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Risk Factors for Infectious Complications after Surgical Treatment of Spinal Metastases in Patients with Breast and Kidney Cancer

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Abstract

Relevance. In patients with the most common malignant new growth such as breast, kidney and lung cancer the rate of spinal metastases amounts to 70%. Increasing number of surgical procedures results in growing frequency of postoperative complications including surgical site infection (SSI) which do not only deteriorate the quality of patient's life but change the timelines for renewal of therapy for the primary disease. Study design — case control study. ***Purpose of the study*** — to identify key risk factors as well as impact of tumor therapy on development of infectious complications in patients with breast and kidney cancer after surgical management of metastatic spine lesion. ***Materials and Methods.*** The authors collected and compiled the data on 2023 oncological patients who underwent specialized neuroorthopaedic treatment in the period from 2000 until 2017 due to tumor spine lesions. Inclusion criteria: malignant breast and kidney tumors with spine metastases, continued systemic tumor therapy, decompression and stabilization spine surgery irrespective of used implants. Patients that corresponded to inclusion criteria were divided into two groups. The first (main) group included patients (n = 22) with infectious complications after surgery. The second (control) group (n = 23) was formed by propensity score matching. ***Results.*** The analysis of obtained data resulted in identification of severe significant factors (p<0.05): diabetes mellitus, postoperative liquorrhea, certain classes by ASA (3, 4) and ECOG (2, 3, 4) scales, volume of blood loss, time of surgery and type of tumor therapy. However, the three latter have the highest statistical significance (p<0.01): surgical factors (blood loss volume and time of procedure) and type of tumor therapy. ***Conclusion.*** Postoperative SSI remains a common severe complication after surgeries due to metastatic spine lesions. The causes of postoperative infection after tumor resection are compromised immune status of the patient; long time of procedure with heavy blood loss and adjuvant tumor therapy.

Keywords: spinal metastases, surgical treatment, spinal infection, risk factors, adjuvant tumor therapy.

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Introduction

Every year the number of patients with oncological diseases is growing and the number of spine procedures increases accordingly [1]. In patients with the most common malignant new growth such as breast, kidney and lung cancer the rate of spinal metastases amounts to 70% [2, 3]. Increasing number of surgical procedures results in growing frequency of postoperative complications including surgical site infection (SSI) which do not only deteriorate the quality of patient's life but change the timelines for renewal of therapy for the primary disease [4].

Key factors contributing to surgical site infection can be divided into three categories: patient related; related to the progress of the main disease; and related to the type of tumor therapy [5, 6]. Besides, length and severity of surgical procedure has a serious impact on development of early inflammatory changes [7].

Parameters of infectious complications after spine surgery for different pathologies vary from 1.9 to 4.4% in the recent 10 years [6, 8, 9]. In case of spinal metastases the surgical procedures result to significant increase of deep SSI rate, up to 12-20% according to literature [10, 11]. Long term follow-up of patients with infectious complications is difficult due to limited survival of oncological patients.

Purpose of the study — to identify key risk factors as well as impact of tumor therapy on development of infectious complications in patients with breast and kidney cancer after surgical management of metastatic spine lesions.

Material and Methods

Study design — case control study. The authors collected and compiled the data on 2023 oncological patients who underwent specialized neuro-orthopaedic treatment in the period from 2000 until 2017 due to tumor spine lesions. The analysis data included medical histories, questionnaires and surveys.

Inclusion criteria: malignant breast and kidney tumors with spine metastases, continued systemic tumor therapy, decompression and stabilization spine surgery irrespective of used implants. *Exclusion criteria:* benign tumor-like spinal formations, radiotherapy in preoperative period, presence of primary spine infection (spinal tuberculosis), skin infectious diseases.

The choice of such groups was not random while frequency of spinal metastases is higher than in any other malignancies. Currently both diseases respond well to tumor therapy allowing to significantly increase life span and improvement of life quality in such patients.

Patients that corresponded to inclusion criteria were divided into two groups. The first (main) group included patients (n = 22) with infectious complications after surgery. The second (control) group (n = 23) was formed by propensity score matching. Patient' characteristics of both groups are presented in the Table 1.

The study included patients only with infectious complications developed in early postoperative period. SSI was considered early if developed within first 90 days after surgery, while late infectious complications manifested after 90 days after surgery [6, 8]. All patients underwent revisions, implants were not removed due to inevitable iatrogenic instability of the operated spine segment. Secondary revisions were not required.

Data collection included evaluation of demography (age, gender), comorbidities (diabetes mellitus, chronic obstructive pulmonary disease COPD, obesity, heart diseases), scale of American Society of Anesthesiologists (ASA) and ECOG scale as well as neurological status (motor and sensory disorders, pelvic organ dysfunction). Oncological history included defining the morphological type of tumor, amount of spinal metastases, pattern of systemic tumor therapy. Surgical data comprised of type of procedure, blood loss

volume, time of intervention. Besides, evaluation of pain by VAS scale and neurological dynamics by Frankel scale was done in pre- and postoperative periods.

Table 1

Characteristics of patients

Characteristics	Group 1 (patients with infectious complications)	Group 2 (patients without infectious complications)
Gender		
Male	10 (22.2%)	6 (13.4%)
Female	12 (26.6%)	17 (37.8%)
Primary tumor		
Breast cancer	12 (26.7%)	15 (33.3%)
Kidney cancer	10 (22.2%)	8 (17.8%)

Statistical analysis

Statistical processing was made using software environment R (version 3.5.3). Median was given for mean values. Confidence intervals for the median are obtained by bootstrap. Group comparison by quantitative criteria was conducted using Fisher — Pitman permutation test. To compare groups according to their qualitative characteristics, c^2 Pearson was used with approximation of indicators by resampling using Monte Carlo methods. Critical significance level was established as $p<0.05$.

Results

During the follow-up SSI frequency in early postoperative period in patients with metastatic spine lesions against breast and kidney cancer was 1.84%. Mean time from surgery to manifestation of postoperative complication was 13.2±3.6 days.

Among registered infectious complication one microorganism was identified in 20 patients, and two microorganisms — in two cases. Frequency of SSI agents is given in Table 2.

Table 2

Structure of infection agents of SSI in group 1

Microorganisms	Number of cases
S. aureus (MRSA)	4 (18.2%)
S. epidermidis (MRSE)	13 (59.1%)
E. coli (ESBL)	2 (9.2%)
P. aeruginosa	1 (4.5%)
S. epidermidis (MRSE) + K. pneumoniae	1 (4.5%)
S. aureus (MRSA) + Enterobacter	1 (4.5%)

Factors impacting the risk of SSI can be divided into several groups: related to medical history and somatic condition of the patient; related to surgical procedure; factors related to tumor therapy. Analysis of risk factors for infectious complications after surgical treatment of spinal metastases in patients with breast and kidney cancer is given in Tables 3 and 4.

All patients with diabetes mellitus included into the study received oral medications. Diabetes was a significant risk factor in the present research ($p = 0.021$). Such comorbidities as COPD ($p = 0.286$) and increased BMI ($p = 0.098$) did not have a significant impact on infection development. ASA scores indicate grade and severity of disease. According to obtained data ASA was a statistically significant risk factor ($p = 0.027$). 8 patients from group 1 demonstrated neurological deficit due to compression of spinal cord but it had no impact of SSI ($p = 0.128$).

Table 3

Analysis of qualitative risk factors in the groups by Pearson chi-squared test, number of cases

Risk factors	Group 1	Group 2	χ^2	p
Diabetes mellitus	7 (15.6%)	1 (2.2%)	5.805	0.021
COPD	4 (8.9%)	1 (2.2%)	2.995	0.286
ASA (3. 4)	12 (26.6%)	6 (7.3%)	8.648	0.027
Neurological complications	8 (20%)	3 (7.5%)	4.917	0.128
Urinary infection	8 (17.8%)	2 (4.44%)	4.980	0.106
Secondary procedures	7 (15.6%)	4 (8.9%)	1.267	0.308
Fixation levels (>5 levels)	15 (33.4%)	18 (40%)	8.682	0.167
Spondylectomy	2 (4.5%)	6 (13.3%)	2.221	0.240
Postoperative liquirrhea	5 (11.1%)	0 (0%)	5.880	0.025
Intraoperative vertebroplasty	4 (8.9%)	3 (7.5%)	2.780	0.334
ECOG (>2)	21 (46.7%)	13 (28.9%)	10.993	0.021
Multiple MTS spine lesions	16 (35.5%)	17 (37.7%)	0.684	0.784

Table 4

Analysis of quantitative risk factors in the groups using Fisher-Pitman permutation test (Z)

Risk factor	Group 1	Group 2	Z	*p*
Age, years	58.5 (95% CI 54.8–63.0)	59 (95% CI 55.6–62.9)	-0.653	0.520
BMI, kg/m^2	28.4 (95% CI 28.4–30.7)	27.3 (95% CI 25.3–30.2)	-1.630	0.098
Incision, cm	17.5 (95% CI 7.8–30.3)	18.4 (95% CI 10.1–31.4)	-0.363	0.845
Time of surgery, min	208.5 (95% CI 175–245.5)	170.5 (95% CI 134.5–205.0)	-3.146	0.001
Blood loss, ml	1096 (95% CI 844–1321)	450 (95% CI 53.7–728)	-2.890	0.001
Drainage blood loss, ml	340 (95% CI 113–520)	296 (95% CI 96–412)	-0.298	0.811

Two patients from the study group underwent spondylectomy, 20 patients underwent palliative surgery for laminectomy with or without circular decompression. No significant dependency of SSI after spondylectomy was observed (p = 0.240). Univariate analysis did not prove impact of secondary surgeries on SSI development (p = 0.308). The majority of procedures for management of spinal metastases were lengthy and accompanied with rather high blood loss. According to the obtained data time of surgery (p = 0.001) and blood loss volume (p = 0.001) had significant impact on development of infectious complications after spinal surgery. Dura mater lesions with postoperative liquorrhea contributed to development of SSI (p = 0.25).

All patients from the present research received systemic tumor therapy for treatment of primary tumor. Medical history of hormone therapy for patients with breast cancer and target therapy for patients with kidney cancer was a statistically significant risk factor (p = 0,008 and p = 0.001, respectively). SSI parameters after such therapy was much higher than in patients receiving alternative systemic tumor therapy (Table 5).

Based on the conducted analysis seven significant factors were defined (p<0.05): diabetes mellitus, postoperative liquorrhea, certain classes by ASA (3, 4) and ECOG (2, 3, 4) scales, blood loss volume, time of surgery and type of tumor therapy. However, the three latter have the highest statistical significance (p<0.01): surgical factors (blood loss volume and time of procedure) and type of tumor therapy.

Discussion

Prevention of infectious complications have a highest importance for patient, physician and society as a whole for several reasons. SSI can be a devastating consequence of any operative procedure. During surgeries related to implantation of metal fixators (for the majority of cases with spinal metastases) surgical site infection can result in removal of implants and seriously deteriorate surgical outcome. Besides, longer hospital stay, orthopaedic limitations, medication (including antibiotics) and revisions — all of these affects not only life quality of patient but the ability of patient to receive the therapy for main disease.

Purpose of this study was to identify risk factors for SSI after surgical management of metastatic spine lesion. Factors increasing the risk for SSI can be classified as related to medical history and somatic status of patient, as well as related to surgical management and to tumor therapy received by patient [12, 13].

Table 5

Evaluation of tumor therapy impact on development of SSI

Type of therapy	Group 1	Group 2	χ^2	p
Type of breast cancer therapy				
chemotherapy	1 (4.5%)	8 (34.8%)	3.074	0.231
hormonotherapy	10 (45.5%)	4 (17.4%)	7.769	0.008
Type of kidney cancer therapy				
target therapy	10 (45.5%)	2 (8.7%)	10.288	0.001
immunotherapy	1 (4.5%)	9 (39.1%)	1.198	0.351

According to some authors the frequency of postoperative infection after management of metastatic spinal lesions varies from 0.9 to 36% [14, 15]. I.B. McPhee et al found that SSI was observed in 20% of cases in early postoperative period [10]. In the present study the average SSI rate was 1.84%.

Some publications report on higher risk for SSI after spine surgery in patients with diabetes mellitus [16, 17]. Diabetic patients have pathologically changed blood vessels, especially in microvasculature. Ischemia and hypoxia of blood vessels occurring in result of significant damage to soft tissues contributes to active infectious process. Immune function in inhibited in patients with diabetes due to serious functional cells damage [18]. Results of the present research confirm the conclusion that patients with diabetes mellitus have a higher risk for SSI. Glycemic control and correction of blood glucose indicators with its increase is needed for prevention.

Higher BMI in the present study was not a statistically significant risk factor for SSI, but literature demonstrates that MBI increase over 25 kg/m^2 is related to 15% increased rate of postoperative infection [5, 7].

ASA and ECOG scales prove their prognostic value with respect to the general status of oncological patient [3, 6, 10].

Some researchers established that the risk of infectious complications in patients after open surgeries was much higher than after minimally invasive procedures [19, 20]. This is related not only to a larger traumatic impact on soft tissues and bleeding but also with long contact of soft tissues with the air and surgical instruments, which increases the risk of SSI. R. Schwarzkopf et al report that with blood loss >800 ml the risk of postoperative infection increases [21]. The authors of the present analysis also demonstrated that higher blood loss volume is the risk factor for SSI. Due to this the preference should be given to minimally invasive procedures whenever possible.

According to the findings of the present research no clear correlation was observed between postoperative infection and chemotherapy. Hormone therapy for breast cancer and target therapy for kidney cancer are statistically significant risk factor for SSI. It's considered that leukopenia, neutropenia, deficiency of local immune status and secondary damage to microcirculation due to chemotherapy as well as soft tissue damage directly contribute to development of postoperative infection. However, according to other data, adjuvant chemotherapy and radiotherapy weren't significant risk factors for infection [22]. On the other hand, according to S. Demura et al study of spinal metastases the hormone therapy is an independent risk factor for postoperative infection [23].

Postoperative SSI is a common and severe complication after surgical management of metastatic spine lesions. The causes of postoperative infection after tumor resection are compromised immune status of the patient, long time of procedure with heavy blood loss and adjuvant tumor therapy. Surgeons should analyze and adequately assess risk factors in oncological patients. After diagnosing the infection it's required to do the revision for removal of infection focus, preferably preserving the implants, secondary drainage of postoperative wound and in some cases flow rinsing of postoperative wound by antiseptic solution. Besides, antibiotic therapy should be selected in accordance with results of bacteriological cultures.

The present research is limited due to a small sample of infected patients (n = 22). However, the homogeneous study group, long follow up, type and scope of surgeries allowed to define statistically significant risk factors for spinal infection in early postoperative period.

Publication ethics

All patients provided informed written consent for inclusion into the study.

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Authors' contribution

Smekalyonkov O.A. — literature review, processing of clinical material, statistical processing, discussion, conclusions.

Ptashnikov D.A. — design.

Zaborovsky N.S. — statistical evaluation of material.

Mikhailov D.A. — literature review, processing of clinical material.

Masevnin S.V. — literature review, processing of clinical material.

Denison A.A. — processing of clinical material.

Литература [References]

1. [Malignant neoplasms in Russia in 2017 (morbidity and mortality)]. Kaprin A.D., Starinsky V.V., Petrova G.V. (eds.). M., 2018. p. 4-6. (In Russian).
2. Coleman R.E. Clinical features of metastatic bone disease and risk of skeletal morbidity. *Clin Cancer Res.* 2006;12(20 Pt 2):6243s-6249s. doi: 10.1158/1078-0432.CCR-06-0931.
3. Atkinson R.A., Jones A., Ousey K., Stephenson J. Management and cost of surgical site infection in patients undergoing surgery for spinal metastasis. *J Hosp Infect.* 2017;95(2):148-153. doi: 10.1016/j.jhin.2016.11.016.
4. Sugita S., Hozumi T., Yamakawa K., Goto T., Kondo T. Risk factors for surgical site infection after posterior fixation surgery and intraoperative radiotherapy for spinal metastases. *Eur Spine J.* 2016;25(4):1034-1038. doi: 10.1007/s00586-015-4116-6.
5. Sebaaly A., Shedid D., Boubez G., Zairi F., Kanhonou M., Yuh S.J., Wang Z. Surgical site infection in spinal metastasis: incidence and risk factors. *Spine J.* 2018;18(8):1382-1387. doi: 10.1016/j.spinee.2018.01.002.
6. Dowdell J., Brochin R., Kim J., Overley S., Oren J., Freedman B., Cho S. Postoperative Spine Infection: Diagnosis and Management. *Global Spine J.* 2018;8 (4 Suppl):37S-43S. doi:10.1177/2192568217745512.
7. Olsen M.A., Nepple J.J., Riew K.D., Lenke L.G., Bridwell K.H., Mayfield J., Fraser V.J. Risk factors for surgical site infection following orthopaedic spinal operations. *J Bone Joint Surg Am.* 2008;90(1):62-69. doi: 10.2106/JBJS.F.01515.
8. Weinstein M.A., McCabe J.P., Cammisa F.P. Jr. Postoperative spinal wound infection: a review of 2,391 consecutive index procedures. *J Spinal Disord.* 2000;13(5):422-426.
9. Pull ter Gunne A.F., Cohen D.B. Incidence, prevalence, and analysis of risk factors for surgical site infection following adult spinal surgery. *Spine (Phila Pa 1976).* 2009;34(13):1422-1428. doi: 10.1097/BRS.0b013e3181a03013.
10. McPhee I.B., Williams R.P., Swanson C.E. Factors influencing wound healing after surgery for metastatic disease of the spine. *Spine (Phila Pa 1976).* 1998;23(6):726-732. doi: 10.1097/00007632-199803150-00015.
11. Sundaresan N., Rothman A., Manhart K., Kelliher K. Surgery for solitary metastases of the spine: rationale and results of treatment. *Spine (Phila Pa 1976).* 2002;27(16):1802-1806. doi: 10.1097/00007632-200208150-00021.
12. Pull ter Gunne A.F., Hosman A.J., Cohen D.B., Schuetz M., Habil D., van Laarhoven C.J., van Middendorp J.J. A methodological systematic review on surgical site infections following spinal surgery: part 1: risk factors. *Spine (Phila Pa 1976).* 2012;37(24):2017-2033. doi: 10.1097/BRS.0b013e31825bfca8.
13. van Middendorp J.J., Pull ter Gunne A.F., Schuetz M., Habil D., Cohen D.B., Hosman A.J., van Laarhoven C.J. A methodological systematic review on surgical site infections following spinal surgery: part 2: prophylactic treatments. *Spine (Phila Pa 1976).* 2012;37(24):2034-2045. doi: 10.1097/BRS.0b013e31825f6652.
14. Peel T., May D., Buising K., Thursky K., Slavin M., Choong P. Infective complications following tumour endoprosthesis surgery for bone and soft tissue tumours. *Eur J Surg Oncol.* 2014;40(9):1087-1094. doi: 10.1016/j.ejso.2014.02.241.
15. Dierselhuis E.F., Gerbers J.G., Ploegmakers J.J., Stevens M., Suurmeijer A.J., Jutte P.C. Local Treatment with Adjuvant Therapy for Central Atypical Cartilaginous Tumors in the Long Bones: Analysis of Outcome and Complications in One Hundred and Eight Patients with a Minimum Follow-up of Two Years. *J Bone Joint Surg Am.* 2016;98(4):303-313. doi: 10.2106/JBJS.O.00472.
16. Fang A., Hu S.S., Endres N., Bradford D.S. Risk factors for infection after spinal surgery. *Spine (Phila Pa 1976).* 2005;30(12):1460-1465. doi: 10.1097/01.brs.0000166532.58227.4f.
17. Browne J.A., Cook C., Pietrobon R., Bethel M.A., Richardson W.J. Diabetes and early postoperative outcomes following lumbar fusion. *Spine (Phila Pa 1976).* 2007;32(20):2214-2219. doi: 10.1097/BRS.0b013e31814b1bc0.
18. Chen S., Anderson M.V., Cheng W.K., Wongworawat M.D. Diabetes associated with increased surgical site infections in spinal arthrodesis. *Clin Orthop Relat Res.* 2009;467(7):1670-1673. doi: 10.1007/s11999-009-0740-y.
19. Koutsoumbelis S., Hughes A.P., Girardi F.P., Cammisa F.P. Jr., Finerty E.A., Nguyen J.T. et al. Risk factors for postoperative infection following posterior lumbar instrumented arthrodesis. *J Bone Joint Surg Am.* 2011;93(17):1627-1633. doi: 10.2106/JBJS.J.00039.
20. Parker S.L., Adogwa O., Witham T.F., Aaronson O.S., Cheng J., McGirt M.J. Post-operative infection after minimally invasive versus open transforaminal lumbar interbody fusion (TLIF): literature review and cost analysis. *Minim Invasive Neurosurg.* 2011;54(1):33-37. doi: 10.1055/s-0030-1269904.
21. Schwarzkopf R., Chung C., Park J.J., Walsh M., Spivak J.M., Steiger D. Effects of perioperative blood product use on surgical site infection following thoracic and lumbar spinal surgery. *Spine (Phila Pa 1976).* 2010;35(3):340-346. doi: 10.1097/BRS.0b013e3181b86eda.

22. Morris C.D., Sepkowitz K., Fonshell C., Margetson N., Eagan J., Miransky J. et al. Prospective identification of risk factors for wound infection after lower extremity oncologic surgery. *Ann Surg Oncol.* 2003;10(7):778-782. doi: 10.1245/aso.2003.07.023.

23. Demura S., Kawahara N., Murakami H., Nambu K., Kato S., Yoshioka K., Okayama T., Tomita K. Surgical site infection in spinal metastasis: risk factors and countermeasures. *Spine (Phila Pa 1976).* 2009;34(6): 635-639. doi: 10.1097/BRS.0b013e31819712ca.

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