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Current possibilities of surgical treatment for infectious spondylitis in children

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Aim To analyze the immediate and long-term results of the surgical treatment of infectious spondylitis in children. **Materials and methods** A retrospective cohort design was implemented with the following inclusion criteria: 1) age below 18 years, 2) titanium mesh block cage for anterior spondylodesis, and 3) follow up period of 24 months. The mean age was 15.3 ± 2.8 years. The patients were divided into two groups according to diagnosis: active tuberculous spondylitis (n_1 = 42) and chronic non-specific spondylitis and its consequences (n_2 = 41). **Results** There were no complications or process aggravation within a period of 6 months after surgery. However, there was one case of mesh cage destabilization when tuberculous spondylitis progressed in the period from 6 to 12 months. The amount of kyphosis correction was 26.5° ± 10.1°. The postoperative deformity increase at 18 months after surgery did not exceed 5°. Bone block was estimated at 3 points in 95 % of cases 6 months after surgery and at 4 or 5 points in 97 % of cases 12 months after surgery. Neurological disorders, based on Frankel evaluation before surgery, were identified in 5 patients (Type D in 3 patients, Type B in 2), and complete regression was observed after surgery in 4 cases up to Type E and 1 case up to Type D. Operative blood loss was M ± m = 207.9 ± 139.1. **Conclusion** The use of titanium mesh block cages in children with infectious spondylitis is a safe procedure that reduces the number of complications in the immediate and long-term postoperative period as well as maintains the stability of surgical correction of the spine deformity.

Keywords: spondylitis, tuberculosis, spondylodesis, titanium mesh block cages, children

Infectious spondylitis encompasses a large group of diseases of the spine characterized by the destruction of the vertebrae and intervertebral disks, as well as the involvement of paravertebral soft tissues and the spinal canal. Given the etiology of spondylitis, two variants are most frequently diagnosed [1]:

1) non-specific spondylitis and ***osteomyelitis of the spine*** (primary, secondary hematogenous or septic, and secondary post-traumatic. Given the destructive lesions limited by one segment, the term “spondylodiscitis” is also often used [2]);

2) tuberculous spondylitis (spinal osteomyelitis) or ***Pott's disease***, which develops as a result of the dissemination of the *Mycobacterium tuberculosis* complex from infected lungs or lymph nodes. A rare simple form of tuberculous spondylitis is so-called “TB-spondylitis of BCG etiology,” which involves damage caused by the dissemination of the vaccine strain of *M. tubersulosis bovis,* BCG [3, 4].

The characteristic features of these diseases in children are as follows:

• the tendency of multisegmental destruction with a complete or partial destruction of the vertebral bodies involved in the pathological process for specific spondylitus, and monosegmental destruction is involved in the case of non-specific spondylitus (spondylodiscitis);

• the possible onset of the disease in early childhood (before the age of three years);

• the rapid development of gross kyphotic deformation in infants with multisegmental processes [5, 6];

• low frequency of neurological disorders, even in the case of gross deformation of the spine due to highly compensatory mechanisms.

The main objectives of surgical treatment for infectious spondylitis include the radical removal of the destroyed tissue, recovery of the supporting ability, stability, sagittal balance, and the preservation of the capacity for further spinal growth [7, 8]. The traditional material used for the replacement of post-resection defects of the anterior column is bone autografts (i.e., fragments of the rib and iliac crest); however, their use is associated with a high risk of developing pseudoarthrosis (≥40 %), the long-term loss of surgical correction, and the development of pain syndrome in the area of auto-bone sampling (donor site disease) [9].

The introduction of modern posterior spinal instrumentation enables effective reconstruction of the affected region of spine. However, the possibility of the use of anterior stabilization implants in pediatric spine surgery have not been studied to date. [10].

The gathered experience of the Clinic of Pediatric Surgery and Orthopedics of the Saint Petersburg Research Institute of Phthisiopulmonology has provided the long-term results of children who have received surgical treatment for infectious spondylitis by reparative surgery of the spine with the use of titanium mesh block cages for front spine stabilization (Harms meshes).

The aim was to study the potential use of titanium mesh block cages to form anterior interbody fusion for the surgical treatment for infectious spondylitis in children.

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Study design. This was a monocentre retrospective cohort (level of evidence – III). The patient recruitment period was from 2011 to 2014.

The inclusion criteria:

• age at the time of the surgery less than 18 years;

• the surgery was performed at a single location: Clinic of Pediatric Surgery and the Orthopedics of Saint Petersburg Research Institute of phthisiopulmonology;

• use of titanium mesh for anterior fusion;

• etiologically verified diagnosis of infection (tuberculous or nonspecific) spondylitis

• follow-up period of at least 24 months;

• availability of a full imaging (i.e., X-ray, CT) archive.

PATIENTS AND METHODS

During the study period, 319 surgeries on the spine in children were performed at the clinic. The data of 83 patients corresponding to the inclusion criteria was included in the overall analysis. The average age at the time of the surgery was 15.3 ± 2.8 years (minimum: 7 months; maximum: 17 years). Indications for surgery included: the presence of infectious destruction of the vertebrae; the presence of kyphotic deformation of the spine; neurological disorders; and the ineffectiveness of conservative antibacterial (for non-specific processes) and antituberculous (for specific spondylitis) chemotherapy for at least two months. The average duration of a therapeutic timeout (the time from establishing the diagnosis to surgery) was 16 months (minimum: 4 months; maximum: 13 years).

According to the diagnosis based on a compilation of morphological, bacteriological, and molecular genetic (PCR) studies of surgical material, the patients were divided into two groups:

Group 1 (n_1 = 42): tuberculous spondylitis, including 33 patients with an active disease and nine patients with consequences of tuberculosis. After surgery, all patients underwent a course of comprehensive antituberculous chemotherapy in accordance with the regulated regimes, for at least 12 months.

Group 2 (n_2 = 41): chronic non-specific spondylitis and consequences of tuberculosis, including 16 patients with monosegmental spondylodiscitis. Following surgery, at least two courses of antibacterial therapy were administered to the patients in accordance with the isolated microflora.

The general scheme of the study, including the distribution of patients according to etiology and age is presented in **Figure 1**.

The distribution of patients according to the localization of lesions: cervical (n = 7); thoracic (n = 27); thoracolumbar (n = 12); lumbar (n = 36); and lumbosacral (n = 3) regions, respectively. The surgeries were performed under endotracheal anesthesia. Surgical access to the reconstructed region was chosen by accounting for the localization and extent of the destruction. The anterior cervical access was used for the cervical region; the lateral transthoracic extrapleural access with the resection of the corresponding rib was used for the thoracic region; the thoraco-diaphragmal access was used for the thoracolumbar region; and the extraperitoneal access was used for the lumbar and lumbosacral spine. In cases involving the reconstruction of more than one spinal motion segment (SMS) (three or more vertebrae) or the initial presence of a spine deformation, the surgery was performed simultaneously with posterior instrumental fixation (n = 45). This involved transpedicular, hooked, or hybrid third-generation designs (CDI) adapted for each age group (rod diameter: 3.5–5.5 mm). The average number of support elements for posterior fixation was 6. All patients underwent the radical removal of the destroyed tissues, as well as the drainage of pre-, paravertebral, and epidural abscesses. Reconstruction of the anterior column was performed using a titanium mesh block cage pre-filled with an auto-bone fragment (n = 83). A mesh was implanted into the interbody diastasis in maximum possible reclination. After surgery, a drainage tube was fixed with a layered closure of the wound. The vertical positioning of patients was performed on the Day 4 in orthesis.

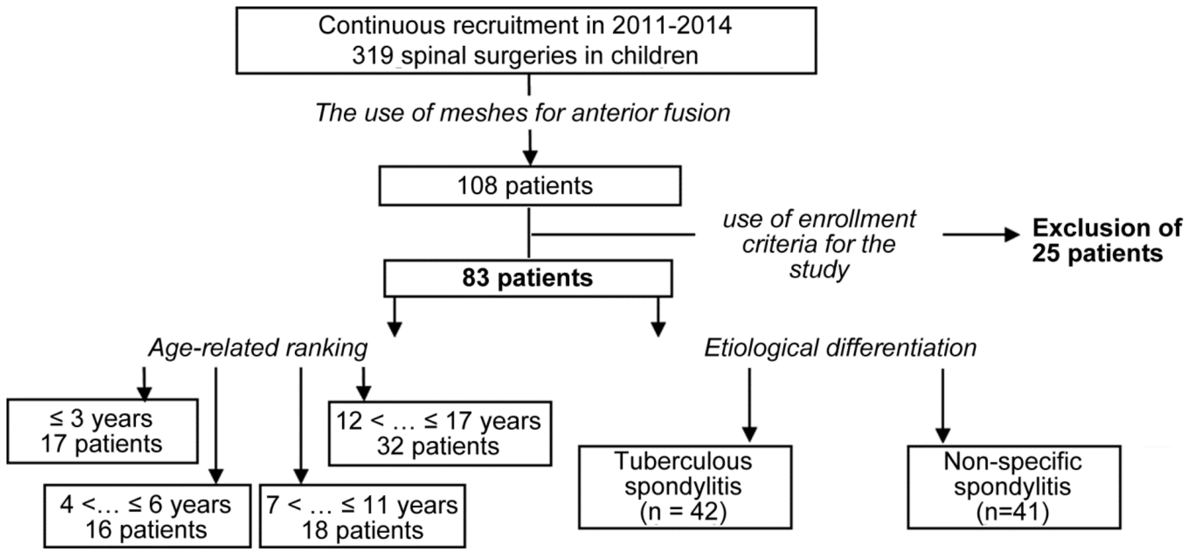

Fig. 1 General study design with age-related ranking and etiological differentiation of the diagnosis

The results were analyzed for all children immediately after the surgery, 6, 12, and 18 months postoperatively, and then annually. The evaluation of the long-term results of the study was performed in accordance with the regression schedule **(Fig. 2**).

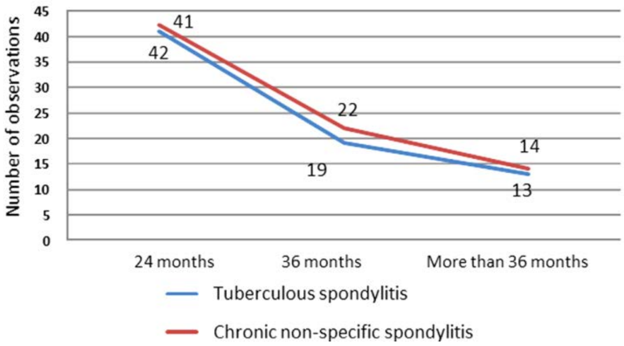

Fig. 2 Dynamics of the number of patients monitored over a period greater than 18 months

Analyzed parameters:

1) exacerbation of the infection;

2) frequency of complications associated with the implanted interbody titanium mesh (e.g., dislocation, protrusion, etc.);

3) surgical correction of the spinal deformity (in Cobb degrees);

4) dynamics in the Cobb angle (in degrees) after the surgery;

5) dynamics of bone block formation at the site of anterior fusion (5-point quantitative scale) [11];

6) dynamics of neurological disorders (Frankel scale) [12];

7) intraoperative blood loss;

8) time of surgery.

Statistical analysis. Software Statistical Package for the Social Sciences (SPSS) version 22.0 (SPSS Inc., Chicago, IL, USA); t-criteria: 1) comparison of the average values of the angular kyphotic deformation before and after the surgery; 2) comparison of average values for the dynamics of bone block formation at the site of anterior fusion 6 and 12 months after the surgery; 3) comparison of values of operative blood loss and the time of surgery. The differences are recognized to be statistically significant at a bilateral p-level of <0.05. The pairwise correlation analysis with the ranking of the Pearson coefficient values ($p \leq 0.5$ indicates a weak relationship; $0.5 < p \leq 0.7$ indicates medium power; and $p > 0.7$ indicates a strong relationship).

RESULTS

Exacerbation of the infection. In accordance with the post-operative examination deadline, no cases of infectious complications or exacerbation of the infectious process were identified six months after surgery; after 12 months, one case of exacerbation of the initial tuberculous spondylitis was registered; and after 24 months, no infectious complications were found (*no statistically significant differences in the indices of exacerbation of the infectious process were found between the study groups; p = 0.199*).

Complications commonly associated with the implanted interbody mesh (e.g., fractures, dislocations, and pseudarthrosis) were not identified in the study groups.

The indices of the **angular kyphosis correction value (in Cobb degrees)** are shown in **Table 1**.

Table 1

The kyphosis correction value (according to Cobb)

Kyphosis	Min	Max	M ± m
Before surgery*	15.00	92.00	48.7 ± 23.6
After surgery*	2.00	46.00	22.3 ± 13.5

* *t*-test for the paired samples of 83 patients: the differences between the average values of the variables “Kyphosis before the surgery” and “Kyphosis after the surgery” proved to be statistically significant with a significance level of $p < 0.001$. The correlation between the variables was $r = 0.944$ ($p < 0.001$), indicating variable dependence.

Indices of a postoperative increase in deformation by the 18th month* (Cobb sagittal angle):

• Group 1 (TB spondylitis): M ± m = 4.5 ± 1.2° Cobb;

• Group 2 (Chronic nonspecific spondylitis): M ± m = 3.2 ± 0.7°s Cobb

(* No statistically significant differences in the indices for the loss of surgical correction were found by the 18th month between the study groups; p = 0.324).

The intensity of bone block formation at the site of anterior fusion* six months after the surgery, vertebrae locking was evaluated as 3 out of 5 points in 88 % of observations; 12 months after the surgery it was evaluated as 4 points or higher for 95 % of the observations.

Table 2

Indices of bone block formation

The evaluated segment	Terms of observations	Points				
		1	2	3	4	5
Cranial	6 months	0	0	78	5	0
	12 months.	0	0	0	57	26
Caudal	6 months	0	10	71	2	0
	12 months	1	0	3	60	19

* statistically significant differences in the rate of bone block formation were revealed during the postoperative period (p = 0.009), and by the 12th month, the degree of bone block manifestation (4 and 5 out of 5 points) was significantly higher than six months after surgery.

Neurological disorders* were initially detected in 5 out of 83 patients. In all cases, the leveling of movement disorders was registered following the reconstruction of the spine. In four patients, the regression of neurological disorders appeared to be complete.

Indices of **operative blood loss***:

• Group 1 (tuberculous spondylitis): M ± m = 184.1 ± 122.6 mL;

• Group 2 (chronic non-specific spondylitis): M ± m = 137.3 ± 88.4 mL.

* the criterion for Livin dispersion equality indicates that the dispersions of two distributions do not differ significantly (p = 0.245). Therefore, the use of a *t*-test was adequate. No statistically significant differences in the rates of operative blood loss were found between the study groups (p = 0.214).

Time of surgery*:

• Group 1 (TB spondylitis): M ± m = 3 h 10 min ± 43 min;

• Group 2 (Chronic non-specific spondylitis): M ± m = 2 h 40 min ± 32 min.

* the criterion for Livin dispersion equality indicates that the dispersion of two distributions do not differ significantly (p = 0.592). Therefore, the use of a *t*-test was adequate. No statistically significant differences in the indices for the time of surgery were found between the study groups (p = 0.361).

Table 3

Peculiarities of neurological disorders in children of the study group

№	Sex	Age (years)	Pathology level	Evaluation on the Frankel scale		Diagnosis
				Before the surgery*	After the surgery*	
1	f	17	Th6-L4	D	E	TB spondylitis complicated with abscesses
2	m	4 y 6 mos.	Th9-12	B	C	Consequences of TB spondylitis
3	f	11	Th8-10	D	E	Chronic non-specific spondylitis
4	m	1 y 3 mos.	Th3-4	B	E	Tuberculous spondylitis
5	f	12	Th6-9	D	E	Consequences of TB spondylitis

* *t*-test for the paired samples of 83 patients: the differences between the average values of the variables "Evaluation on the Frankel scale before the surgery" and "Evaluation on the Frankel scale after the surgery" were statistically significant (p = 0.007). Moreover, as indicated from the results, there is a significant correlation between the variables (r = 0.843; p < 0.001), indicating that these variables can be considered dependent.

DISCUSSION

When commenting the obtained results, the physical and mechanical properties of the implant should be primarily noted, particularly the strength and biological inertness of the titanium. This enables the extended (more than 2 x SMS) anterior column defects to simultaneously and effectively be replaced without causing a biological reaction in the body of the child.

In the analysis of Russian and international medical literature databases, we could not find any information on the use of titanium mesh in children. In this regard, we compared our results with the studies that analyzed surgical treatment of infectious spondylitis in adults [13, 14].

According to Hadjipavlou et al. [15], Skaf et al. [16], and Chen et al [17], the use of bone autografts for the treatment of spondylodiscitis results in an increased risk of infectious complications; however, according to Arrington et al., grafting of an auto-bone is accompanied by chronic pain in more than 40 % of cases [9]. This forces the surgeons who do not have modern implants at their disposal to follow conservative treatment for spondylitis with the use of antibacterial chemotherapy, orthoses, and bed rest. However, this strategy is aimed only at the infectious agent and it is not possible to reconstruct the destroyed region, eventually resulting in the development of spinal deformities.

Zhang et al. [18] presented a retrospective clinical series which included data on 28 patients (average age: 42.7 ± 5.8 years) who underwent surgery for tuberculous spondylitis using titanium mesh block cages for anterior fusion. The average term for the formation of a stable bone block was eight months, and the correction of the kyphotic deformation was 38.9 ± 6.6° with the loss of correction over a long-term follow-up period (4 years), which does not exceed 2°.

Won Heo et al. presented a study with similar number of patients (n = 28) [19]. Radical spinal reconstruction was performed for infectious spondylitis with the use of titanium mesh in all cases. The average age of the patients was 55.7 years and the long-term observation period was 6 to 64 months. There were no complications associated with implanted titanium mesh and the surgical correction loss at the end of the observation period was 4.8°.

There are only single reports of the complications associated with the fracture and migration of titanium mesh block cages, which are not of statistical significance [20, 21, 22].

CONCLUSIONS

The treatment for infectious spondylitis in children requires a comprehensive approach which includes: 1) the early diagnosis and chemotherapy (in the case of non-specific spondylitis, antibacterial therapy of narrow spectrum of action is required; in case of tuberculosis spondylitis, antituberculous chemotherapy is required); 2) the implementation of spine reconstruction using titanium mesh block cages. This enables a reduction in the risk of both immediate and long-term postoperative complications. The formation of a reliable bone block in the region of the anterior reconstruction contributes to shortening the term for the removal of posterior retaining structures while maintaining reliable intraoperative correction of the deformity and the potential for further growth of the child.

Clinical case. Patient M., aged 2 years 11 months with the consequences of previous generalized tuberculosis: tuberculous spondylitis, soft tissue tuberculosis of the right foot. Neurological status: type E by Frankel scale.

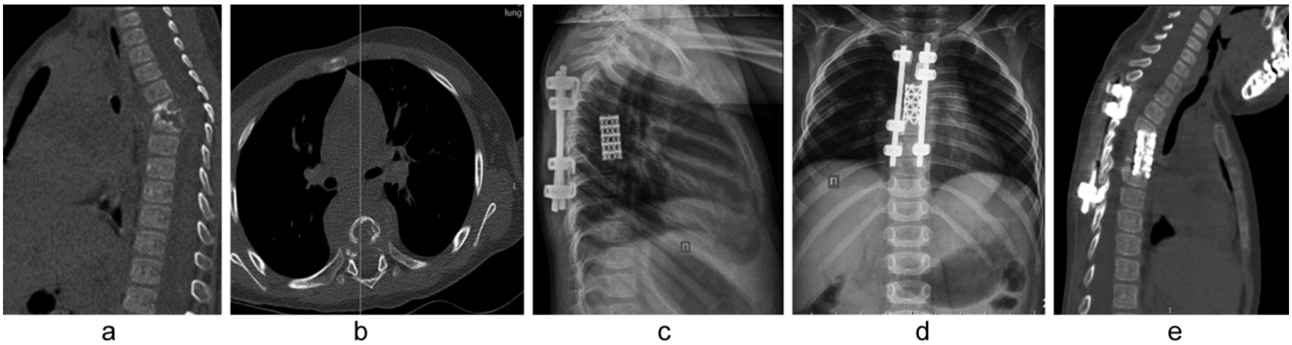

Fig. 3 Patient M. aged 2 years 11 months: CT (a and b) before the surgey, kyphotic deformation of Th4-8 41°. X-rays (c and d) after surgery of Th4-8 (anterior interbody fusion using titanium mesh with an auto-bone, posterior instrumental fixation of Th3-9 with a multi-support system of eight hooks). Thoracic CT eight months after surgery (e). Formation of the block inside the mesh is estimated at 4 points (no area of resorption with contact associated with reactive contact sclerosis)

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