



# ANALYSIS OF RISK FACTORS OF LATE COMPLICATIONS AFTER SPINE RECONSTRUCTION SURGERY FOR NON-TRAUMATIC PATHOLOGY IN CHILDREN

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**Objective.** To analyze the structure and frequency of complications after surgical treatment of non-traumatic spinal disorders in children and to identify factors affecting the development of the disorders.

**Material and Methods.** The study included follow-up data of 218 children who underwent no less than 2-level reconstructions of the spine for infectious and neoplastic destruction, as well as for congenital malformations of the spine in 2005–2015. The average period of long-term follow-up was 5 years 4 months. Sixteen patients developed complications requiring repeated surgical treatment in the long-term period (at least 12 months). Clinical and X-ray factors that influenced the risk of developing long-term complications were studied.

**Results.** Four groups of complications were identified: recurrence (progression) of primary pathology ( $n = 5$ ), pseudoarthrosis in the interface between bone graft and recipient vertebra ( $n = 6$ ), proximal junctional kyphosis ( $n = 4$ ), and bone graft resorption ( $n = 1$ ). The influence of thoracic lesions on the risk of pathology recurrence ( $p = 0.039$ ) and of lumbar spine surgery on earlier complication development ( $p = 0.016$ ) and pseudoarthrosis formation ( $p = 0.047$ ), as well as on earlier appearance of secondary deformities as compared to other complications ( $p = 0.035$ ) was statistically proved. The predictor value of such factors as etiology, age, gender and material used for anterior fusion (bone alone or titanium mesh with bone autograft) was not confirmed.

**Conclusion.** The frequency of late complications after 360° vertebral reconstruction in children is 7.3 %, with most of them developing several years after surgery. Increase in surgical activity, number of operated patients and length of follow-up will possibly prove the presence of new predictors of complication development.

**Key Words:** children, spinal pathology, spondylitis, spinal tumors, spine reconstruction, spine surgery.

Please cite this paper as: Naumov DG, Mushkin AYu. Analysis of risk factors of late complications after spine reconstruction surgery for non-traumatic pathology in children. *Hir. Pozvonoc.* 2017;14(3):84–92. In Russian.

DOI: <http://dx.doi.org/10.14531/ss2017.3.84-92>.

One of the basic principles of modern surgical treatment of non-traumatic (destructive and congenital) pathology of the spine is restoration of stability (supporting capacity) for anterior column after removal of pathological/destroyed tissue, so-called debridement, or decompression of the spinal cord [6, 14]. For a long time, bone allo- and autografts considered to be the gold standard for spinal fusion [8], however the analysis of long-term outcomes of these reconstructions refined the understanding of the main causes of unsatisfactory outcomes, which were registered in adults with an incidence of up to 40 % [11, 12]:

1) progression of the disease accompanied by exacerbation or recurrence of infectious spondylitis, continued growth of the tumor;

2) changes in the position and structure of the graft - its dislocation and resorption;

3) disruption of osteoadaptation and regeneration in the area of contact between the graft and the recipient bone, which manifests as delayed formation or absence of bone fusion.

The widespread use of stable fixation of the spine is an important principle for prevention of complications and it can be achieved not only with posterior metal structures, but also by non-biolog-

ical supporting implants (in addition to bone grafts) for anterior fusion [1, 2]. The most widely used implants are titanium mesh cages (TMC) which provide reliable postoperative stability, are durable and bioinert, and enable additional incorporation of osteoinductive materials (bone autografts, biocomposites) to stimulate osteoreparation [7, 9, 10]. Nevertheless, their use, like the use of any other technology, does not preclude development of complications that could be associated with both progression of the underlying disease and extrusion of the ends of the implant into the blocked vertebral bodies due to their insufficient strength [15, 16].

Spine reconstruction in children occupies a special place in spine surgery. In this age, destruction of the vertebrae can be a manifestation of diseases with various etiologies: infectious spondylitis, benign and malignant lytic tumors, and less often non-bacterial (aseptic) inflammatory processes. Many of them are characterized by early-onset polysegmentary destruction, development of severe deformities and extravertebral dissemination [3]. The relative scarcity of such pathologies and small number of clinics specializing in their surgical treatment can explain almost complete absence of articles on the complications of vertebral reconstructions in children in domestic and foreign literature. The experience of the Clinic for pediatric surgery and orthopedics of the St. Petersburg Research Institute of Phthisiopulmonology allows us to fill this gap.

The aim of the study was to analyze the structure and incidence of post-op complications in non-traumatic spine lesions in children and to determine factors that affect their development.

The design of the study was a mono-centre retrospective cohort (Level of evidence – III).

## Material and Methods

A total of 236 patients were selected from among 548 patients operated on the spine in 2005–2015 based on the following criteria:

1) spine non-traumatic pathology, whose nature was verified by bacteriological, molecular genetic, or morphological methods;

2) surgery involving the removal of pathological tissues and/or vertebral bodies with mandatory performing of anterior fusion and, if necessary, posterior instrumental fixation;

3) reconstruction of two or more spinal motion segments (SMS);

4) documented follow-up for 12 months or more.

The analysis of outcomes was performed on out-patient clinical documents and radiological data (most patients live in different regions of Russian Federation) and on findings of in-

patient examinations. The assessment was carried out 3, 6, 12 months after surgery, and then once a year. Due to lack of X-ray or clinical data documented at the time points specified in the inclusion criteria, 18 (less than 7%) of 236 patients were excluded from the study, but the validity of the sample was not affected.

As a result, a group of 16 children who developed complications at different times after surgery were identified for primary clinical cohort. The analysis of the spine reconstructions' results within the group was the subject of the study.

We have also examined the structure of complications and the impact of such factors as gender and age of patients, disease's etiology, level of the lesion, number of vertebrae destroyed and scope of the spine reconstruction, as well as materials used for anterior fusion (bone alone or a TMC and bone autograft) on the development of complications.

Statistics were performed by Statistical Package for the Social Sciences (SPSS). Single-factor ANOVA analysis was used to identify factors potentially affecting the development of postoperative complications; a factor was considered to be statistically significant at two-sided  $p < 0.05$ . The results are presented as  $M \pm m$ .

## Results

The overall scheme of the study is presented in Fig. 1.

The average age of patients at the time of primary surgery was 5 years 4 months  $\pm$  4 years 10 months (min – 8 months, max – 14 years). The classification by age and patients' distribution by the level of pathology are presented in Tables 1, 2. The general characteristics of pathology and complications, identified in 16 patients, are presented in Table 3. The patients were classified into five groups based on the etiology of the underlying disease: tuberculous spondylitis – 9; nonspecific spondylitis – 2; tumors – 3; congenital malformations – 1; pathological fracture (presumably, non-bacterial osteomyelitis, the patient was operated on before this pathology was considered to be an independent disease) – 1.

Primary surgeries were performed in one surgical session (under one narcosis), which included two stages: radical (removal of destroyed tissues and abscesses) and reconstructive. Until 2011, the inter-body bone auto- and allografts were used for anterior fusion; since 2011 they were replaced with TMC filled with bone autografts. In cases of polysegmentary lesions (affecting more than two SMS) and in case of spinal deformity, posterior instrumentation was used as an obligatory component of the reconstruction. In all cases, CD instrumentation corresponding to the age and weight criteria was used, dynamic implants were not used due to absolute necessity to achieve stable fixation in the spine reconstructions in children.

The average duration of long-term follow-up after the primary surgery was 5 years 4 months  $\pm$  2 years 6 months; after the revision surgery, 2 years 5 months  $\pm$  1 year 9 months. Complications developed in 7.3% of the total number of patients who underwent reconstructive surgery on the spine. Among the most common infectious spinal lesions, the incidence of late complications of tuberculous spondylitis was 7.9% (9 of 114 reconstructions), and of nonspecific spondylitis, 3.6% (2 of 83 reconstructions).

Evaluation of potential complication risk factors revealed the following:

1) "Level of lesion" factor: in patients with thoracic vertebrae lesion, the risk of postoperative recurrence of the deformity is significantly higher ( $p = 0.039$ ) than other complications; in case of surgeries in the lumbar spine, the risk of development of pseudoarthrosis ( $p = 0.016$ ) is significantly higher and the time to onset of complications increases ( $p = 0.047$ );

2) despite the fact that 10 from 16 patients (62.5%) were in early childhood (up to 3 years), and the fact that infections (tuberculosis, nonspecific spondylitis) were initially registered in 11 (68.7%), such factors as "etiology of the disease", "gender" and "age" had no statistically significant effect on the development of complications ( $p = 0.697$ ;  $p = 0.151$ ;  $p = 0.180$ ); however, in five patients progression of tuberculous spondylitis (3) and the tumor process (2) resulted in

destabilization of anterior reconstruction zone;

3) the average time of complication development, regardless of the etiology, was 2 years 9 months ± 2 years 4 months (min – 6 months, max – 9 years), and the dynamics of their onset depending on pathology is presented in Table 4. Among the analyzed complications, secondary deformity of the spine developed significantly earlier (11 ± 4 months, p = 0.035); for pseudoarthrosis this period was 4 years 1 month ± 3 years 2 months; for progression of disease, 2 years 7 months ± 1 year 7 months, and for graft lysis, 4 years 6 months;

4) in a total of 12 (75.0 %) cases, the complications developed after the reconstruction of two SMS, however, no relationship was identified between the number of affected SMS and the time of complication onset (p = 0.476);

5) the effect of the material used for anterior fusion on the risk of complications was not statistically significant (p = 0.561), but it was noted that the use of bone grafts more often led to the development of pseudoarthrosis (66.6 %) and lysis (this complication was not detected with TMC).

*Tactics of complications management.* Recurrence of the underlying disease (tuberculosis, 3, tumor, 2) was accompanied by re-appearance of clinical manifestations, such as reactivation of inflammatory process or continued growth of the tumor, as well as the involvement of adjacent vertebrae with junctional instability. Fistulonecrosequesterectomy and anterior re-fusion with a TMC with bone autograft were performed in 3 patients, remounting of the posterior instrumental fixation was performed in 2 patients (long-term follow-up was 3 years 8 months). In one case, rapid continued growth of the malignant tumor resulted in fatal outcome within 3 months after the main intervention. In case of pseudoarthrosis, which more often (4 of 6 cases) developed in patients with bone graft, restoration of stability was achieved through anterior re-fusion with TMC with bone autograft (long-term follow-up was 2 years 3 months, Fig. 2).

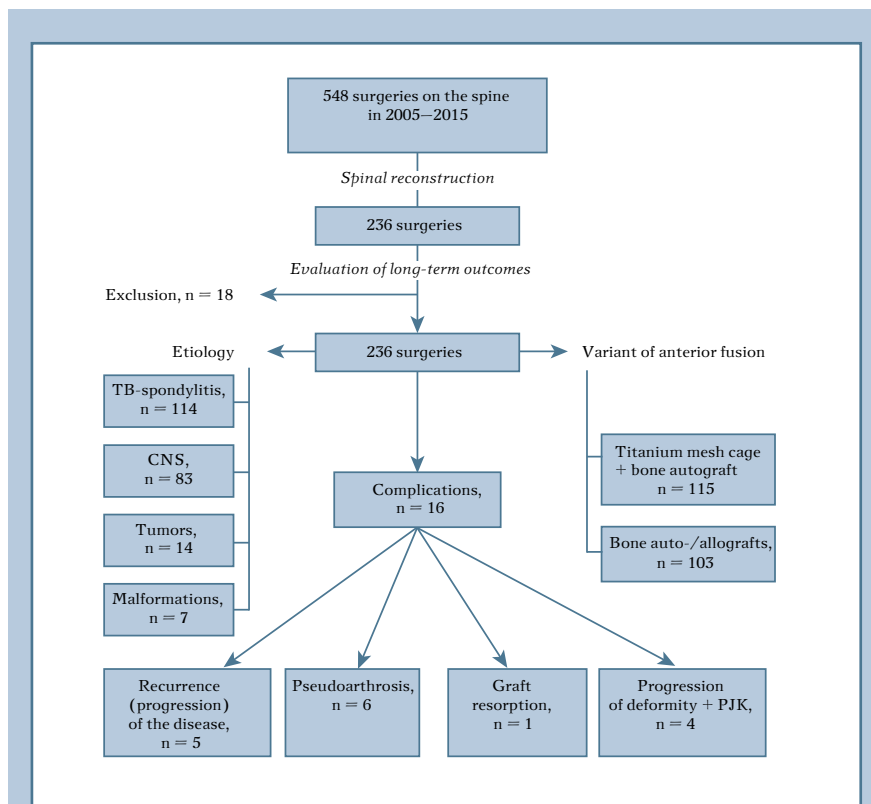


Fig. 1

Scheme of the study: TB-spondylitis – tuberculous spondylitis; CNS – chronic nonspecific spondylitis; PJK – proximal junctional kyphosis

Table 1

Age characteristics of patients

Age group	Age bracket (full years)	Patients, n
Early childhood	≤3	10
Pre-school	4 ≤ ... ≤ 6	1
Primary school	7 ≤ ... ≤ 11	0
Secondary school	12 ≤ ... ≤ 17	5

Table 2

Level of spine reconstruction

Localization	C	C/T	T	T/L	L	L/S
Patients, n	0	1	7	1	6	1

In 3 of 4 cases of deformity progression cranial expansion of the posterior instrumentation was performed (long-term follow-up was 2 years 4 months); in 1 case there was anterior re-fusion by

TMC with bone autograft and expansion of the posterior instrumental fixation on the background of PJK (Fig. 3a–d).

Lysis of the graft (n = 1) was accompanied by the development of instability

Table 3

## Patients' characteristics

Patient	Age at the time of surgery	Gender	Diagnosis	Primary surgery: AF, PIF (date of surgery)	Time of onset and nature of complications after surgery	Revision surgery, duration of the follow-up
1	2 years 3 months	F	Generalized tuberculosis, tuberculosis spondylitis L3, L5–L6	AF A: L4–L6, PIF L1–L6 (02.2009)	3 years 3 months, recurrence	Fistulonecrosequesteromy, AF M+A: L4–L6, 5 years 3 months
2	13 years	M	Mixed infection (MDR MbT + chlamydia) C7–T2, T4–T6	AF M+A: C7–T2, PIF C4–T5 (07.2012)	4 years 5 months, recurrence	AF M+A: T4–T6, PIF, re-mounting, C7–T9, 4 months
3	3 years 10 months	M	Generalized tuberculosis, tuberculosis spondylitis L3–L4	AF A: L3–L5, PIF L2–L5 (07.2011)	1 year 4 months, recurrence	PF M+A: L3–L5, 4 years 3 months
4	12 years	M	Giant cell tumor of L2–L4	AF M+A: L1–L5, L2–L4 PIF T11–S1 (04.2010)	2 years, recurrence	Fistulotomy, abscessotomy, remounting, PIF, 4 years 10 months
5	5 years 11 months	F	Ewing's sarcoma T1–T2	AF M+A: C7–T3, PIF (04.2012)	3 months, recurrence	Fatal outcome
6	3 years	F	Tuberculosis spondylitis L3–L5	AF M+A: L3–L5, PIF L2–S1 (12.2014)	1 year 10 months, pseudoarthrosis	AF M+A: L3–L5, PIF, 4 months
7	3 years	M	Tuberculosis spondylitis L5–S2	AF A: L4–S3 (11.2006)	9 years, pseudoarthrosis	AF M+A: L4–S3, PIF L3–S2, 1 year 3 months
8	3 years 1 month	M	Generalized tuberculosis, tuberculosis spondylitis L2–L3	AF A: L1–L2, PIF T11–L4 (04.2011)	1 year, pseudoarthrosis	AF M+A: L1–L4, PIF T11–L4, 4 years 8 months
9	1 year 11 months	F	BCG spondylitis, T10–T12	AF M+A: T10–T12, PIF T8–L1 (06.2013)	1 year after the removal of PIF, pseudoarthrosis	PIF Th8–L1, PS, 1 year 11 months
10	2 year 2 months	M	SSD, L1–L5	AF A: L1–L5, PIF T9–S1 (10.2010)	3 years 6 months, pseudoarthrosis	AF M+A: L2–L5, 2 years 10 months
11	1 year 5 months	M	Chronic non-specified spondylitis, T11–T12	AF A: T11–T12, PIF T11–L1 (11.2009)	5 years 5 months, pseudoarthrosis	AF M+A: T11–T12, PIF T11–L1, 4 months
12	3 years 5 months	F	Tuberculosis spondylitis T11–L1	AF M+A: T11–L1 (01.2014)	1 year 1 month, progression of deformity	PIF T7–L4, 1 years 10 months
13	14 years	M	ABC, T10	AF M+A: T9–T11, PIF T9–T11 (11.2011)	6 months, progression of deformity	PIF (re-mounting, extension), T9–T11, 4 years 9 months
14	8 months	F	LONS, XHC T6–T9	AF A: T6–T9, PIF T5–T10 (02.2014)	1 year 5 months, progression of deformity	AF M+A: T6–T9, PIF Th5–T10, 1 year 9 months
15	14 years	M	PF, T5, T7, T8	AF M+A: T6–T9, PIF T5–T10 (02.2014)	8 months, PJK	PIF, extension "Domino" T1–T11, 1 year 1 month
16	2 years 1 month	F	Generalized tuberculosis, tuberculosis spondylitis T8–T10	AF A: T7–T12, PIF Th5–L2 (03.2015)	5 years 6 months, graft lysis	AF M+A: T7–T12, PIF, 4 years 6 months

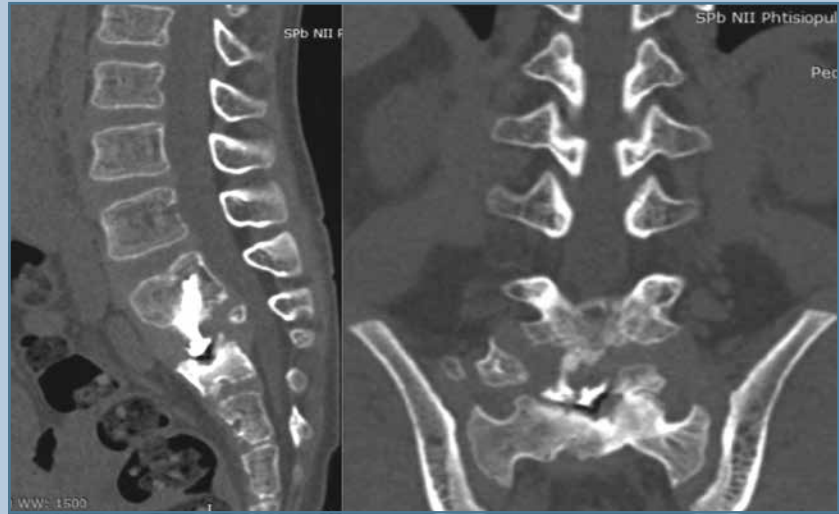
AF – anterior fusion; M+A – mesh with bone autograft; A – bone auto-/allograft; PIF – posterior instrumental fixation; SSD – segmental spinal dysgenesis; PF – pathological fracture: infectious/tumor etiology of the disease is excluded bacteriologically, molecularly-genetically and morphologically; PJK – proximal junctional kyphosis; MbT – Mycobacterium tuberculosis; MDR – multiple drug resistance; BCG – vaccine strain of mycobacteria; ABC – aneurysmal bone cyst; LONS – late onset neonatal sepsis; PS – posterior fusion (osteoplastic).

and increase in angular kyphosis, which required a 360-degree reconstruction with the correction of the defect in the anterior column by TMC with bone autografts and performing posterior instrumental fixation (Fig. 4a–d).

No repeated complications were observed in 14 of 16 patients after revision surgery during the subsequent follow-up. In two cases (aneurysmal bone cyst and generalized mixed infection with multiresistant mycobacteria), a second revision was required due to repeated recurrence of the disease in the long-term period.

## Discussion

Comparison of our data with the experience of other researchers is extremely difficult in the absence of analysis of revision spinal surgeries in children who underwent reconstruction surgeries. It draws our attention to similar publications related to adult patients operated on for comparable pathology. For example, Qureshi et al. [13], who described the results of treatment of 87 patients with tuberculous spondylitis (mean age 36 years), mentioned 7 (8.1 %) complications related to destabilization of the bone graft in the area of the anterior reconstruction, but did not indicate their causes and time to onset. Yoshioka et al. [17], who presented the experience of total reconstructions using titanium mesh with bone autograft in 26 patients with spinal tumors at a level of three or more SMS, reported that within a period of more than 2 years (26.5 months) mesh cages sagged by more than 2 mm in 11 patients, however, only one case required revision surgery with



**Fig. 2**

Data of the patient M., 12 years old, with the effect of L4–S2 tuberculous spondylitis: radical reconstruction using L4–S3 anterior fusion with autograft from the iliac wing at the age of 3; 9 years later, reports of back pain, CT reveals pseudoarthrosis of the distal end of the graft with a vacuum phenomenon; revision surgery: refusion with a titanium mesh with bone autograft, posterior instrumental fixation

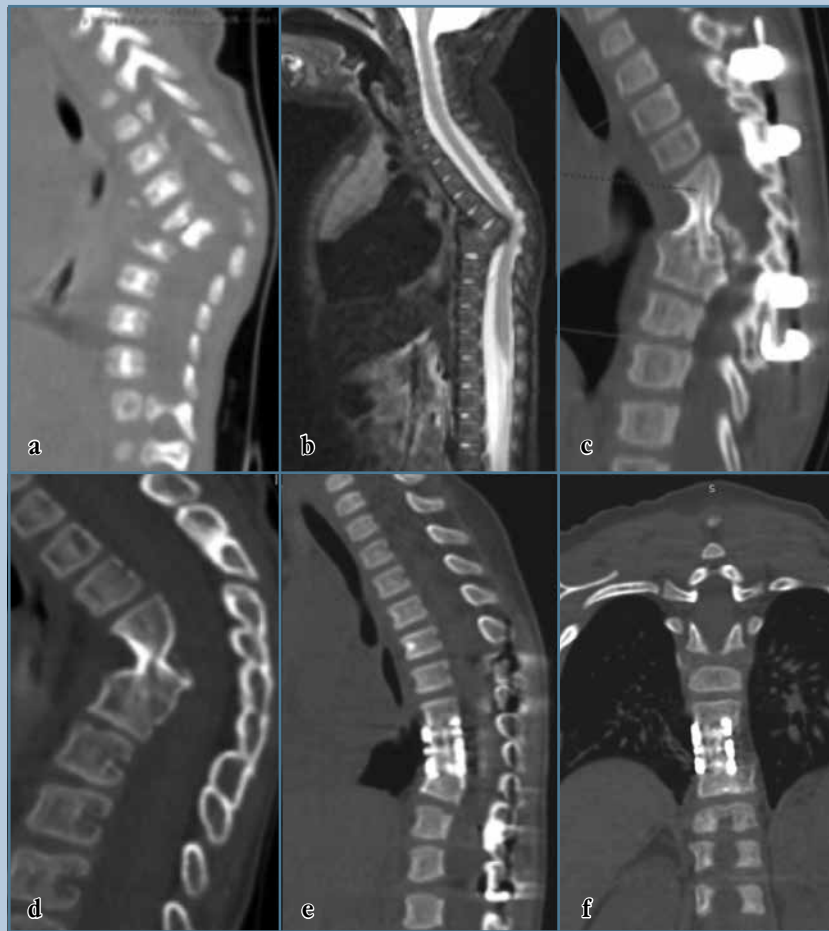
the installation of additional posterior structures due to further sagging of the mesh cage to 13 mm in 6 months. Therefore, the sagging of TMC in the postoperative period is, in the opinion of the authors, a common phenomenon in polysegmental reconstructions and requires correction only in case of progression and development of instability. Alam et al. [4] in a multicentre study combining the experience of surgical treatment of 582 patients with tuberculous spondylitis (mean age 35.2 years) reported four fractures of the graft, 11 cases of infection in the

zone of intervention and 6 revision surgeries with re-fusion with titanium mesh cage with bone autograft in 113 reconstructions of the anterior column performed using bone grafts. The number of late complications of vertebral reconstructions presented in our study is not high, but it is the highest among the available publications. Remarkably, despite high number of cases of infectious spondylitis in our group of patients, we, on the one hand, did not observe any cases of peri-implant infection, and, on the other hand, were unable to prove statistically significant

**Table 4**

Dynamics of complications onset depending on pathology

Diagnosis	Observations, n	M, years + months	m, years + months
Tuberculous spondylitis	9	3 + 1	2 + 8
Chronic non-specific spondylitis	2	3 + 5	2 + 9
Tumor	3	1 + 3	1 + 0
Congenital malformation	1	3 + 6	–
Pathological fracture	1	0 + 8	–



**Fig. 3**

Data of the patient M., with the effects of T6–T9 spondylitis in the presence of late neonatal sepsis: septic condition (pneumonia, bullous epidermolysis, spondylitis) at the age of 1–2 months; deformity of the thoracic region was noted at the age of 2 months; at 8 months, CT and MRI revealed subtotal destruction of T7–T8, T6–T9 contact, kyphosis of 41.7°; reconstruction with anterior fusion with bone autograft, posterior instrumental fixation (a, b); 1 year 3 months after the surgery in the presence of stable anterior block, the posterior instrumental fixation (c) was removed, which led to the growth of kyphosis to 65° (d); revision surgery (refusion with titanium mesh with bone autograft, posterior instrumental fixation) was performed at the age of 3 (e, f)

effect of etiology of the disease on the risk of late complications. Obviously, further collection of material, expansion of statistical processing capabilities and development of algorithms for correcting complications require combining the data from different clinics and creation, if feasible, of one common register of complications. It should be noted that the experience of foreign databases

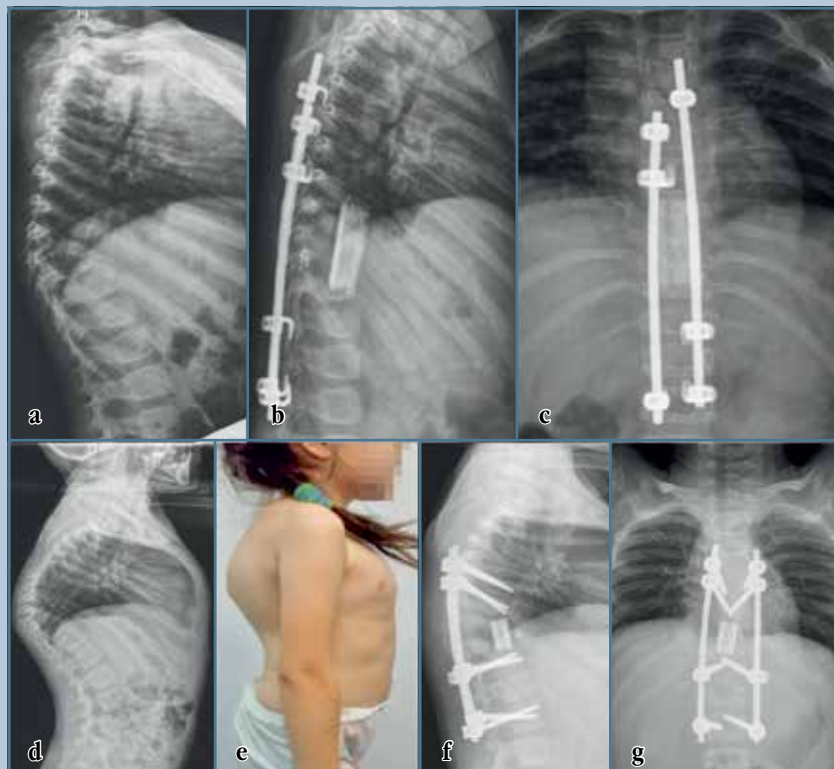
(Kids' Inpatient Database, National Trauma Data Bank), which allows to systematize and evaluate various parameters including complications of surgical treatment of vertebral pathology in children, has one significant drawback: they include only early complications, arising during the period of a patient's immediate stay in the hospital after the surgery. This is also indicated by users

of these databases, who simultaneously note that significant part of the complications occurs in the long-term period after the surgery [5], which fully corresponds to our data.

### Conclusion

Surgical treatment of spinal disorders involving vertebral destruction in children requires detailed analysis of the long-term outcomes with stage-by-stage X-ray and clinical control. The development of complications after such surgeries can occur over a sufficiently long period and may be associated with progression of the disease (infection, tumor). Understanding the risk factors for such complications should contribute not only to more careful choice of tactics of anterior and posterior stabilization of the spine in children, but also to a targeted dynamic follow-up observation. Particular attention should be given to patients with infectious pathology of the spine, and it should be borne in mind that even though modern non-biological implants for anterior fusion reduce the risk of pseudoarthrosis and preclude the possibility of graft fracture, they do not exclude the possibility of progression of the underlying disease and associated development of delayed spinal instability.

*The study did not have sponsorship. The authors state that there is no conflict of interest.*



**Fig. 4**

Data of the patient I., with the effects of T8–T10 tuberculosis spondylitis: at the age of 2 years 1 month with an active process complicated by kyphosis of 48.2° (a) reconstruction of the spine with anterior fusion using T7–T12 cortical allograft, posterior instrumental fixation at T5–L2 (b, c); 3 years later the posterior structures were removed at the place of residence without providing the reason, another 1.5 years later graft resorption was detected with increase of kyphosis to 95.3° (d, e); revision surgery, refusion with a mesh of porous titanium with bone autograft, posterior instrumental fixation (f, g), correction of kyphosis by 55°

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Received 27.03.2017

Review completed 30.03.2017

Passed for printing 12.04.2017

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