HOSPITAL MORTALITY IN HEMATOGENOUS VERTEBRAL OSTEOMYELITIS

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Objective. To analyze lethal outcomes in patients with hematogenous vertebral osteomyelitis.

Material and Methods. Study design: retrospective analysis of medical records. A total of 209 medical records of inpatients who underwent treatment for hematogenous vertebral osteomyelitis in 2006–2017 were analyzed. Out of them 68 patients (32.5 %) were treated conservatively, and 141 (67.5 %) – surgically. The risk factors for lethal outcomes were studied for various methods of treatment, and a statistical analysis was performed.

Results. Hospital mortality (n = 9) was 4.3 %. In patients who died in hospital, average time for diagnosis making was 4 times less (p = 0.092). The main factors affecting mortality were diabetes mellitus (p = 0.033), type C lesion according to the Pola classification (p = 0.014) and age over 70 years (p = 0.006). To assess the relationship between hospital mortality and the revealed differences between the groups, a regression analysis was performed, which showed that factors associated with mortality were Pola type C.4 lesions (OR 9.73; 95 % CI 1.75–54.20), diabetes mellitus (OR 5.86; 95 % CI 1.14–30.15) and age over 70 years (OR 12.58; 95 % CI 2.50–63.34). The combination of these factors increased the likelihood of hospital mortality (p = 0.001). Sensitivity (77.8 %) and specificity (84.2 %) were calculated using the ROC curve. In the group with mortality, the comorbidity index (CCI) was significantly higher (≥4) than in the group without mortality (p = 0.002). With a CCI of 4 or more, the probability of hospital death increases significantly (OR 10.23; 95 % CI 2.06–50.82), p = 0.005. Long-term mortality was 4.3 % (n = 9), in 77.8 % of cases the cause was acute cardiovascular pathology, and no recurrence of vertebral osteomyelitis was detected.

Conclusion. Hospital mortality was 4.3 %, and there was no mortality among patients treated conservatively. The main risk factors were diabetes mellitus, type C lesion according to Pola and age over 70 years. There was a significant mutual burdening of these factors (p = 0.001). With CCI ≥4, the probability of death is higher (p = 0.005).

Key Words: hematogenous vertebral osteomyelitis, spondylodiscitis, spondylitis, hospital mortality.

Please cite this paper as: *Bazarov AYu, Sergyeev KS, Faryon AO, Paskov RV, Lebedev IA. Hospital mortality in hematogenous vertebral osteomyelitis. Hir. Pozvonoc. 2021;18(3):86–93. In Russian.*

DOI: http://dx.doi.org/10.14531/ss2021.3.86-93.

Hematogenous vertebral osteomyelitis is a severe infectious disease with a potentially unpredictable outcome. The largest number of dead patients is recorded during the first year from the disease onset [1, 2]. The mortality ratio, according to most papers, does not exceed 5.0 % [3, 4], but rises to 20.0 % in the absence of early treatment. The mortality in the early stages from the start of treatment is related to complications (sepsis, co-morbidity), as well as to the disease caused by *S. Aureus* and neurologic impairment [5, 6]. Within two years after diagnosis, up to 23 % of patients die [7, 8].

In the paper of Zadran et al. [9] there were no differences in mortality during conservative and surgical treatment of vertebral osteomyelitis for two years. Certainly, the candidates for surgery are patients with the most advanced disease. Considering that mortality in hematogenous vertebral osteomyelitis of patients of the older age group is high, the authors doubt that these rather weak elderly patients will feel better after surgery [9]. S.A. Tichodeev et al. uphold these views [10]. This concept is familiar to few researchers. Segreto et al. [11] draw attention to the fact that the suspension of the necessary surgical treatment for more than 24 hours is attended by a significant risk of complications, permanent neurologic impairment and death. An essential fact is a significant increase in the total cost of treatment. If the operation was delayed for 24 hours and for 14–30 days, the cost of treatment in the United States increased from $63,390.78 to $245,752.40, respectively [11]. The overall cost of treatment of vertebral osteomyelitis in this country reaches $1.3 billion [4].

The significant differences in the number of deaths mentioned in a number of papers are associated with distinctions in the timing of follow-up and reflect hospital and long-term mortality over several years.

Diabetes mellitus is not accepted in all studies as a significant risk factor affecting mortality and the total number of unsatisfactory treatment results [9]. However, in most studies this fact is unquestionable [12, 13]. There is a significant influence of the pathogen on the outcome of the disease, in particu-

lar, methicillin-resistant Staphylococcus aureus (MRSA) accumulates the number of deaths, thus, timely surgeries are a factor contributing to survival [14].

Based on regression analysis, the cut-off points are the age over 60 years, the Charlson comorbidity index (CCI > 1), the severity of neurological impairment on the Frankel E grade (normal neurological status), the Karnovsky scale – 80 % (ability to work), the level of C-reactive protein (CRP) – 30 mg/l 14 days after the treatment onset [9].

The anatomical localization of the lesion in thoracic spine or thoracolumbar junction is accompanied by a more severe course of the disease [15], and in the presence of two co-morbidities (CCI ⩾ 2) increases mortality [16].

The conservative treatment is safe and effective with careful selection of patients suffering from spondylodiscitis without complications. The researchers do not observe a direct link between surgical treatment and an increase in mortality in comparison with patients treated conservatively [17].

The objective is to analyze lethal outcomes in patients with hematogenous vertebral osteomyelitis.

Material and Methods

A retrospective analysis of 209 medical records of indoor patients who were treated at the Regional Clinical Hospital No. 2 (Tyumen) with a diagnosis of "hematogenous vertebral osteomyelitis" was performed. Group A included patients who died in hospital, and group B (control) included patients discharged from the hospital. Details are given in the diagram (Fig. 1). Exclusion criteria: outpatient treatment, tuberculous or brucellosis spondylodiscitis, postoperative osteomyelitis, the absence of a follow-up during a year.

The paper demonstrates clinical information for 2006–2017. We used data from medical records, questionnaires taken no earlier than a year after the patient's discharge, as well as data from control CT and/or MRI, CBC, ESR, CRP and statistical analysis.

Men were 73.2 % (n = 153), women – 26.8 % (n = 56), the ratio of 3 : 1. The average age of patients was 50.39 ± 14.00 y.o.

The lesion localization in the cervical spine was observed in 19 (9.1 %) cases; the ratio of discharged and dead in hospital was 8.5: 1.0; in the thoracic spine – 70 (33.5 %), the ratio was 22.3 : 1.0; in the lumbar spine – 115 (55.0 %), the ratio was 27.8 : 1.0; multilevel lesions – 5 (2.4 %), no deaths were noted. Lesions of the junctional parts were referred to the superposed spine department.

The patients with acute and subacute forms of the disease accounted for 58.9 % (n = 123), with chronic ones – 41.1 % (n = 86). The process activity was defined on the basis of the disease duration and the type of tissue inflammatory response. 68 (32.5 %) patients were treated conservatively, 141 (67.5 %) surgically. Indications for the conservative method of treatment were uncomplicated, minor destructive disease forms. An antibacterial therapy was performed for at least 6 weeks, including 3 weeks intravenously. There were no deaths in hospital among the patients receiving conservative treatment. The distribution of patients by types of surgeries and outcomes is presented in Fig. 2.

All patients who died in the hospital underwent debridement and drainage, which in 66.7 % of cases were supplemented by stabilization or reconstruction of the affected spine.

Statistical analysis was performed in IBM SPSS Statistics 21.0 and Statistica 6.0 software. The quantitative data is given in the form of the mean and standard deviation of the mean (M ± SD) or in the form of the median and interquartile range of Me [25–75 %]. The Kolmogorov – Smirnov criterion was used to check the distribution of quantitative attributes. Depending on the distribution of variables, the Student's t-test for independent samples or the Mann – Whitney test were applied for analysis. The differences between the qualitative indicators were estimated by the χ-square criterion or the Fisher Exact test. For determining the factors connected with mortality, logit regression was applied accompanied by a step-by-step approach of variable inclusion. The quality of the obtained model was estimated using the ROC curve. The differences in indicators were considered significant if the level of $p < 0.05$.

Results

The patients were divided into two groups depending on the outcome: the ones discharged from the hospital and those who died during hospital stay.

The general features of the groups are given in Table 1.

The average time of diagnosis in patients who died in hospital was 4 times less than in the control group: 0.5 and 2 months, respectively (p = 0.092).

The distribution of patients by lesion types and outcomes, according to the Pola classification [18], is shown in Table 2.

The C type lesion (p = 0.014) was observed in 55.6% of cases of hospital deaths.

The analyzed risk factors depending on the outcome of the disease are shown in Table 3.

The distribution of patients by age and outcomes is given in Table 4.

In order to evaluate the relationship of hospital mortality with the revealed differences between the groups, a regression analysis was conducted. It showed that the factors related to mortality are lesions of type C.4 according to Pola (OR 9.73; 95% CI 1.75–54.20), the presence of diabetes mellitus (OR 5.86; 95% CI 1.14–30.15) and age over 70 (OR 12.58; 95% CI 2.50–63.34). The combination of these factors enhances the likelihood of a fatal outcome in the hospital. The sensitivity (77.8 %) and specificity (84.2 %) were estimated using the ROC curve (Fig. 3).

The value of the area under the curve (AUC)– 0.822 with an error probability of p = 0.001 signifies a good predictive value of the model used.

We have conducted an analysis of the comorbidity index, accounting for the presence of co-morbidities in many patients. In the group with mortality, CCI is significantly higher (⩾4) than without mortality (p = 0.002). If comorbidity is 4 or more, the probability of a fatal out-

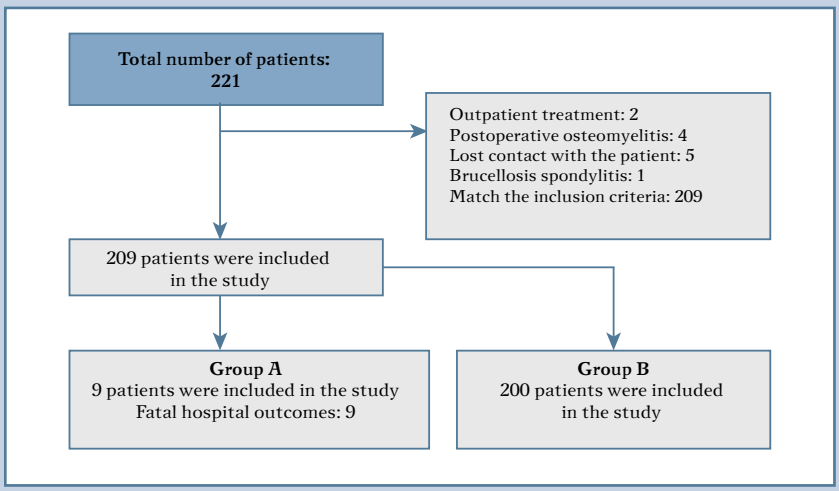

Fig. 1
Criteria for patients' inclusion in the study

come in a hospital significantly increases (OR 10.23; 95% CI 2.06–50.82; p = 0.005).

The following reasons resulted in patients' deaths in the hospital: uncontrolled sepsis – 2 cases, ascending spinal cord edema with lesions of the cervical spine – 2, pneumonia – 2, multiple-organ-failure syndrome – 3.

The long-term fatal outcomes were observed in 9 (4.3 %) patients in terms from a week to seven years after hospital discharge. Acute cardiovascular pathology was the reason of death in 7 (77.8 %) patients, meningoencephalitis – in 1 (11.1 %); the cause of death in one patient is unknown; no repeated hospitalizations were reported.

Discussion

Notwithstanding the technological progress in diagnostic methods and tools as well as increasing their availability, hematogenous vertebral osteomyelitis remains a difficult-to-diagnose disease.

The time of diagnosis is 2–12 months [19]; according to Pola al. [18], the average is 49.9 days; according to our data, 0.5 and 2 months for the dead and discharged from the hospital, respectively. In case of a complicated course of the disease with a fatal outcome, the time consumed for diagnostic search is decreased, which reflects the initial severity of the disease. Out of nine dead patients, three were diagnosed within the first week, and two within two weeks. During bacteriological study of the surgical specimen, positive results were received in 44.4 % of cases (n = 4); methicillin-sensitive *St. Aureus* (MSSA) was separated in three patients; MRSA was found only in

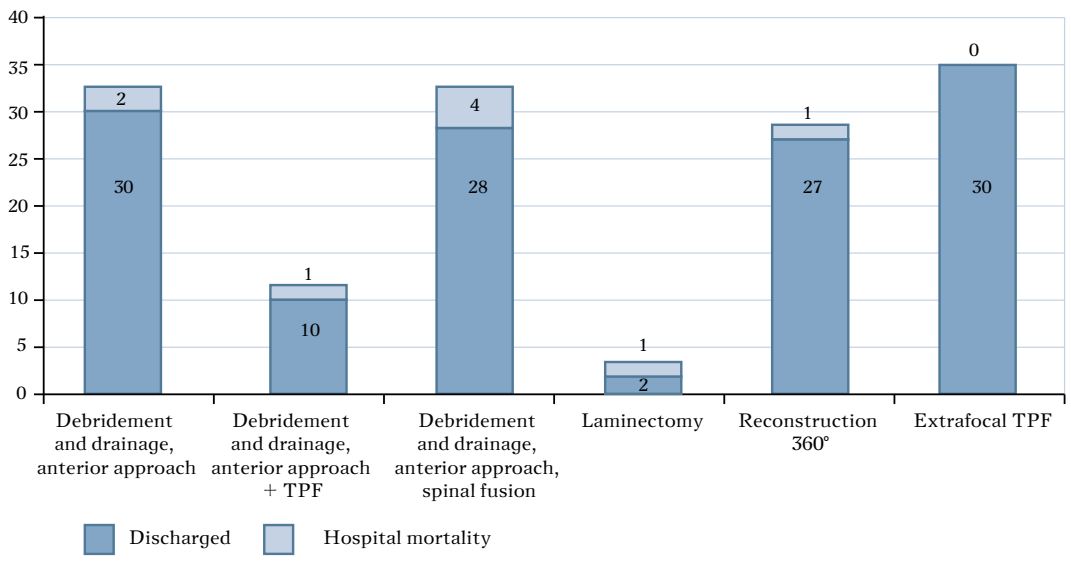

Fig. 2
Surgical distribution of patients and outcomes: TPF – transpedicular fixation

one patient. In two specimens, pathogens were isolated during a blood test. Polymicrobial infestation was noted in both cases: *St. epidermidis, E. faecium and A. baumani, Ps. Aeruginosa*. A lot of papers have reported on the significance of *St. Aureus*, its resistant form, as well as polymicrobial infestations as risk factors for adverse outcomes of vertebral osteomyelitis [12, 14].

The vast number of deaths was observed among patients who underwent surgeries [9]. The death rate in hospital is typical only for operated patients, according to our data. It is still not clear whether surgery is a significant risk factor.

An increasing neurological impairment, uncontrolled sepsis with an undrained infection focus, the formation of extended epidural and paravertebral abscesses, septic instability are clear evidence for surgery [8, 20]. The patients with complications of osteomyelitis are primarily undergone surgery. For them, the death risk from the primary disease is higher than the risks from the proposed surgery.

Out of 39 patients with type C lesion, 19 (48.7 %) had a neurological impairment with the formation of an epidural abscess and segmental instability (type C.4); out of three dead, one had an increase in neurological disorders (from B to A) on the Frankel scale. One patient had an improvement in the condition (from B to C), and another had no dynamics (C degree of neurological impairment). The direct causes of death were different: ascending spinal cord edema, progression of the prior disease and sepsis, as well as destructive pneumonia with multi-organ failure.

Chang et al. [21] did not observe the effect of abscess formation on the mortality rate (p = 0.952), recurrence (p = 0.906) and recovery (p = 0.906). With regard to polymicrobial etiology, it significantly increased this indicator. There were no differences in the mortality rate during the antibiotic therapy duration of 6 and 12 weeks [5].

The majority of papers describe male patients with lesion of the lumbar spine [21, 22]. This ratio is maintained among those who died in the hospital (M : W = 3.5 : 2.0).

The analysis of the surgical findings of patients over 65 years of age is not followed in all studies by an increase in mortality at the hospital stage and in the long-term period (3.1 and 12.5 %, respectively). Meanwhile, there were significantly more complications (21.9 and 40.6 %) [23]. The risk of an unfavorable outcome in multisegmental lesion grows with increasing age [7].

According to the presented data, the hospital mortality rate in persons over 60 was 66.7%. In group A, 88.9 % (n = 8) of patients underwent single- or bilateral restorative surgery (n = 2), which were supplemented by transpedicular fixation (n = 1), anterior fusion (n = 4), and 360° reconstruction (n = 1). The bilat-

Table 1
General features of patient groups

Criterion	Group A (n = 9)	Group B (n = 200)	p
Age, y.o.	61.9 ± 12.3	48.1 ± 14.7	0.006
Bed day	34.1 ± 29.2	30.5 ± 16.5	0.733
The time of diagnosis, months	0.5 [0.25; 2.00]	2.0 [1.00; 3.00]	0.092

There was a statistically significant rise in age in the group of patients who died in hospital (p = 0.006).

Table 2
The distribution of patients into groups according to the Pola type of lesion [18], n (%)

Pola type of lesion	Group A (n = 9)	Group B (n = 196*)	p
A	2 (22.2)	60 (30.6)	0.726
B	2 (22.2)	102 (52.0)	0.098
C	5 (55.6)	34 (17.3)	0.014

* Four patients were not classified. They had a lesion of the posterior spinal structures without involvement of the vertebral-motor segment.

Table 3
Distribution of patients by risk factors, n (%)

Risk factor	Group A (n = 9)	Group B (n = 200)	p
Diabetes mellitus	3 (33.3)	15 (7.5)	0.033
Cirrhosis, alcoholism	0 (0.0)	4 (2.0)	0.668
Viral hepatitis	1 (11.1)	62 (31.0)	0.283
HIV	1 (11.1)	40 (20.0)	0.511
HIV + hepatitis	1 (11.1)	33 (16.5)	0.668
Implants	0 (0.0)	3 (1.5)	0.711
Steroid therapy	0 (0.0)	4 (2.0)	0.668
Drug addiction	1 (11.1)	54 (27.0)	0.447
Purulent infections	2 (22.2)	50 (25.0)	0.850

If patients suffering from concomitant diabetes mellitus, the risk of death is significantly higher (p = 0.033).

Table 4
Distribution of patients by age and outcomes, n (%)

Age, y.o.	Group A	Group B	p
30 and younger	0 (0.0)	19 (9.5)	0.332
31–40	0 (0.0)	59 (29.5)	0.064
41–50	2 (22.2)	35 (17.5)	0.717
51–60	1 (11.1)	37 (18.5)	0.574
61–70	2 (22.2)	34 (17.0)	0.655
older than 70	4 (44.4)	16 (8.0)	0.006

There is a tendency to decrease mortality in the age group of 31–40 (p = 0.064) and a significant rise in the group older than 70 (p = 0.006).

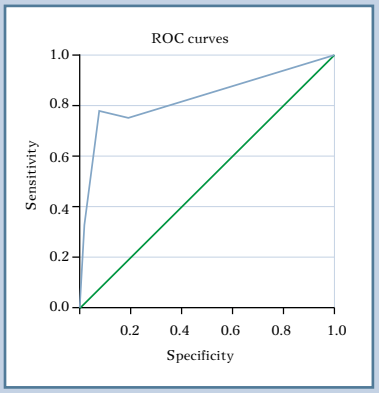

Fig. 3
ROC curve: AUC – 0.822; p = 0.001

eral restoration through retroperitoneal approach was required in two patients due to the extended bilateral iliopsoas abscesses. Eight patients were diagnosed with a monosegmental type of lesion, one – with multisegmental.

The relatively low mortality rate in the long-term period, according to our data, is related to a lower average age: among discharged patients – 48.07 y.o., in the group with hospital mortality – 61.89 y.o. Many researchers [9, 24] report that 74 % of patients are over 60, and the average age is 67.

In the paper by Akiyama et al. [25] there was a significant reduction in mortality in the treatment of patients with vertebral osteomyelitis in large multidisciplinary and academic clinics (p = 0.003).

The aforementioned data are heterogeneous and vary depending on the sample size and the study design. Multiple risk factors were assessed separately in different groups of patients and their prognostic significance was identified. Nevertheless, when they are mixed in one patient, the probability of a fatal outcome significantly increases.

Conclusions

Hospital mortality (n = 9) was 4.3 %. In patients who died in hospital, the average time of diagnosis was 4 times less (p = 0.092). The main factors influencing mortality are diabetes mellitus (p = 0.033), lesion type C according to the Pola classification (p = 0.014), age over 70 (p = 0.006). To evaluate the relationship of hospital mortality with the identified differences between the groups, a regression analysis was conducted. It showed that the factors related to mortality are lesions of type C.4 according to Pola (OR 9.73; 95 % CI 1.75–54.20), the presence of diabetes mellitus (OR 5.86; 95 % CI 1.14–30.15) and age over 70 (OR 12.58; 95 % CI 2.50–63.34). The combination of these factors increases the likelihood of a fatal outcome. ROC curve was applied to determine sensitivity (77.8 %) and specificity (84.2 %). In the group with mortality, CCI is significantly higher (⩾4) than without mortality (p = 0.002). If the comorbidity index is 4 or more, the probability of hospital death significantly grows (OR 10.23; 95 % CI 2.06–50.82).

The long-term mortality in terms from a week after discharge to 7 years was 4.3 %. The key cause was an acute cardiovascular pathology. There were no data concerning the recurrence of the primary disease.

The study had no sponsors. The authors declare that they have no conflict of interest.

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Received 29.06.2020
Review completed 17.05.2021
Passed for printing 20.05.2021

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