Original Article

Evaluation of Anesthesia Applications and Postoperative Care Results in Patients Who Underwent Reconstruction Surgery with Tumor Resection Prosthesis in Primary and Metastatic Bone Tumors

Primer ve Metastatik Kemik Tümörlerinde Tümör Rezeksiyon Protezi ile Rekonstrüksiyon Cerrahisi Yapılan Hastalarda Anestezi Uygulamaları ve Postoperatif Bakım Sonuçlarının Değerlendirilmesi

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ABSTRACT

Introduction: Patients scheduled for orthopedic oncological surgery often receive various treatments, such as chemotherapy or radiotherapy, before the operation. The treatments applied and related side effects, accompanying co-morbidities and the characteristics of the surgery to be performed affect the choice of anesthesia and require specificity. In this study, it was planned to retrospectively evaluate the patients who underwent tumor resection prosthesis with the diagnosis of primary or metastatic bone tumor in our hospital.
Materials and methods: 72 patients between the ages of 6-84 who underwent tumor resection prosthesis operation with the diagnosis of primary or metastatic bone tumor and who are in American Society of Anesthesiologists (ASA) I-III group were included in the present study. Demographic characteristics of patients, accompanying diseases, malignity diagnoses, ASA scores, surgical intervention carried out and anesthesia method, duration of anesthesia and operation, pre and postoperative hemoglobin values, amount of intraoperative bleeding, intraoperative fluid management and need for blood transfusion, need for and duration of postoperative intensive care and/or mechanic ventilation were recorded.
Results: The most frequently diagnosed primary bone tumor was osteosarcoma, and the most common operation was wide tumor resection and femoral proximal tumor resection prosthesis. Parameters such as duration of anesthesia, amount of bleeding, age, ASA, and comorbidity were shown to be associated with the need for postoperative mechanical ventilation or intensive care. In the postoperative analgesia methods applied to the patients, it was seen that the most frequently preferred method was intravenous analgesia.
Discussion: In orthopedic oncologic surgeries, anesthesia management should encompass evaluating the patient with a holistic approach starting from the preoperative period, and considering the need for postoperative analgesia and/or for intensive care in addition to intraoperative anesthesia. Communication between members of anesthesia and surgery teams is important for providing optimal surgical care.

Keywords: Bone neoplazms, reconstructıon surgery. anaesthesia. postoperatıve care, tumor resectıon, prosthesıs

ÖZET

Giriş: Ortopedik onkolojik cerrahi planlanan hastalar sıklıkla operasyondan önce kemoterapi veya radyoterapi gibi çeşitli tedaviler almaktadır. Uygulanan tedaviler ve bunlara bağlı yan etkiler, eşlik eden ko-morbiditeler ve yapılacak olan cerrahinin özellikleri anestezi seçimini etkileyerek spesifikleşmeyi

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gerektirir. Bu çalışmada, hastanemizde primer veya metastatik kemik tümörü tanısı ile tümör rezeksiyon protezi uygulanan hastaların retrospektif olarak değerlendirilmesi planlandı.
Gereç ve yöntemler: Çalışmaya hastanemiz Ortopedi ve Travmatoloji Kliniği tarafından Ocak 2015 ve Aralık 2016 tarihleri arasında Primer veya metastatik kemik tümörü tanısı ile tümör rezeksiyonu protez operasyonu uygulanan, American Society of Anesthesiologists (ASA) I-III grubunda yer alan 6-84 yaş arası 72 hasta bu çalışmaya dahil edildi. Hastaların demografik özellikleri, eşlik eden hastalıkları, malignite tanıları, ASA skorları, yapılan cerrahi girişim ve anestezi yöntemi, anestezi ve operasyon süresi, ameliyat öncesi ve sonrası hemoglobin değerleri, intraoperatif kanama miktarı, intraoperatif sıvı yönetimi ve kan transfüzyon ihtiyacı, ve postoperatif yoğun bakım ve/veya mekanik ventilasyon süreleri kaydedildi.
Bulgular: En sık tanı alan primer kemik tümörü osteosarkom, en çok yapılan ameliyat ise geniş tümör rezeksiyonu ve femur proksimal tümör rezeksiyon protezi olarak bulundu. Anestezi süresi, kanama miktarı, yaş, ASA ve ek hastalık gibi parametrelerin postoperatif mekanik ventilasyon veya yoğun bakım ihtiyacıyla ilişkili olduğu gösterildi. Hastalarda uygulanan postoperatif analjezi yöntemlerinde ise en sık olarak intravenöz analjezi yöntemi tercih edildiği görüldü.
Tartışma: Ortopedik onkolojik cerrahilerde anestezi yönetimi, preoperatif dönemden başlayarak hastayı bütüncül bir yaklaşımla değerlendirmeyi, intraoperatif anesteziyle birlikte postoperatif analjezi ve / veya yoğun bakım gereksinimini belirlemeyi kapsamalıdır. Anestezi ve cerrahi ekip üyeleri arasında iletişim optimal onkolojik cerrahi bakımın sağlanması açısından önemlidir.

Anahtar kelimeler: Kemik tümörleri, rekonstrüksiyon cerrahisi, anestezi, ameliyat sonrası bakım, tümör rezeksiyonu, protez

Introduction

In 2009, approximately 2600 new cases of primary bone malignancies and a more significant number of metastatic bone tumors were reported in the USA [1]. Osteosarcoma, Ewing sarcoma, and chondrosarcoma are the three most common types of sarcoma. The recent employment of new chemotherapy treatment agents and radiological imaging methods, treatment options conserving extremity have become more popular [2].

Patients planned to undergo orthopedical oncological surgery commonly receive treatments such as chemotherapy or radiotherapy before the operation. The treatment administered and associated side effects and the characteristics of the surgery influence choice of anesthesia, making it necessary to be more specific. In operations of tumors with rich vascular structure, fluid resuscitation, and adequate intravenous intervention for probable blood transfusion, invasive monitorization or preoperative tumor embolization may be required [3]. It is known that sufficient postoperative analgesic efficacy enables early mobilization and rehabilitation, decreasing morbidity [1].

In the present study, retrospective analysis of the patients who underwent tumor resection prosthesis between January 2015- December 2016 with the diagnosis of the primary or metastatic bone tumor was planned. It was aimed to evaluate demographic characteristics of patients, malignity diagnoses, surgical operation and anesthesia method used, amount of intraoperative bleeding and fluid management, need for blood transfusion, methods used for postoperative analgesia, duration of stay in postoperative ICU, complications developing and need for mechanic ventilation. In addition, the relation between duration of stay in intensive care and mechanic ventilation with other parameters were investigated.

Material and Method

The present study was carried out at University of Health Sciences Ankara Abdurrahman Yurtarslan Oncology Education and Research Hospital Anesthesiology and Reanimation Clinic after ethical approval numbered 2017-05/01 was obtained on 10/5/2017. The study was planned as a retrospective descriptive.72 patients between the ages of 6-84 who underwent tumor resection prosthesis operation with the

diagnosis of primary or metastatic bone tumor between January 2015 and December 2016 and who are in American Society of Anesthesiologists (ASA) I-III group were included in the present study. Cases who were planned to undergo tumor resection prosthesis but who turned out to have benign masses after biopsy were excluded from the study. The study was planned as a retrospective evaluation.

The files of patients who underwent tumor resection between the dates mentioned above were retrieved from hospıtal archive and preoperative anesthesia examination forms, anesthesia monitorization forms, post-operative anesthetic care unit monitorization forms and records of patients who needed monitorization in intensive care unit and/or mechanical ventilation were investigated.

Demographic characteristics of patients, accompanying diseases, malignity diagnoses, ASA scores, surgical intervention carried out and anesthesia method, duration of anesthesia and operation, pre and postoperative hemoglobin values, amount of intraoperative bleeding, intraoperative fluid management and need for blood transfusion, need for and duration of postoperative intensive care and/or mechanic ventilation duratıon were recorded. The relation between evaluated parameters and the need for postoperative intensive care duratıon and/or mechanical ventilation duratıon was investigated.

The number of patients administered regional or general anesthesia was determined and demographic characteristics and differences in the need for postoperative intensive care and/or mechanic ventilation between regional and general anesthesia groups were investigated (Group R, n:28, regional anesthesia - Group G, n:44, general anesthesia). Postoperative analgesia methods and drugs used and their doses were recorded

Statistical analysis

Statistical evaluation was made with SPSS 20.0 program using the tests listed below. $P<0.05$ was considered statistically significant. Statistical analysis was presented as follows: [mean ±standard deviation, minimum- maximum), median (minimum-maximum), n (%)]. Inter groups differences in age, hemoglobin levels, duration of anesthesia and surgical intervention, blood products and fluids used were evaluated with Student's t-test. Data on duration of stay in intensive care and mechanic ventilation, which were not normallly distributed, were evaluated with Mann Whitney U test. Data on ASA class, and additional disease, and the number of patients requiring intensive care and mechanic ventilation were evaluated with Chi-square or Fisher's exact tests.Correlation between data of patients that need intensive care and mechanic ventilation and duration of operation, ASA class, products used, and other parameters were evaluated with Spearman or Pearson correlation test.

Results

Demographic characteristics and accompanying diseases were as follows. 5.6% of the patients were in ASA I, 62.5% in ASA II and 31.9% in ASA III risk group. The most common accompanying disease was hypertension (13.9%) and 62.5% of patients had no additional disease (Table 1). Cancer diagnoses of the patients are shown in (Table 2).The most commonly diagnosed primary bone tumor was established to be osteosarcoma (21%) and the type of operation carried out most commonly wide tumor resection + Femur proximal tumor resection prosthesis with 32 (44%) patients. Upper extremity operation was performed in only one patient out of 72 patients. In 71 patients, the operation was in the lower extremities.

Postoperative analgesia methods used in patients. It was established that epidural PCA (Patient controlled analgesia) method was used in 33% of the patients. The most commonly used intravenous anesthesia method was tramadol bolus administration and PCA prepared with tramadol. (n=14, 19%). It was also determined that two patients underwent femoral plexus, and one patient brachial plexus block and two patients were administered i.v. NSAII (Non steroidal antiinflamatuar drug).

Table1.Demographic characteristics of patients and accompanying diseases [mean ± SD, n (%)]

		(n=72)
Age(year)		47.22±19.12
Weight(kg)		72.35±18.61
ASA(I/II/III)		4 (5.6)/45 (62.5)/23(31.9)
Additional diseases	Acute renal failure	1 (1.4)
	Asthma	1 (1.4)
	Asthma + Goitre	1 (1.4)
	Diabetes Mellitus	3 (4.2)
	Diabetes Mellitus + Hypertension	3 (4.2)
	Hepatitis B	1 (1.4)
	Hypertension	10 (13.9)
	Hypertension + Coronary Artery Disease	4(5.6)
	Hypertension + Chronic Obstructive Pulmonary Disease	1 (1.4)
	Obesity	1 (1.4)
	Pulmonary Hypertension	1 (1.4)
	No additional disease	45 (62.5)

Correlation between the need for duratıon of intensive care and evaluated parameters is shown in table 3. A positive correlation was found between the need for intensive care and duration of anesthesia, amount of bleeding and the amount of erythrocyte suspension used (p=0.025, p=0.003, p<0.0001, respectively). A negative correlation was found, however, between preoperative hemoglobin amount and need for duratıon of intensive care (p<0.0001). No correlation was found between the need for duratıon of intensive care and other parameters evaluated (Table 3).

The correlation between the need for duratıon of mechanic ventilation and the investigated parameters is demonstrated in (Table 4). A positive correlation was found between need for mechanic ventilation and age, ASA, additional disease, duration of anesthesia and amount of erythrocyte suspension used (p=0.005, p=0.012, p=0.041, p<0.0001, respectively). A negative correlation was found between the amount of preoperative hemoglobin and need for duration of mechanic ventilation (p<0.0001). No correlation was found between other parameters and the need for duratıon of mechanic ventilation (Table 4).

In the present study, the number of patients administered regional anesthesia was 28 (39%) (Group R), while the number of patients administered general anesthesia was 44 (61%) (Group G). Combined spinal epidural anesthesia was applied to 28 patients in the regional anesthesia group. Our rate of application of regional anesthesia was similar to the literatüre [1].

Table2.Cancer diagnoses of patients [n (%)]

Cancer diagnoses (n=72)	n (%)
Metastatic adenocarcinoma with unknown primary	4 (%5)
Lung Ca +Bone metastasis	4 (% 5)
Stage 4 Lung Ca+Primary bone malignant mesenchymal tumor	1 (% 1.4)
Giant cell tumor in Femur distal	1 (% 1.4)
Chondrosarcoma	10 (% 14)
Malignant melanoma bone metastasis+ Lung metastasis	1 (% 1.4)
Breast Ca +Bone metastasis	11 (% 15)
Bladder Ca+ left femur metastasis	2 (% 2.8)
Metastatic larynx Ca+ Right femur metastasis	1 (% 1.4)
Multiple myeloma+Humerus proximal carcinoma metastasis	3 (% 4.2)
Nasopharynx Ca +Right humerus proximal and left femur subtrochanteric fracture	1 (% 1.4)
Osteosarcoma	15 (% 21)
Prostat Ca + Bone metastasis	3 (% 4.2)
RCC +Bone metastasis	2 (% 2.8)
Right femur proximal fibrous dysplasia	1 (% 1.4)
Right tibia proximal Ewing sarcoma	1 (% 1.4)
Right tibia proximal giant cell tumor	1 (% 1.4)
Pleomorphic sarcoma in thigh	2 (% 2.8)
Femur malignant mesenchimal tumor	3 (% 4.2)
Left femur distal desmoid tumor	1 (% 1.4)
Left femur proximal pleomorphic rhabdomyosarcoma	1 (% 1.4)
Left thigh posterior mixoid liposarcoma	1 (% 1.4)
Tibia proximal malignant mesenchimal tumor	1 (% 1.4)
Thyroid carcinoma metastasis lytic lesion in proximal of left femur	1 (% 1.4)

Table 3. Correlation between the need for intensive care and other parameters

	R	*P*
Age(year)	0.139	*0.244*
Weight (kg)	0.108	*0.367*
ASA(I/II/III)	0.137	*0.251*
Additional disease	0.085	*0.489*
Duration of anesthesia (min)	0.265	*0.025**
Duration of operation (min)	0.211	*0.075*
Preoperative hemoglobin(g/dl)	-0.403	*<0.0001**
Postoperative hemoglobin(g/dl)	-0.163	*0.173*
Amount of bleeding (ml)	0.340	*0.003**
Erithrocyte suspension (unit)	0.490	*<0.0001**
Cristalloid (ml)	0.185	*0.119*
Colloid (ml)	0.191	*0.331*

Table 4. Correlation between the need for mechanic ventilation and other parameters

	R	*P*
Age(year)	0.330	*0.005**
Weight (kg)	0.058	*0.627*
ASA(1/2/3)	0.259	*0.012**
Additional disease	0.283	*0.018**
Duration of anesthesia(min)	0.242	*0.041**
Duration ofsurgery(min)	0.183	*0.123*
Preoperative hemoglobin (g/dl)	-0.400	*0.001**
Postoperative hemoglobin (g/dl)	-0.184	*0.122*
Amount of bleeding (ml)	0.162	*0.309*
Erithrocyte suspension (unit)	0.613	*<0.0001**
Crystalloid(ml)	0.155	*0.194*
Colloid (ml)	0.206	*0.294*

The comparison of the amount of crystalloid, colloid fluids, erythrocyte suspension, pre and postoperative hemoglobin, and duration of surgical intervention and anesthesia between groups were similar between groups.The amount of preoperative hemoglobin was found to be significantly higher in Group R (p=0.015).

The need for duration of mechanical ventilation was found to be significantly higher in Group R than Group G (p=0.031). Mechanic ventilation was required in eight patients (28.8%) in Group R, and four patients (9.1%) in Group G. Other findings were found to be similar between groups. Death did not occur within 24 hours, preoperatively or postoperatively in any patient.

Discussion

The most commonly diagnosed primary bone tumor was established to be osteosarcoma, and the operation carried out most commonly was found to be wide tumor resection and femur proximal tumor resection prosthesis. Metastatic bone tumors occur more commonly than primary tumors. As many primary cancers metastasize to bone, it is difficult to determine the exact incidence of metastatic bone cancer. Breast and prostate cancers are those that metastasize most commonly to the bone and do so at the rate of 70% in advanced stages [4]. In the present study, metastatic bone cancer was detected in 46% of patients. Of these patients, 11 had breast cancer metastasis, which is similar to the incidence reported in other studies [4]. The increase in developed countries in the prevalence of cancer with the increasing elderly population necessitates more care to be given for cancer patients in the routine practice of health professionals. Anesthetists work with cancer patients not only in operating theaters but also in supportive treatment processes such as pain, nutrition, and intensive care. Although various surgical guidelines have been developed in oncology patients according to cancer types, there are not adequate studies on anesthesia management in these patients [5]. Patients planned to undergo an operation for bone tumors experience an intensive treatment process before surgery. Cancer patients are immune-suppressed due to their disease inducing apoptosis of immune cells,

chemotherapy, and radiotherapy they undergo, malnutrition and psychological stress [6]. Along with immunosuppressive factors, surgical inflammation, pain, hypoxia, hypothermia, hyperglycemia, and immuno-modulation triggered with blood transfusion markedly influence the function of T lymphocytes and natural killer cells (NK) which are active in antitumor activity [7,8]. Recognition of these immune factors and selection of suitable methods in anesthesia management will decrease perioperative risks leading to tumor progression in cancer patients. Volatile anesthetics, morphine and blood transfusion promote immune suppression directly, while propofol, regional anesthesia, and cyclooxygenase inhibitors have been reported to exert positive effects on the immune system [5]. In patients undergoing chemotherapy or radiotherapy, anemia and thrombocytopenia occur frequently. Tumors are generally of vascular structure and tend to bleed at intraoperative period. It has been reported that perioperative tumor embolization may be useful if abundant bleeding is expected associated with a highly vascular tumor [3]. Adequate intravenous access for fluid resuscitation and probable transfusions and preparations for invasive monitorization should be incorporated into preoperative planning. Accompanying co-morbidities such as hypertension, diabetes mellitus, and chronic obstructive lung disease, may make anesthesia management more difficult. Communication with the surgical team is important in that characteristics of the operation can be learned, and anesthesia preparations can be made appropriately [3]. In the present study, the highest amount of bleeding occurred in the case who underwent wide resection, femur and humerus proximal tumor prosthesis operation due to metastasis of the renal cell tumor. As there was about 3000 ml loss of blood in the patient, intensive fluid and blood transfusion was required.

As primary bone tumors and metastases may arise at different sites in the body, anesthesia techniques specialized for certain anatomic localizations provide postoperative analgesia in addition to intraoperative analgesia. In upper extremity tumor resections, regional anesthesia methods may be used as in other surgical operations. If there are a large surgical area and excessive blood loss, difficulty in positioning or long duration of the operation is expected, general anesthesia may be used. In operations carried out under general anesthesia, postoperative analgesia may be given by local anesthetic infiltration via placement of perineural, subfascial or subcutaneous catheters in wound region. In lower extremity tumor resections, regional anesthesia methods may be used on their own or along with general anesthesia[1]. In the present study, 39% of the patients (n=28) were administered regional anesthesia and the remaining patients 61% (n=44) were administered general anesthesia.

Among metastatic tumor resection operations, the most difficult ones are surgeries involving femur. It may be difficult to position patients and use regional anesthesia methods due to primary lesion and other present metastases [1,9]. In cases with excessive bleeding together with sympathetic block associated with neuraxial anesthesia, it may not be easy to control intraoperative blood pressure. In the present study, no significant difference was found between regional and general anesthesia groups in terms of bleeding and the amount of blood transfusion.

It is known that sufficient postoperative analgesia after surgery decreases morbidity by enabling early mobilization and rehabilitation and shortens the duration of hospitalization [10,11]. In oncological surgical operations, postoperative analgesia may be carried out with multimodal analgesia approach, in which drugs and methods exerting effect on different regions in pain pathway such as central or peripheric nerve blocks, local anesthetic infusion via catheters placed in nerve sheath, local infiltration and PCA are used in combination [1]. In the present study, it was established that 33% of the patients used epidural PCA method. Operating theaters with the heavy workload, lack of a separate room for the administration of peripheric blocks in advance, lack of time for the anesthetist and

surgeon, difficulties in the supply of material may be the reasons why peripheric nerve blocks are not used commonly. Orthopedic oncology patients usually use strong opioids due to their pain in the preoperative period. This should be considered when planning postoperative opioid doses and opioid need and tolerance characteristics should be adjusted according to patients. In the study of Chung et al in which pain patterns in recovery unit were investigated, it was reported that the highest pain was described by orthopedics patients in ambulatory surgery [12]. In the study of Barbosa et al, similar results were obtained and 65.6% of patients complained of pain. It was also suggested that physicians and nurses do not adequately evaluate the pain of patients [13]. The efficacy of adjuvant drugs in postoperative pain management has been demonstrated in various studies [14-16]. There are publications reporting the efficacy of alpha 2 agonists such as Dextro-methorphan, NMDA antagonists, gaba-pentinoids, and clonidine[15-17] . NSAII drugs are commonly added to treatment in order to enhance the analgesic efficacy of opioids. The multimodal analgesic approach will decrease the need for intravenous opioids and hence the incidence of probable opioid side effects such as nausea-vomiting, somnolence, ileus and urine retention will also decline.

Orthopedic tumors are quite vascular and may lead to massive intraoperative bleeding[18] . For control and management of intraoperative bleeding, many methods such as preoperative embolization, acute normovolemic hemo-dilution, preoperative blood transfusion, controlled hypotension and antifibrinolytic treatment have been tried and each has its own characteristics [1]. Blood transfusion is an important risk factor in-hospital morbidity[19]. Bower et al investigated the effect of blood transfusion in non-cardiac patients on hospitalization, recovery, and cost and demonstrated that in patients undergoing blood transfusion, duration of hospitalization and frequency of complications was higher [20]. They also reported that in such patients the risk of surgical wound infection increased two-fold and hospital mortality increased 1.4 fold for every unit of blood transfused. Ogura et al in their study on 5716 patients, reported that female sex, age over 80, Charlson Comorbidity Index score of 4 or over, duration of anesthesia longer than 240 minutes, and blood transfusion increased morbidity and mortality [21]. In the present study, a positive correlation was found between duration of anesthesia, amount of bleeding, and amount of erythrocyte suspension used and the need for duration intensive care ($p=0.025$, $p=0.003$, $p<0.0001$, respectively). However, a negative correlation was found between the amount of perioperative hemoglobin and need for intensive care ($p<0.0001$). In patients with high intraoperative bleeding and transfusion need, duration of admission to intensive care was longer. A positive correlation was also found between age, ASA class, additional disease, duration of anesthesia, and the amount of erythrocyte suspension used and the need for duratıon of mechanic ventilation. Similar to other studies, increasing age, comorbidity, high ASA values, prolonged duration of anesthesia and bleeding, and complications increase the need for intensive care [21-27]. In the present study, it was established that the need for duration of mechanic ventilation was higher in the regional anesthesia group (28.6%) than in the general anesthesia group. We believe that this is because ASA class and mean age was higher in the regional anesthesia group and that anesthetists prefer regional methods in patients considered risky.

Bone cancers are usually metastatic tumors rich in vascular structure and localized in various regions of the body. Intense medical treatment patients receive before operation, radiotherapy and accompanying diseases, malnutrition and immune suppression render the operation that will be carried out more critical, necessitating more care to be taken. Bleeding, transfusion and intraoperative complications such as hemodynamic disturbances or embolus may lead to the need for intensive care and mechanic ventilation. The limited number of patients included in the

study and the fact that almost all of the patients were in the lower extremities are the limitations of the study. If larger patient series and patients with tumors in the upper extremity were included in the study, different results could be obtained.

Conclusion

In orthopedic oncological surgery, the need for intensive care may be greater in groups of patients who are older,have a higher ASA score,the duration of anesthesia is longer,the amount of bleeding and the amount of erythrocyte suspension used is excessive. In addition, the hemoglobin value should be optimized in terms of postoperative results before such major surgeries.

In orthopedic oncologic surgeries, anesthesia management should encompass evaluating the patient with a holistic approach starting from the preoperative period, and considering the need for postoperative analgesia and/or for intensive care in addition to intraoperative anesthesia. Communication between members of anesthesia and surgery teams is important for providing optimal surgical care.

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