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Analysis of postoperative prognostic factors in patients with long bones metastatic lesions

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Abstract

Currently, with the development of the concept of cancer treatment, the survival rate of patients has increased significantly, but the percentage of the frequency of various metastatic lesions remains high. The bones of the skeleton are one of the main parts of metastases. In cancer patients, bone metastases usually mean that the disease is at an advanced stage, and the prognosis is not good. These patients often suffer from many complications, including pain, decreased mobility, pathological fractures, etc. The quality of life of patients is seriously deteriorating. Therefore, the main goal of surgical treatment of patients with bone metastases is the earliest possible restoration the function of the affected limb, pain relief, prevention of pathological fractures and the improvement of the quality of life of patients after surgery. This literature review analyzes the incidence of bone metastases in patients, and the dependence of metastatic lesions of long tubular bones on localization incidence of bone metastases in different body parts. The domestic and foreign literature on the surgical treatment of patients with metastatic bone lesions was analyzed. The results of the analysis show that the features of surgical treatment are becoming the main factors influencing the prognosis in patients with metastatic lesions of the long bones.

Keywords: bone metastases, long tubular bones, surgical treatment, cancer patients, osteosynthesis.

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The bones can be one of the main sites of metastatic lesions in malignant neoplasms. The development of bone metastases (BM) depends largely on the primary site. BMs most often occur in patients with breast, kidney, thyroid, or prostate cancer or in those with erythroid myeloma. In addition to prostate cancer, most metastases are lytic or mixed; thus, patients have high risk for pathological fractures [1].

In breast cancer, the bones can be the most common site of metastasis [2]. On initial visit and examination, approximately 5%–6% of women with breast cancer have BM. In advanced stages of breast cancer, BMs eventually occur in 65%–75% of the patients [3].

In prostate cancer, metastatic bone lesions are found in 90% of the patients [4]. BMs often develop in patients with kidney cancer [5]. In lung cancer, the bones are also the most common location of metastases, which occur in 30%–40% of the patients [6].

BMs are considered a rare and late event in patients with head and neck cancer, and its frequency varies depending on the tumor location, that is, from 50% to 80% in patients with nasopharyngeal cancer and from 2% to 22% in patients with squamous cell tumors but not nasopharyngeal cancer [7, 8].

The causes of BMs have not yet been fully known, but the molecular and biological characteristics of tumor cells and tissues to which they metastasize are important and influence the spread of metastasis. Some risk factors for BM show conflicting or vague associations, which can be due to the high heterogeneity of the populations under investigation, cancer treatment options, and methodologies [9].

Menopausal status is suggested to influence BM development; however, this finding is refuted in some studies; in particular, researchers state that the protective effect of estrogens on bone density did not prevent the spread of tumors in the bones [10, 11]. Other factors, such as gene mutations, molecular changes associated with oncogenesis, therapy, and bone metabolism, can also influence BM development [12].

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BMs weaken the structural integrity of the bones, increasing ones risk for complications often clustered in a group of skeletal-related events (SRE), such as a pathological fracture, spinal cord compression, hypercalcemia, and severe bone pain syndrome, which require palliative radiotherapy or surgical treatment [4,13].

The prognosis in BM patients is usually poor, and the expected overall survival is often less than 8 months [14]. In addition, bone lesions reduce significantly the quality of life, since they cause pain, can compress the main neurovascular structures, and lead to a pathological fracture. The quality of life is diminished due to deteriorating health and independent functioning. Studies have shown that at least one SRE occurs in nearly 50% of female breast cancer patients with BM [15].

In BM, metastases mainly occur in long tubular bones. The frequency of metastatic lesions in the sections of long tubular bones varies. According to the Scandinavian BM registry, the femur, humerus, and pelvic bones are affected in 64%, 21%, and 9% of the patients, respectively. Three-quarters of the lesions are recorded in the proximal femur, while the diaphysis is the most commonly affected area in the humerus [16]. Proximal femur metastases occur in approximately 10% of patients with primary malignant tumors. In metastatic lesions of the femur, metastases are localized in the femoral neck, subtrochanteric region, and intertrochanteric region in 50%, 30%, and 20% of the cases, respectively. This is due to the well-developed vascular system in the intertrochanteric region.

Given the high prevalence of oncological pathology, the incidence of BM among the population is significant. Therefore, it is important to study the factors influencing the prognosis of patients in the context of the treatment. Thus, this work was based on the analysis of articles by various authors, including 35 international authors and one Russian researcher.

Surgical treatment of BM is usually not the main treatment option. In multiple BMs, treatment is started with chemotherapy, radiotherapy, hormonal therapy, or targeted therapy, depending on the histological type of the primary tumor. SRE can be effectively reduced by administering bisphosphonates and denosumab [2,9,10,14,17].

In some tumor histotypes, for example, in renal cancer, one of the BM characteristics is resistance to radiation and drug treatment [18,19]. In this regard, surgical treatment of metastatic lesions of the bones has become more actively used for palliative care. Surgical treatment is mainly aimed at relieving pain, preventing pathological fracture, osteosynthesis in cases with pathological fracture, restoration of patient mobility, and improvement of the quality of life [13,16,17,20–22].

When selecting a treatment option, specialists always face the question of which method to choose, especially if there are several treatment options. Cho et al. [6] present interesting data rationalizing orthopedic surgeries. In their report, among lung cancer patients with metastatic lesions of the bones, the overall survival rate was significantly longer in patients who had undergone orthopedic surgery than those who did not receive surgical treatment [6].

Unbearable pain and pathological fracture are indications for surgery. Treatment decisions should consider various aspects, such as the patient's overall health status, histological type of the primary tumor, and effectiveness of other feasible treatment methods. Although surgical intervention carries a risk for the patient and affects the immune status, drug or radiation therapy will not cause a pathological fracture. This problem is also described by Szendrői, who reported that 74.2% of 1,195 patients who underwent surgery for BMs had a pathological fracture and 18.3% were at risk of fracture [17].

Nowadays, numerous surgical techniques are available for the repair of bone defects, including osteosynthesis, but choosing the appropriate treatment that can provide the best prognosis is very important.

Orthopedic stabilization of bones with metastatic lesions remains the basis for the treatment of pathological bone fractures [20,23]. Reconstruction is mainly aimed at achieving stability and reduction of pain at the site of the lesion or fracture. Pathological fractures resulting from metastatic disease are usually treated by repairing or removing the existing bone [24]. The most common methods are intramedullary nailing or implantation of a plate supplemented with polymethyl methacrylate. If there was massive bone resection or a destroyed joint surface, the bone can be removed and replaced with prosthesis [6].

Most authors prefer unipolar or modular endoprostheses that enable early activation and mobilization of patients and are associated with fewer complications than intramedullary nails or plates [1,25,26]. If the diaphysis of the long bones is affected, a plate, an intramedullary nail, or a prosthesis can be implanted. All these methods have advantages and disadvantages [27,28].

In case of a poor prognosis, intramedullary osteosynthesis using retaining screws by a minimally invasive technique and supplemented with bone cement is optimal. The patient can weight bear immediately. Postoperative radiation therapy (when appropriate) can be started early. However, the

incidence of pathological fractures increases with time [12,25,29]. For the treatment of metastases near the knee joint, intramedullary nails, and angle plates with screws supplemented with bone cement are good options for patients with a poor prognosis, while an endoprosthesis should be used for patients with a better prognosis [1,30].

Weiss et al. presented good results of using a cemented plate for stabilization of pathological fractures of the proximal humerus, while Wedin et al. recommended hemiprosthesis for more destructive lesions of the proximal humerus and interlocking with intramedullary nails for the treatment of pathological fractures of the diaphyseal segment [31,32].

The histological type of the primary tumor (cancer is controlled versus not controlled), patient's general health status, other predictors of estimated survival, and degree of metastasis are significant in surgery planning. In rare cases, such as a single metastasis, a slight injury, or if the tumor can be removed without complicated surgery, the tumor should be removed completely to avoid further local complications. However, in most cases, the minimally invasive technique is reasonable to avoid repeated surgeries in case of complications, with the initiation of specialized drug or radiation treatment [4,33].

The incidence of complications associated with surgical treatment of metastatic bone lesions is quite high, ranging from 9% to 22% for the humerus [31,32] and from 10% to 30% for the femur [16,30,34,35]. This is mainly due to low bone quality, use of inappropriate implant, disease progression, patient's health status, prosthesis displacement or loosening, periprosthetic infection, and implant fracture [17]. Thus, researchers also focused on identifying factors that influence the condition and prognosis of patients after surgical treatment of BM in long tubular bones.

Scott et al. assessed the factors influencing surgical outcomes in patients with BMs in the extremities. They showed that the ineffectiveness of surgical treatment, which accounted for 16.8% of the cases, was associated with the histological type of the tumor ($p = 0.008$). According to radiographic data, male sex ($p < 0.001$) and use of bone cement ($p = 0.019$) further influenced tumor progression. Additional tumors also developed in 43.8% of the patients. As a result, they concluded that the histological type of the tumor may be very important when considering surgical treatment of metastatic bone disease [36].

According to Radchenko et al. [5], who analyzed the results of surgical treatment of renal cancer metastases in long tubular bones, the timing of distant metastases appeared to be a significant factor influencing overall survival. Thus, the median survival duration of patients whose distant metastasis was established during the first year of follow-up was 19.0 months. With later progression, the median survival duration was 42.0 months ($p = 0.001$).

As regards surgical treatment of BM in tubular bones, preventive surgical interventions should be prioritized, as they can reduce the volume of blood loss during surgery and the duration of hospitalization and can provide better functional results.

Radchenko et al. also revealed statistically significant difference in the duration of hospitalization in patients with a pathological fracture compared with patients who did not have a fracture. Thus, among patients with a pathological fracture, the average duration of hospitalization of patients who underwent resection of affected bone segments was 16.7 bed-days and those at risk for a pathological fracture was 13.1 bed-days. In addition to the direct immediate economic effect of preventive surgeries, extreme technical complexity should be considered, as well as the unfeasibility of adhering to the principles of ablastics when performing organ-sparing surgical interventions for a pathological fracture, which is of particular relevance for metastases of chemo- and radioresistant tumors [5].

Thus, according to the literature, among those factors that affect the prognosis of a patient who received surgical treatment of metastatic lesions of long tubular bones, the histological type of the tumor, timing of metastases, patient's sex, and aspects of surgical treatment can be noteworthy. The bone tissue condition (occurrence of a pathological fracture or risk of pathological fracture) can be also an important factor affecting overall survival. Definitely, by taking into account oncological pathology, it is difficult to distinguish single prognostic factors, since they all depend on many aspects. For accurate prognoses, a multicenter study, which includes a large number of patients, is required to provide more exact numerical data.

Thus, contemporary achievements in the treatment of disseminated forms of cancer can increase the life expectancy of patients. However, at present, there is no consensus on the factors influencing the results of surgical treatment of BMs in long tubular bones. Therefore, further scientific research in this field is necessary.

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