Neurosurgery, University of Florida Health Jacksonville, Jacksonville, Florida; [**]Division of Pediatric Neurosurgery, Department of Neurosurgery, University of Alabama at Birmingham, Children's of Alabama, Birmingham, Alabama; [‡‡]Division of Neurosurgery, University of Vermont, Burlington, Vermont; [§§]Kids Specialty Center, Women's & Children's Hospital, Lafayette, Louisiana; [¶¶]Semmes Murphey, Memphis, Tennessee; [‖‖]Department of Neurosurgery, University of Tennessee Health Science Center, Memphis, Tennessee; [##]Le Bonheur Children's Hospital, Memphis, Tennessee; [***]Department of Neurological Surgery, Palmetto Health USC Medical Group, Columbia, South Carolina; [‡‡‡]Division of Pediatric Neurosurgery, Advocate Children's Hospital, Oak Lawn, Illinois; [§§§]Congress of Neurological Surgeons, Schaumburg, Illinois; [¶¶¶]Division of Pediatric Neurosurgery, British Columbia Children's Hospital, University of British Columbia, Vancouver, Canada; [‖‖‖]Department of Neurosurgery, Mercer University Medical School, Macon, Georgia

RECCOMMENDATIONS

PICO Question

Is there a difference in the proportion of patients who develop shunt-dependent HC between fetuses who underwent prenatal MM closure compared to infants who underwent postnatal MM repair?

Target Population

Infants with MM who meet eligibility criteria as fetuses for prenatal MM repair.

Recommendation(s)

Prenatal repair of MM is recommended for those fetuses who meet maternal and fetal Management of Myelomeningocele Study (MOMS) specified criteria for prenatal surgery to reduce the risk of developing shunt-dependent HC (Level I). Differences between prenatal and postnatal repair with respect to the requirement for permanent cerebrospinal fluid diversion should be considered along with other relevant maternal and fetal factors when deciding upon a preferred method of MM closure.

PICO Question

In patients with MM, does prenatal or postnatal closure improve the ability to ambulate?

Target Population

MM patients diagnosed prenatally.

RECOMMENDATION(S)

1. When possible, for prenatally diagnosed fetuses with MM who meet maternal and fetal MOMS inclusion criteria, prenatal closure of MM should be performed, which may improve ambulatory status for patients in the short term (at 30 mo of age) (Level II).
2. Long term benefit for ambulatory status with prenatal closure is unknown. Children who have had either prenatal or postnatal closure should be carefully followed for the development of tethered spinal cord with the associated loss of ambulatory function (Level III).

PICO Question

In patients born with a MM, does closure of the defect within 48 hours reduce the rate of infection?

Target Population

Infants born with a MM.

RECOMMENDATION(S)

1. There is insufficient evidence to confirm that closure of MMs within 48 hours decreases the risk of wound infection.

2. It is recommended that if MM closure is delayed beyond 48 hours, antibiotics should be initiated. (Level III)

PICO Question

In MM patients with HC, does persistent enlargement of the ventricles adversely impact neurocognitive development?

Target Population

MM patients with HC.

Recommendation

Currently, there is insufficient data to conclude that ventricular size and morphology impact neurocognitive development.

PICO Question

Is there a difference in the rate of development of tethered cord syndrome in infants who had prenatal MM closure compared to infants who had MM closure after birth?

Target Population

Infants and children with MM.

Recommendation(s)

Continued surveillance for tethered cord syndrome and/or the development of inclusion cysts in children with prenatal and postnatal closure of MM is indicated (Level II), as there is evidence that prenatal closure increases the risk of recurrent tethered cord over the baseline rate seen with postnatal closure.

CONCLUSION

This evidence based guideline and systematic review of the literature relevant to children with MM were accomplished in order to improve the quality of life for patients with MM.

Disclosures

These evidence-based clinical practice guidelines were funded exclusively by the CNS, which received no funding from outside commercial sources to support the development of this document.

Conflicts of Interest

All Guideline Task Force members were required to disclose all potential conflicts of interests (COIs) prior to beginning work on the guideline, using the COI disclosure form of the AANS/CNS Joint Guidelines Review Committee. The CNS Guidelines Committee and Guideline Task Force Chair reviewed the disclosures and either approved or disapproved the nomination and participation on the task force. The CNS Guidelines Committee and Guideline Task Force Chair may approve nominations of task force members with possible conflicts and restrict the writing, reviewing, and/or voting privileges of that person to topics that are unrelated to the possible COIs. See Appendix I for a complete list of disclosures.

Disclaimer of Liability

This clinical, systematic, evidence-based clinical practice guideline was developed by a multi-disciplinary physician volunteer taskforce and is provided as an educational tool based on an assessment of the current scientific and clinical information regarding the management and treatment of pediatric patients with MM. These guidelines are disseminated with the understanding that the recommendations by the authors and consultants who have collaborated in their development are not meant to replace the individualized care and treatment advice from a patient's physician(s). If medical advice or assistance is required, the services of a physician should be sought. The proposals contained in these guidelines may not be suitable for use in all circumstances. The choice to implement any particular recommendation contained in these guidelines must be made by a managing physician in light of the situation in each particular patient and on the basis of existing resources.

REFERENCES

1. Shurtleff DB, Luthy DA, Nyberg DA, Benedetti TJ, Mack LA. Meningomyelocele: management in utero and post natum. *Ciba Found Symp*. 1994;181:270-280; discussion 280-276. https://www.ncbi.nlm.nih.gov/pubmed/8005029.
2. Hunt GM. 'The median survival time in open spina bifida'. *Dev Med Child Neurol*. 1997;39(8):568.
3. Manning SM, Jennings R, Madsen JR. Pathophysiology, prevention, and potential treatment of neural tube defects. *Ment Retard Dev Disabil Res Rev*. 2000;6(1):6-14.

Acknowledgments

The guidelines task force would like to acknowledge the CNS Guidelines Committee for their contributions throughout the development of the guideline, the AANS/CNS Joint Guidelines Review Committee, as well as the American Academy of Pediatrics, Child Neurology Society and Spina Bifida Association for their review, comments, and suggestions throughout peer review, as well as the contributions of Trish Rehring, MPH, CHES, Senior Manager of Clinical Practice Guidelines for the CNS, and Gretchen Kuntz, MSW MLIS, for assistance with the literature searches. Throughout the review process, the reviewers and authors were blinded from one another. At this time the Guidelines Task Force would like to acknowledge the following individual peer reviewers for their contributions: Kimon Bekelis, MD; Robin Bowman, MD; Timothy J. Brei, MD; Andrew P Carlson, MD; John Chi, MD; Mark Dias, MD; Jeffrey Olson, MD; John O'Toole, MD; Michael Partington, MD; Curtis Rozzelle, MD; Krystal Tomei, MD; and Jan B. Wollack, MD, PhD.