EVALUATION OF THE EFFECTIVENESS OF SURGICAL TREATMENT OF TETHERED SPINAL CORD SYNDROME OF SECONDARY ORIGIN IN SPINA BIFIDA: A SYSTEMATIC REVIEW

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Objective. To present a literature review assessing the effectiveness of surgical treatment methods for tethered spinal cord syndrome of secondary origin in *spina bifida*.

Material and Methods. The Pubmed, EMBASE, eLibrary, and Cochrane Library databases were searched for prospective cohort clinical studies published from 2009 to 2024 and evaluating the effectiveness of methods for correcting tethered spinal cord syndrome in *spina bifida*. The study was carried out in accordance with the guidelines for Preferred Reporting Items for writing Systematic Reviews and Meta-Analyses (PRISMA).

Results. During this period, 20 articles were published assessing the effectiveness of surgical methods for correcting tethered spinal cord syndrome. Of these, 15 are pragmatic clinical trials and 5 are randomized clinical trials. The average level of evidence is III.

Conclusion. Currently, it can be stated that there is an intra-expert consensus regarding functional radiological criteria for tethered spinal cord syndrome of secondary origin in *spina bifida*. However, the issue of the effectiveness of surgical intervention directly depends on the availability of objective methods for clinical assessment of the severity of functional deficit and the reversibility of morphofunctional changes in the nervous tissue. Despite the variety of clinical scales and questionnaires, there is no unified assessment system for neurological, urological and orthopedic deficits in patients with tethered spinal cord syndrome. In this context, functional MRI (spinal MR tractography) can be considered a promising method for objectifying the pathological process. However, the phenomena revealed during the examination are not fully studied and require further research.

Key Words: children, *spina bifida*, tethered spinal cord syndrome, surgical treatment.

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Tethered spinal cord syndrome (TSCS) of secondary origin is a complex of functional disorders caused by the spinal cord tension associated with fixation of its caudal sections in the lumbosacral spinal canal [1]. Clinical signs of TSCS of secondary origin include neurological, orthopedic, and urological manifestations; the most common symptoms are motor and sensory disorders in the lower extremities, dysfunction of the pelvic organs, and pain syndrome [2, 3]. The primary goal of the surgical management of TSCS is to release the spinal cord structures from excessive tension.

Conventional methods for correction of TSCS of secondary origin in the presence of spinal dysraphism include surgical removal of tethering causal factors (lipomas, dermoid cysts, bone and/or fibrous septa of the spinal canal, etc.), separation of arachnoid and cicatrical adhesions, and dissection of a tight filum terminale [4, 5]. At that, surgical innovations implemented during recent years include only options for monitoring surgical activities, such as intraoperative neuromonitoring of somatosensory or motor evoked potentials, neuronavigation, etc. Repeated surgical interventions increase the risk of injury to the spinal cord and nerve roots; therefore, in several cases, complete elimination of tethering causal factors cannot be performed [6].

Clinical presentation of TSCS of secondary origin associated with *spina bifida* can be very diverse and depends on the grade of lesion of the spinal cord and its meninges. Symptoms may include bladder and bowel dysfunctions, sensory and motor dysfunctions of the lower extremities, cerebral disorders, and mental retardation. It is the assessment of changes in these symptoms over time that is the key aspect in analyzing the development, need for the surgical treatment for tethered spinal cord syndrome of secondary origin and its effectiveness [7].

The purpose of this research was to provide a review of literature sources that include the assessment of the effectiveness of surgical treatment methods for secondary TSCS associated with *spina bifida*.

Material and Methods

Search and selection strategy for literature data

A search for prospective cohort clinical trials that assessed the effectiveness of correction techniques for TSCS of secondary origin associated with *spina bifida* and were published in 2009–2024 was performed in the Pubmed, EMBASE, eLibrary, and Cochrane Library databases. The research was carried out in accordance with the PRISMA international guideline for systematic reviews and meta-analyses [9].

At the first stage, a search of literature sources was carried out using the following keywords: "tethered spinal cord syndrome", "*spina bifida*", "tethered cord syndrome", "meningomyelocele", and "post-MMC syndrome". At the second stage, abstracts of articles were reviewed, and publications that did not meet the criteria of this research were excluded. At the third stage, full-text versions of the selected articles were analyzed for compliance with the inclusion and exclusion criteria for the relevant trials (Fig.).

Evaluation criteria

For these papers, clinical and instrumental criteria were analyzed depending on their frequency in inter- and intradisciplinary papers, the presence of inter- and intra-rater reliability, the level of evidence and grading of recommendations, if there was reference to this information in the article.

Results and Discussion

In 2009–2024, 20 articles were published that assessed the effectiveness of surgical techniques for correction of TSCS of secondary origin. Out of them, 15 papers are pragmatic clinical trials, and 5 are randomized clinical trials. Mean level of evidence is III.

In cases of the development of clinical and neuroimaging signs of TSCS of secondary origin after the surgical intervention aimed at tethering factor correction, an issue arises that requires the choice of further treatment strategy. The solution to this issue is based on an objective assessment of the appropriate analysis of the pathological process and the effectiveness of the primary intervention. There are several aspects to consider:

1) what objective clinical diagnostic criteria and scores should be used for determining indications for surgical intervention?

2) what is the role of spinal cord MR tractography as an auxiliary diagnostic method?

3) what objective clinical and instrumental parameters can be used to assess the results of microsurgical spinal cord untethering?

1. It is true that currently there are no validated scores for this category of patients that would allow assessing the grade of urodynamic, motor, as well as neurological and orthopaedic deficit. The use of standard scores (mJOA, Ashworth, Tardieu, SBNS) in regard to *spina bifida* is problematic, since they were developed on the basis of more typical nosologic groups and require further standardization of criteria to ensure the comparability of study results.

However, when analyzing the MR symptoms of TSCS, all authors identified the following signs (Table): cone dystopia, myelopathy, terminal syringomyelia, arachnoid cysts (dermoids are less common) and abnormal filum terminale, lumbosacral lipomas, meningocele, and encephalomyelocele. This allows concluding that intra-rater reliability was achieved for these clinical and diagnostic criteria.

2. Considering various clinical manifestations of TSCS, a need to identify structural changes in the spinal cord, including spinal tracts, seems to be clear. Assessment of functional criteria for myelino- and axonopathy based on spinal cord MR tractography was found in 17 out of 20 analyzed publications; this fact also suggests that intra-rater reliability has been reached.

The tractographic method is based on the determination of the total orientation of water molecules in 3D space. It is considered that the diffusion-weighted MR mode allows assessing the direction of the diffusion of water molecules in tissues, and the integration of these data determines its overall direction in 3D space. Taking into account the fact that water diffusion in the CNS is limited by the membranes of axons, 3D images obtained using MR tractography are proposed to be considered as the brain and spinal cord conduction tracts [10].

One of the main parameters for tractography evaluation is the fractional anisotropy value that quantifies unidirectional diffusion of water molecules and varies from 0 (anisotropy) to 1 (isotropy). It is assumed that decreased fractional anisotropy in the presence of spinal cord lesions is associated with the rupture of longitudinally oriented axons of white matter what indicates interruption of tracts associated with spinal cord tension [11–13]. The presence of pathological changes in the spinal cord tracts in patients, for example, with lipoma of the filum terminale, suggests the spinal cord stretching as a single influencing factor, and clinical manifestations of this pathology can be characterized as TSCS or, more precisely, spinal cord tension syndrome.

In 10 of 20 papers, the authors evaluate decreased fractional anisotropy value of less than 1 as a criterion for this syndrome, and this fact also allows confirming insufficient intra-rater reliability on this issue. Thus, spinal MR tractography allows finding stretching and isch-

emia of the spinal cord; this is an important criterion for spinal cord tension syndrome and, considering the physical condition of the patient, a key indication for surgical intervention [14, 15].

3. When it comes to the diagnosis and choice of surgical treatment strategy in patients who have previously undergone surgery on the caudal parts of the spinal cord in order to untether the spinal cord, specialists take it with a dose of skepticism. It is obvious that spinal cord tethering factors could appear and persist after the intervention.

The natural progression of the disease with retethering of the spinal cord was analyzed; however, the need for surgical treatment is still debatable. Although intervention can in most cases help to improve or stabilize the condition, some patients demonstrate progressive deterioration even after short-term improvement. A reasonable approach in the future could be the use of multivariate intraoperative electrophysiological monitoring that includes the assessment of a larger number of somites and the condition of pelvic organs to eliminate spinal cord tethering in the safest way.

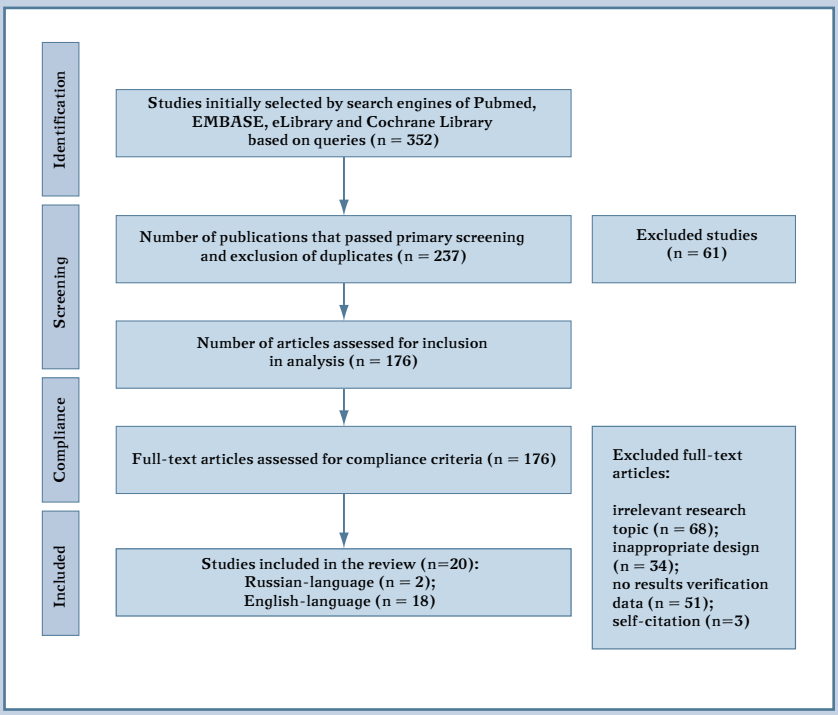

Fig.
Schematic algorithm for selecting thematic publications in accordance with PRISMA criteria

Conclusion

At present, one can confirm an intra-rater reliability regarding the clinical and neuroimaging criteria for TSCS of secondary origin according to MRI results. These are cone dystopia, myelopathy, terminal syringomyelia, arachnoid cysts and dermoids, abnormal filum terminale, lipomas, and signs of meningocele and encephalomyelocele.

However, the matter of the effectiveness of surgical intervention directly depends on the available objective methods for the clinical assessment of functional deficit severity and the reversibility of morphofunctional changes in the nervous tissue. Despite the variety of clinical scores and questionnaires, currently, there is no single system for the assessment of neurological, urological, and orthopedic deficit and its changes over time in patients with TSCS.

For this purpose, functional MRI (spinal MR tractography) can be considered a high-potential method for objective assessment of the pathological process; the need for this procedure also indicates intra-rater reliability. However, the signs that it reveals are understudied and require further research.

Limitations of the research

1. Low level of evidence in papers that are mainly represented by cohort trials.

2. Lack of structured data on the long-term outcome and functional status of patients.

3. Lack of cohort identity in regard to the number of cases and criteria for assessing changes in patient status over time.

4. Lack of possibility to reliably consider and analyze factors that may have an effect on outcomes (availability of medical care in the regions, compliance of parents, etc.).

These aspects raise difficulties for performing a meta-analysis on this important issue.

The study had no sponsors. The authors declare that they have no conflict of interest.
The study was approved by the local ethics committees of the institutions. All authors contributed significantly to the research and preparation of the article, read and approved the final version before publication.

Table
Main clinical and diagnostic criteria for the effectiveness of surgical treatment of tethered spinal cord syndrome in *spina bifida* and the frequency of their mention in thematic articles

Study	Year	Type of study	Patients, n	Clinical criteria/ scales	Radiological criteria	MR tractography	Methods of surgical untethering — direct (D) / indirect (N)*	LE	GR
Adzick et al. [1]	2011	PCT	17	Ashworth scale, Tardieu scale	Dystopia of the SC conus, myelopathy, terminal syringomyelia, lipomas, arachnoid cysts, less often dermoids and abnormal filum terminale. Functional criteria for myelino- and axonopathy**	N/A	D	IV	C
Barf et al. [2]	2013	PCT	34	Ashworth scale, Tardieu scale	Dystopia of the SC conus, myelopathy, lumbosacral lipomas, meningomyeloceles and encephalomyeloceles. Functional criteria for myelino- and axonopathy	Reduction in fractional anisotropy index <1	D/I	III	B
Chehroudi et al. [3]	2016	PCT	26	Ashworth scale, Tardieu scale	Arachnoid cysts, less commonly dermoids and abnormal filum terminale, lumbosacral lipomas, meningomyeloceles and encephalomyeloceles. Functional criteria for myelino- and axonopathy	Reduction in fractional anisotropy index <1	D	III	C
Choi et al. [4]	2021	PCT	18	Ashworth scale, Tardieu scale	Dystopia of the SC conus, myelopathy, terminal syringomyelia, arachnoid cysts, less commonly dermoids and abnormal filum terminale, lumbosacral lipomas, meningomyeloceles and encephalomyeloceles. Functional criteria for myelino- and axonopathy	Reduction in fractional anisotropy index <1	D	IV	B
Copp et al. [5]	2015	RCT	37	Ashworth scale, Tardieu scale	Dystopia of the SC conus, myelopathy, lumbosacral lipomas, meningomyeloceles and encephalomyeloceles	N/A	D	III	B
Cordelli et al. [6]	2021	PCT	31	Modified Ashworth scale, Tardieu scale	Dystopia of the SC conus, myelopathy, terminal syringomyelia, arachnoid cysts, less commonly dermoids and abnormal filum terminale, lumbosacral lipomas, meningomyeloceles and encephalomyeloceles. Functional criteria for myelino- and axonopathy	Reduction in fractional anisotropy index <1	D	IV	B
En'Wezoh [7]	2016	PCT	16	Modified Ashworth scale, Tardieu scale, SBNS, mJOA	Dystopia of the SC conus, myelopathy, terminal syringomyelia, arachnoid cysts, less commonly dermoids and abnormal filum terminale, lumbosacral lipomas, meningomyeloceles and encephalomyeloceles. Functional criteria for myelino- and axonopathy	N/A	D	III	A
Eide, Ringstad [8]	2024	PCT	24	Modified Ashworth scale, Tardieu scale	Dystopia of the SC conus, myelopathy, lumbosacral lipomas, meningomyeloceles and encephalomyeloceles. Functional criteria for myelino- and axonopathy	Reduction in fractional anisotropy index <1	D	III	B
Fieggen et al. [10]	2015	RCT	15	Modified Ashworth scale, Tardieu scale, SBNS, mJOA	Dystopia of the SC conus, myelopathy, terminal syringomyelia, arachnoid cysts, less commonly dermoids and abnormal filum terminale, lumbosacral lipomas, meningomyeloceles and encephalomyeloceles. Functional criteria for myelino- and axonopathy	N/A	D	III	A

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Table continuation
Main clinical and diagnostic criteria for the effectiveness of surgical treatment of tethered spinal cord syndrome in *spina bifida* and the frequency of their mention in thematic articles

Frim [11]	2014	PCT	23	Modified Ashworth scale, Tardieu scale	Dystopia of the SC conus, myelopathy, lumbosacral lipomas, meningomyeloceles and encephalomyelocoele. Functional criteria of myelino- and axonopathy	N/A	D	III	B
Juriloff, Harris [12]	2018	PCT	18	Ashworth scale, Tardieu scale	Dystopia of the SC conus, myelopathy, lumbosacral lipomas, meningomyeloceles and encephalomyelocoele.	N/A	D	III	B
Kellogg et al. [13]	2018	PCT	24	N/A	Dystopia of the SC conus, myelopathy, terminal syringomyelia, arachnoid cysts, less commonly dermoids and abnormal filum terminale, lumbosacral lipomas, meningomyeloceles and encephalomyeloceles. Functional criteria for myelino- and axonopathy	N/A	D	IV	B
Хачатрян, Сысоев [14]	2014	RCT	18	Modified Ashworth scale, Tardieu scale, SBNS, mJOA	Dystopia of the SC conus, myelopathy, terminal syringomyelia, arachnoid cysts, less commonly dermoids and abnormal filum terminale, lumbosacral lipomas, meningomyeloceles and encephalomyeloceles. Functional criteria for myelino- and axonopathy	Reduction in fractional anisotropy index <1	D	III	B
Курцер с соавт. [15]	2018	PCT	24	Modified Ashworth scale, Tardieu scale, mJOA	Dystopia of the SC conus, myelopathy, lumbosacral lipomas, meningomyeloceles and encephalomyeloceles. Functional criteria for myelino- and axonopathy	N/A	D	III	B
Lindquist et al. [16]	2022	RCT	29	Modified Ashworth scale, Tardieu scale, SBNS, mJOA	Dystopia of the SC conus, myelopathy, terminal syringomyelia, arachnoid cysts, less commonly dermoids and abnormal filum terminale, lumbosacral lipomas, meningomyeloceles and encephalomyeloceles. Functional criteria for myelino- and axonopathy	N/A	D	III	B
Rocque et al. [17]	2015	PCT	18	Modified Ashworth scale, Tardieu scale, SBNS, mJOA	Dystopia of the SC conus, myelopathy, terminal syringomyelia, arachnoid cysts, less commonly dermoids and abnormal filum terminale, lumbosacral lipomas, meningomyeloceles and encephalomyeloceles. Functional criteria for myelino- and axonopathy	Reduction in fractional anisotropy index <1	D	III	B
Seki et al. [18]	2016	PCT	27	Ashworth scale, Tardieu scale	Dystopia of the SC conus, myelopathy, terminal syringomyelia, arachnoid cysts, less commonly dermoids and abnormal filum terminale, lumbosacral lipomas, meningomyeloceles and encephalomyeloceles. Functional criteria for myelino- and axonopathy	Reduction in fractional anisotropy index <1	D	III	C
Snow-Lisy et al. [19]	2015	PCT	16	Ashworth scale, Tardieu scale	Dystopia of the SC conus, myelopathy, terminal syringomyelia, arachnoid cysts, less commonly dermoids and abnormal filum terminale, lumbosacral lipomas, meningomyeloceles and encephalomyeloceles. Functional criteria for myelino- and axonopathy	Reduction in fractional anisotropy index <1	D	III	B

The end of the Table
Main clinical and diagnostic criteria for the effectiveness of surgical treatment of tethered spinal cord syndrome in *spina bifida* and the frequency of their mention in thematic articles

Wide [21]	2020	PCT	9	Modified Ashworth scale, Tardieu scale, SBNS, mJOA	Dystopia of the SC conus, myelopathy, terminal syringomyelia, arachnoid cysts, less commonly dermoids and abnormal filum terminale, lumbosacral lipomas, meningomyeloceles and encephalomyeloceles. Functional criteria for myelino- and axonopathy	N/A	D	IV	B
Williams et al. [22]	2015	RCT	34	Modified Ashworth scale, Tardieu scale, SBNS, mJOA	Dystopia of the SC conus, myelopathy, terminal syringomyelia, arachnoid cysts, less commonly dermoids and abnormal filum terminale, lumbosacral lipomas, meningomyeloceles and encephalomyeloceles.	Reduction in fractional anisotropy index <1	D	III	B

PCT — pragmatic clinical trials; RCT — randomized clinical trials; SC — spinal cord; LE — level of evidence of the American Society of Clinical Oncology ASCO [20]; GR — gradation of recommendations according to ASCO; N/A — not available. * Indirect defixation of the SC has been described in spinal osteotomy and is aimed (in addition to correction of deformity) at eliminating its tension; ** functional criteria of myelino- and axonopathy: decreased amplitude of the M-response with preserved nerve conduction velocity.

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