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ORIGINAL ARTICLE

Risk factors associated with surgical site infection in patients with musculoskeletal cancer

Fatores de risco associados à infecção de sítio cirúrgico em portadores de câncer musculoesquelético

Factores de riesgo asociados a la infección del sitio quirúrgico en pacientes con cáncer musculoesquelético

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ABSTRACT

Background and objectives: surgical site infections (SSI) continue to be a major concern in orthopedic oncology and pose as great a challenge as cancer recurrence, despite the preventive potential of surgery. SSI can be avoided if evidence-based measures are taken. The objective was to assess the frequency of infections in oncological orthopedic surgeries and associated risk factors and inflammatory markers in a reference hospital in the state of Pernambuco. **Methods:** the frequency of SSI, the identification of isolated microorganisms, the risk factors and the profile of Th1 and Th2 inflammatory markers (IL-2, IL-4, IL-6, IL-10, TNF and IFN-Y) in patients with musculoskeletal cancer were analyzed. **Results:** SSI were found in 9.1% of patients undergoing orthopedic surgery. Bivariate analysis revealed that a surgical team comprising more than five members (p=0.041) and the need for intraoperative transfusion (p=0.012) were correlated with a higher risk of SSI. The measurement of ultrasensitive C-reactive protein levels to assess the inflammatory response after SSI showed results that were superior to the reference values for each sample, ranging from >5 to >200mg/dl by the immunoturbidimetric method. Of the IL-2, INFγ and TNF (Th1) and IL-4, IL-6, IL-10 (Th2) levels, only interleukin 6 showed high levels, between 6.68 and 58.76 pg/mL. **Conclusion:** the study found that surgical team with five or more members and blood transfusion were factors associated with the development of SSI in orthopedic surgery in patients with musculoskeletal cancer. Among the inflammatory markers, interleukin 6 (IL-6) showed the highest correlation with the outcome.

Keywords: *Surgical Site Infection. Risk Score. Orthopedics. Cancer.*

RESUMO

Justificativa e objetivos: as infecções do sítio cirúrgico (ISC) continuam sendo uma grande preocupação na oncologia ortopédica e representam um desafio tão grande quanto a recorrência do câncer, apesar do potencial

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preventivo da cirurgia. As ISC podem ser evitadas se forem tomadas medidas baseadas em evidências. O objetivo foi avaliar a frequência de infecções em cirurgias ortopédicas oncológicas e os fatores de risco e marcadores inflamatórios associados em um hospital de referência no estado de Pernambuco. **Métodos:** foram analisados a frequência de ISC, a identificação de microrganismos isolados, os fatores de risco e o perfil de marcadores inflamatórios Th1 e Th2 (IL-2, IL-4, IL-6, IL-10, TNF e IFN-Y) em pacientes portadores de câncer musculoesquelético. **Resultados:** as ISC foram encontradas em 9,1% dos pacientes submetidos à cirurgia ortopédica. A análise bivariada revelou que uma equipe cirúrgica composta por mais de cinco membros (p=0,041) e a necessidade de transfusão intraoperatória (p=0,012) foram correlacionadas com maior risco de ISC. A dosagem dos níveis de proteína C reativa ultrassensível para avaliação da resposta inflamatória após ISC apresentou resultados superiores aos valores de referência para cada amostra, variando de >5 a >200mg/dl pelo método imunoturbidimétrico. Dos níveis de IL-2, INFγ e TNF (Th1) e IL-4, IL-6, IL-10 (Th2), apenas a interleucina 6 apresentou níveis elevados, entre 6,68 e 58,76 pg/mL. **Conclusão:** o estudo constatou que equipe cirúrgica com cinco ou mais membros e transfusão sanguínea foram fatores associados ao desenvolvimento de ISC em cirurgia ortopédica em pacientes com câncer musculoesquelético. Entre os marcadores inflamatórios, interleucina 6 (IL-6) apresentou maior correlação com o desfecho.

Palavras-chave: *Infecção de Sítio Operatório. Pontuação de Risco. Ortopedia. Câncer.*

RESUMEN

Justificación y objetivos: las infecciones del sitio quirúrgico (ISQ) siguen siendo una preocupación importante en la oncología ortopédica y representan un desafío tan grande como la recurrencia del cáncer, a pesar del potencial preventivo de la cirugía. Las ISQ se pueden prevenir si se toman medidas basadas en la evidencia. El objetivo fue evaluar la frecuencia de infecciones en cirugías ortopédicas oncológicas y los factores de riesgo y marcadores inflamatorios asociados en un hospital de referencia en el estado de Pernambuco. **Métodos:** se analizaron la frecuencia de ISQ, la identificación de microorganismos aislados, los factores de riesgo y el perfil de marcadores inflamatorios Th1 y Th2 (IL-2, IL-4, IL-6, IL-10, TNF e IFN-Y) en pacientes con cáncer musculoesquelético. **Resultados:** se encontraron ISQ en el 9,1% de los pacientes sometidos a cirugía ortopédica. El análisis bivariado reveló que un equipo quirúrgico compuesto por más de cinco miembros (p=0,041) y la necesidad de transfusión intraoperatoria (p=0,012) se correlacionaron con un mayor riesgo de ISQ. La medición de los niveles de proteína C reactiva ultrasensible para evaluar la respuesta inflamatoria después de la ISQ presentó resultados superiores a los valores de referencia para cada muestra, variando de >5 a >200 mg/dl por el método inmunoturbidimétrico. De los niveles de IL-2, INFγ y TNF (Th1) e IL-4, IL-6, IL-10 (Th2), solo la interleucina 6 mostró niveles elevados, entre 6,68 y 58,76 pg/mL. **Conclusión:** el estudio encontró que el equipo quirúrgico con cinco o más miembros y la transfusión el estudio encontró que un equipo quirúrgico con cinco o más miembros y transfusión de sangre fueron factores asociados con el desarrollo de ISQ en cirugía ortopédica en pacientes con cáncer musculoesquelético. Entre los marcadores inflamatorios, la interleucina 6 (IL-6) mostró la mayor correlación con el resultado.

Palabras clave: *Infección del Sitio Quirúrgico. Puntuación de Riesgo. Ortopedía. Cáncer.*

INTRODUCTION

In recent years, the number of surgical interventions to treat cancer has increased throughout the world, reflecting a worldwide increase in the incidence of malignant neoplasias.[1] It is estimated that there will be 625,000 new cases of cancer in the three-year period between 2020 and 2022 in Brazil.[2] Despite the development of less invasive treatment involving medication, surgery remains a fundamental tool in treatment of musculoskeletal cancer.[3]

Surgery is a treatment method of great importance for patients, as it plays a fundamental role in loco-regional control of the disease and in establishing the parameters of the recommended cancer treatment. Surgical site infections (SSI) have been shown to be the most common complication during treatment.[4]

Despite the significant preventive potential of surgery, it is important that SSI are avoided, given that such infections continue to be a major concern in orthopedic oncology and represent a challenge as great as cancer recurrence, with an incidence between 3, 2 and 35.55%. [1,5,6]

The risk of infection may lead to devastating musculoskeletal complications, requiring bone resection and prosthetic use.[4] This complication may also result in physical, social and/or psychological damage to patients, along with longer stays in hospital, increased risk of re-hospitalization, the need for further surgery, the persistence of painful symptoms, the need for antibiotics, possible loss of implants, limb amputation, infections and death [7] thus substantially increase the cost of treatment.[8]

Numerous factors have been associated with the development of SSI. These risk factors are commonly divided into modifiable and non-modifiable factors. Potentially modifiable factors include a pre-operative antiseptic bath in the case of major surgery and/or implant insertion, routine hair removal discontinuation, hospitalization length of less than 24 hours, blood sugar level control immediately prior to and following surgery, smoking, recent history of immunosuppression, obesity and effective infusion of prophylactic antibiotics for up to 60 minutes prior to surgical incision. Non-modifiable factors include advanced age, history of prior infections, and advanced-stage cancer. SSI also tend to be associated with emergency surgery, lengthy surgery, surgery involving large teams, blood transfusion, an skin antisepsis quality in patients and hand hygiene among the care team.[9,10]

Numerous inflammatory markers have been proposed for infection identification, including high-sensitivity and -specificity cytokines, which are considered to be important mediators in the host's response to infection and C-reactive protein levels and are thus used for early identification of infection, along with clinical evaluation and other laboratory examinations.[11]

Considering the greater complexity of the disease, SSI in patients with bone cancer deserve more extensive studies in the scientific community. In addition to the underlying disease-related disorders, the aggressive nature of cancer treatment causes significant immune imbalance, increasing the risk of infection during surgery. Moreover, treating the infection can, in turn, delay or even prevent cancer treatment.[1,7]

The objective was to assess the frequency of infections in oncological orthopedic surgeries and the associated risk factors and inflammatory markers in a reference hospital in the state of Pernambuco.

METHODS

An observational, analytical, cross-sectional study was carried out with 110 individuals of both sexes, of any age, diagnosed with primary or secondary bone cancer and confirmed by histopathological examination and undergoing orthopedic surgery, between July 2019 and July 2020, at the *Hospital de Câncer de Pernambuco*, in Recife, Brazil. Individuals who, upon hospital admission, had skin/soft tissue infection in the topography of the limb to be surgically treated and individuals with benign tumors were excluded. Written consent was obtained from participants through the Informed Consent Form, for cases over 18 years of age, and the Clarified Assent Form, for those under 18 years of age. The study was approved by the Research Ethics Committee of the *Hospital de Cancer de Pernambuco*, CAAE (13514019.2.0000.5205) ethics opinion (3.399.327) in accordance with Resolution 466/12 of the Brazilian National Health Council (CNS).

The collection of clinical and epidemiological, sociodemographic data, such as lifestyle, tobacco use, Body Mass Index (BMI), immunosuppressant use in the last six months, bacterial infection in the last 30 days, presence of SSI, cancer type and cancer site, preoperative hospital stay, surgery duration, antibiotic prophylaxis, preoperative bath, glycemic control, preoperative shaving, degree of contamination, implant insertion, number of surgery participants ≥5, blood transfusion, was extracted from patients' records. Blood samples were collected to assess inflammatory markers. We found the frequency of SSI, identification of microorganisms isolated in blood samples in SSI, risk factors and profile of Th1 and Th2 inflammatory markers (IL-2, IL-4, IL-6, IL-10, TNF and IFN-Y) using the flow cytometry technique up to 48 hours after the diagnosis of SSI using the SPSS (Statistical Package for the Social Sciences), version 21.0 (IBM, Armonk, NY). After diagnosis of SSI in accordance with the criteria of the Brazilian National Healthcare Safety Network, the Centers for Disease Control and Prevention and the Brazilian Health Regulatory Agency (ANVISA - *Agência Nacional de Vigilância Sanitária*), blood samples were collected, centrifuged and stored at -20°C, and then sent to the Marcelo Magalhães Laboratory, for measuring ultrasensitive C-reactive protein levels using the immunoturbidimetric method, and to the Department of Immunology at the *Instituto Aggeu Magalhãe*/FIOCRUZ, to ascertain the IL-2, INFγ and TNF (Th1) and IL-4, IL-6, IL-10 (Th2) cytokine profile by way of flow cytometry using the Cytometric Bead Array (CBA) method.

Clinical data on patients' lifestyle and previous and current medical history included smoking, BMI, immunosuppressant use in the past six months, bacterial infection in the last 30 days, and type and location of cancer. The variables relating to the healthcare process were length of hospital stay prior to surgery, surgery duration, antibiotic prophylaxis, preoperative bath, blood sugar control, hair removal prior to surgery, contamination level, implant insertion, number of team members participating in surgery ≥5, and blood transfusion. Preoperative, transoperative and postoperative variables for patients with a diagnosis of bone cancer following histopathological examination were taken from medical records in the first 24 hours after surgery.

Sample analysis

Identification of micro-organisms was carried out at the study location using an automated method called VITEK® 2 (*bioMérieux Brasil*) for analyzing samples of tissue fragment culture following diagnosis of SSI and duly recorded. C-reactive protein was measured using the immunoturbidimetric latex agglutination method in serum, and the result for C-reactive protein (CRP) concentration in the sample was read using a spectrophotometer. The benchmark value for the laboratory was considered to be 0-5mg/L.

Cytokine examination was carried out using a CBA (BD) kit for quantification of IL-2, INFγ and TNF (Th1) and IL-4, IL-6, IL-10 (Th2) cytokines in a single sample. Six populations of beads with distinct fluorescence intensities were associated with a capture antibody specific to each cytokine, mixed to form CBA and read using the FL3 channel of a FACScalibur (BD) flow cytometer. The populations of beads were viewed using their respective fluorescence intensities: from brightest to least bright. In CBA, cytokine capture beads are mixed with the detection antibody conjugated to phycoerythrin (PE) fluorochrome, and then incubated together with the samples to form a "sandwich assay". Acquisition tubes were prepared with 50 μL of sample, 50 μL of bead mixture and 50 μL Th1/Th2 PE detection reagent (Human Th1/Th2 PE Detection Reagent/1 vial, 4 mL). The same procedure was performed to obtain the standard curve. The tubes were homogenized and incubated for three hours, at room temperature, in the dark. The flow cytometer was calibrated and its channels/filters adjusted prior to sample collection. The standard curve was obtained, using the same kit, subsequent to sample collection. The results were presented in the form of graphs and tables using FCAP Array™ v3.

Statistical analysis

Frequency comparison of SSI involving qualitative variables were carried out using Pearson's chi-squared test or Fisher's exact test, as appropriate. For quantitative variables, non-parametric Mann-Whitney or Student's t test were used, for non-normal or normally distributed data, respectively. The significance level was set at 5%. Statistical analysis was carried out using SPSS, version 21.0 (IBM, Armonk, NY). The SPSS program (IBM SPSS Statistics 24) was used to calculate the sample size, and the sample was calculated with a 5% sampling error, 95% Confidence Interval and 80% test power, using a population prevalence of 154 individuals, thus obtaining a total of 110 samples. Multivariate analysis was carried out using logistic regression, which enables simultaneous assessment of all the effects, taking SSI to be a dependent variable. Independent variables were included in the regression if they presented a p-value < 0.20 on bivariate analysis (age, length of hospital stay, hair removal, pelvic surgery, number of participants in surgery equal to or greater than five and need for intra-operative transfusion). Variables were selected using the stepwise forward method, with a significance level of 0.05 for inclusion of variables, and 0.10, for removal.

RESULTS

During the study period, 110 patients undergoing orthopedic surgical procedures diagnosed with bone cancer were recruited. Of this total, 10/110 (9.1%) had SSI. Most patients were female, five with SSI and 54 without SSI (59%), and the mean age was 31 years of age for patients with SSI and 26 years of age for patients without SSI (Table 1).

Table 1. Distribution of orthopedic oncology surgery patients by age and sex.

Characteristic	SSI				
	Yes (n=10)		Yes (n=10)		p-value
Gender	N	%	N	%	1.00
Female	5	50	54	54	
Male	5	50	46	46	
Age					0.163_t
Mean (SD)	31 (21 – 34)		26 (21 – 32)		

Caption: SD = standard deviation; t = Student's t test

With regard to the previous and current medical history of patients developing SSI, the most frequent type of musculoskeletal cancer was sarcoma (7/10; 70%) in SSI, and 53/100 (53%) individuals did not have SSI, which is considered to be the most prevalent type of tumor in the population under study. The tumor was mostly located in the pelvis or upper limbs (10/10; 100%) in SSI, and 70/100 (70%) individuals did not have SSI, which also reflected the prevalence in the sample as a whole (Table 2).

With regard to lifestyle, (10/100) 10% of individuals included in the sample were current smokers, although none of these developed an SSI. The mean BMI exceeded 25 in 60% of the group of patients who developed SSI. The mean BMI was similar between the SSI and non-SSI groups. Immunosuppressant use <6 months was more frequent in individuals with SSI (1/10; 10%), and the presence of bacterial infection <4 months was 1/10 (10%) in patients with SSI and 97/100 (97%) in patients without SSI. None of these variables were statistically significant (Table 2).

Table 2. Lifestyle and past and current medical history of orthopedic oncology surgery patients.

Biological Characteristics	SSI				
	Yes (n=10)		Yes (n=10)		p-value
Smoking	N	%	N	%	0.735
Yes	0	0	10	10	
No	10	100	90	90	
BMI					0.733t
Mean (SD)	25 (5.7)		25,5 (4.5)		
Immunosuppressant use <6 months					0.201
Yes	1	10	2	2	
No	9	90	98	98	
Bacterial infection <4 months					0.329
Yes	1	10	97	97	
No	9	90	3	3	
Leukocytes					0.650MW
Median	7515		7450		
(P25 – P75)	(6942– 5775)		(6200–9495)		
Cancer type					0.629
Sarcoma	7	70	53	53	
Chondrosarcoma	1	10	10	10	
Other	2	20	37	37	
Cancer site					0.215
Head/neck	0	0	1	1	
Trunk/upper limbs	0	0	29	29	
Pelvis/lower limbs	10	100	70	70	

Caption: SD = standard deviation; P25 = 25th percentile; P75 = 75th percentile 75; MW = Mann-Whitney test; t= Student's t test.

With regard to healthcare-related variables, all surgical procedures were elective, and most were classified as clean (10/10; 100%) in patients with SSI, and 97/100 (97%) patients did not have SSI, with hospital stay before surgery longer than 24 hours in 60% of patients who developed SSI and mean surgery duration from 61 to 120 minutes, with surgery performed by a care team of five or more participants in 80% of cases that developed ISC. Blood glucose was controlled in 3/100 (2.72%) patients without SSI. None of the surgical procedures were preceded by an antiseptic bath and all involved administration of the recommended prophylactic antibiotic, with no available record of duration of administration. Forty percent 4/10 of patients who received an orthopedic implant during surgery developed SSI (Table 3).

Bivariate analysis showed that a number of team members actively participating in the surgery equal to or greater than five (Odds Ratio [OR] 5.524; Confidence Interval [95%CI] 1.116 – 27.348; p = 0.041) and the need for intraoperative transfusion (OR 7.667; 95%CI 1.786 – 32.910; p = 0.012) suggested an association with SSI. The other independent variables had no significant effect on the risk of developing SSI (Table 3).

Table 3. Healthcare process indicators of orthopedic oncology surgery patients.

Indicators	SSI				
	Yes (n=10)		Yes (n=10)		p-value
Length of hospital stay prior to surgery	N	%	N	%	0.165
≤ 24 h	4	40	66	66	
> 24 h	6	60	34	34	
Surgery duration (hours)					0.143_{MW}
Median (P25 – P75)	1.50 (1.50-2.50)		1.25 (1.25-2.25)		
Blood sugar control					1.00
Yes	0	0	3	2.72	
No	10	100	97	97.28	
Hair removal prior to surgery					0.174
Yes	1	10	1	1	
No	9	90	99	99	
Contamination status					0.857
Clean	10	100	97	97	
Potentially contaminated	0	0	1	1	
Contaminated	0	0	2	2	
Implant insertion					0.456
Yes	4	40	26	26	
No	6	60	74	74	
Number of team members in room ≥5					0.041
Yes	8	80	42	42	
No	2	20	58	58	
Blood transfusion					0.012
Yes	4	40	6	60	
No	6	60	94	94	

Caption: P25 = 25th Percentile; P75 = 75th Percentile; MW = Mann-Whitney test.

Factors with p-value <0.20 in univariate analysis included in multiple logistic regression were age, length of hospital stay, hair removal, pelvic surgery, number of team members who participated in the surgery ≥5 and intraoperative blood transfusion. The variables were selected using the forward stepwise method, with a significance level of 0.05 for inclusion of variables and of 0.10 for removal. Multivariate analysis revealed that the need for intra-operative transfusion (OR 8.22; 95%CI 1.81-27.37; p = 0.006) was the only risk factor for developing SSI.

Outcomes for patients with surgical site infection

According to the classification of infections, all were classified as deep. Patients who developed SSI needed to be admitted to hospital again and underwent further surgery, most of them one or two further procedures, three of these involving amputation of the infected limb. The micro-organism most commonly found in cases with a positive culture was *Staphylococcus aureus*, identified in 50%. In two of these ten patients, the surgeon identified signs and symptoms of purulent secretion, indicating infection at the site of surgery despite a negative culture in accordance with the criteria of the National Health Security Network of the Centers for Disease Control and Prevention. The mean length of hospital stay after diagnosis of infection was 11 to 20 days, and 50% of patients required intensive care. No SSI-related deaths were recorded among these patients. Three patients with SSI underwent amputation. During the study, none of these patients with SSI died (Table 4).

Table 4. Characterization of SSI orthopedic oncology surgery patients.

	SSI N=10	
Clinical characteristics	**N**	**(%)**
Classification of SSI		
Superficial	0	0
Deep	10	100
Organ space	0	0
Culture collected		
Yes	8	80
No	2	20
Micro-organism isolated		
Staphylococcus aureus	5	50.0
Klebsiella pneumoniae	2	20.0
Pseudomonas aeruginosa	1	10.0
Negative culture	2	20.0
Retreatment		
Yes	10	100
No	0	0
Number of retreatments		
1-2	7	70
3-4	2	20
≥5	1	10
Length of hospital stay subsequent to SSI		
≤10 days	2	20
11-20 days	5	50
21-30 days	3	30
>30 days	0	0
Need for transfer to ICU		
Yes	5	50
No	5	50
Amputation		
Yes	3	30
No	7	70
Death		
Yes	0	0
No	10	100

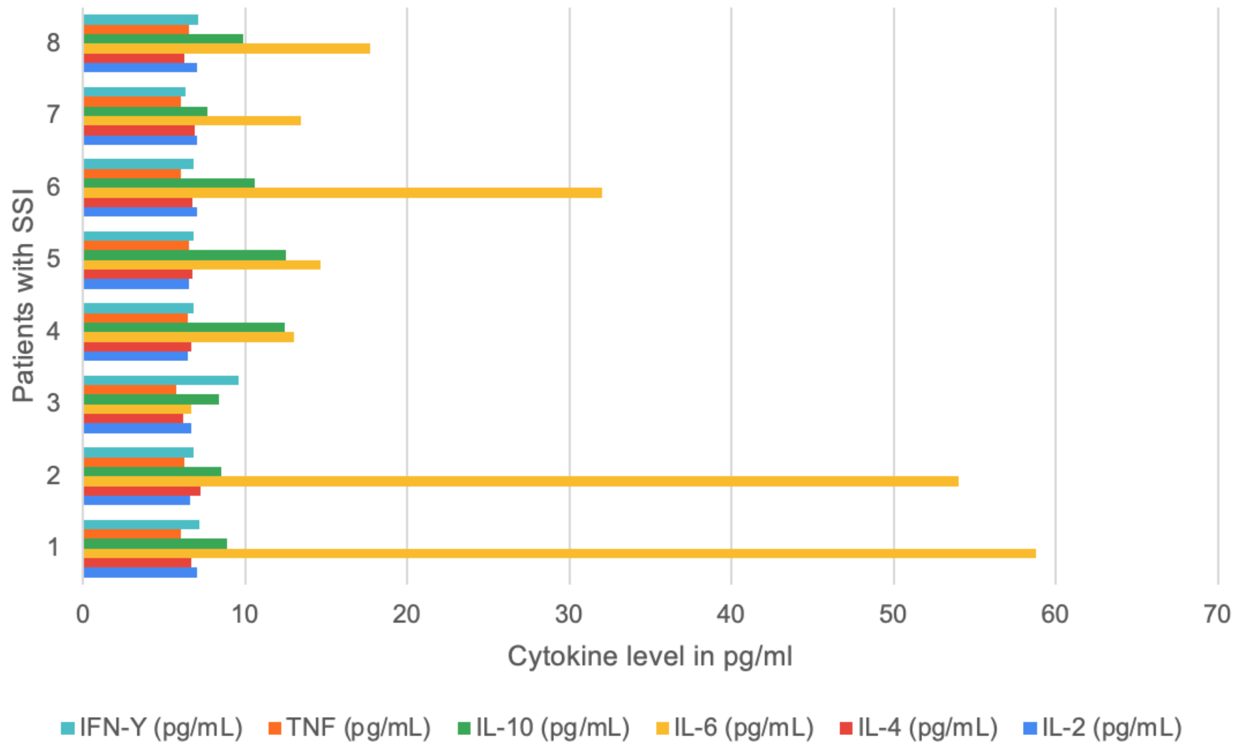

Figure 1. Distribution of cytokine levels measured in pg/ml using the Cytometric Bead Array method.

Inflammatory markers

Ultrasensitive CRP levels, used to assess the immune response after SSI, were >5 mg/dl in 100% of the samples analyzed. Four patients had CRP between 5-25 mg/L (44.44%); two patients had CRP between 26-100mg/L (22.22%); two had CRP between 100-200mg/L (22.22%); and one patient had CRP above 200 mg/L (11.11%).

With regard to cytokines, interleukin 6 (IL-6) presented the highest levels, between 6.68 and 58.76pg/mL. The others did not show any significant variations (Figure 1).

DISCUSSION

The results of this study indicate an incidence of infection of 9.09%, a similar value reported in a study of risk factors for SSI in orthopedic oncology that found that 10.9% of patients developed SSI.[5] On the other hand, the incidence of postoperative infection of deep bone tumors ranged from 3.2% to 10.9%.[1,6] All the procedures included in the study were classified as clean and the incidence of SSI for this category of procedure was higher than the rate considered acceptable (1 to 5%).[9]

The present study found that most cases of SSI involved patients aged over 55 years,[10] who considered belonging to this age group a significant risk factor for SSI, along with overweight and obesity. It also reported obesity to be an independent risk factor for SSI (OR: 1.43; 95%CI: 1.13-2.00) in a study of patients undergoing internal fixation of calcaneal fractures.[12]

The present study also identified that patients receiving a blood transfusion for volume loss were around eight times more likely to have an SSI (OR 8.22; 95%CI 1.81-27.37; p = 0.006) compared to patients with no volume loss. Patients who receive perioperative blood transfusion are at increased risk of developing SSI.[13] In a cohort study with 222 patients undergoing orthopedic surgery with implants, in which those who received perioperative blood transfusion had a three times greater risk of developing SSI compared to the group not submitted to blood transfusion (HR: 3.08; 95%CI: 1.31-7.26,).[8] These findings are supported by a study that found that blood transfusion is a risk factor for developing SSI, being 2.6 times more likely to develop an infection compared to those who did not receive a blood transfusion, in addition to having a longer hospital stay.[14]

The number of colony forming units (CFU) collected in sterile containers in the operating room through microbiological analysis was not significantly associated with the number of individuals in the room.[15] However, the presence of five or more members of the care team at surgery has been an independent risk factor for SSI.[16]

Studies show that implant use in orthopedic oncologic surgery has increased the likelihood of deep infection.[1] General procedures associated with orthopedic diagnosis and treatment, implantation or removal of a musculoskeletal device had the highest prevalence of infections related to implantable orthopedic devices.[17] The study found that 40% of surgeries that led to infection involved the insertion of an implant.

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Smokers are about 6.4 times more likely to develop SSI than non-smokers,[18] despite the fact that in this study none of the patients with SSI reported being a smoker. No patient who developed SSI had a previous or concomitant infection.

Studies show that patients undergoing bone tumor resection at any site followed by reconstruction are risk factors for SSI.[6] Our findings indicate that all infections occurred after surgical interventions involving tumors in the lower limbs and pelvis.

In the present study, length of hospital stay before surgery was greater than 24 hours in 60% of SSI cases, although this number was not statistically significant. Musculoskeletal tumor patients undergoing surgery were at higher risk for SSI.[19]

Surgery duration has been considered an independent risk factor for deep wound infection.[20] The present study found that the mean surgery duration ranged from 85 to 90 minutes, although it was not a risk factor for infections in cancer patients.

Hyperglycemia was associated with a higher incidence of SSI.[21] This study showed the absence of glycemic control in 97.27% of the total sample and 100% of the SSI group.

SSI prevention through an antiseptic bath before major surgeries or implants was not performed in any of the patients, and this can be explained by the lack of an effective protocol at the institution. It was therefore not possible to investigate the effectiveness of this measure.

With regard to prophylactic antibiotics, it is stated in the literature that antibiotic infusion should occur up to 60 minutes prior to surgical incision, in order to ensure serum concentrations sufficient to prevent SSI [1], although no reports of this time being abided by were found in the research.

The microorganism most commonly involved in orthopedic SSI is *Staphylococcus aureus*. The same conclusion was made about infections in orthopedic surgery published between 2015 and 2020.[22] This is corroborated by the findings of the present study.

We found that all patients with SSI were reoperated on and re-hospitalized, requiring intensive care in the most severe cases.

The CRP level, when used with other clinical interventions, has been highly effective in diagnosing SSI and can be used as a criterion to select patients who may need an invasive intervention due to infectious complications,[23] showing a sustained increase in protein levels in cases of postoperative infection. In our study, postoperative levels exceeded the reference level (>5 mg/dl) in all samples.

For cytokines, the study showed that interleukin 6 occurred at high levels in 87.5% of the measured samples. Inflammatory markers such as CRP and IL-6 in lesion fluid hold promise for predicting SSI in the clinic.[24] Serial estimation of postoperative CRP and IL 6 can predict infections and can be used routinely in general surgical practice.[25]

It is not possible to generalize the study findings to other individuals due to the underlying disease character of the population studied. The larger sample size could contribute to a better understanding of the associations studied.

The study found that surgical team with five or more members and blood transfusion were risk factors associated with the development of SSI in orthopedic surgery in patients with bone cancer. Among the inflammatory markers, interleukin 6 (IL-6) showed the highest correlation with the outcome. More studies are needed to determine the degree of modulation of inflammatory responses in this population. Patients who develop SSI require longer hospital stays for adjuvant therapy involving antibiotics and reoperation for infection control and, in some cases, involving amputation.

REFERENCES

1. Miwa S, Shirai T, Yamamoto N, et al. Risk factors for postoperative deep infection in bone tumors. PLoS One. 2017;12(11):e0187438. doi: 10.1371/journal.pone.0187438
2. Instituto Nacional de Câncer José Alencar Gomes da Silva. Estimativa 2020: incidência de câncer no Brasil / Instituto Nacional de Câncer José Alencar Gomes da Silva. – Rio de Janeiro : INCA, 2019. https://www.inca.gov.br/sites/ufu.sti.inca.local/files//media/document//estimativa-2020-incidencia-de-cancer-no-brasil.pdf.
3. Casali PG, Bielack S, Abecassis N, et al. ESMO Guidelines Committee, PaedCan and ERN EURACAN. Bone sarcomas: ESMO-PaedCan-EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2018;29(Suppl 4):iv79-iv95. doi: 10.1093/annonc/mdy310
4. NIHR Global Research Health Unit on Global Surgery. Reducing surgical site infections in low-income and middle-income countries (FALCON): a pragmatic, multicentre, stratified, randomised controlled trial. Lancet. 2021;398(10312):1687-1699. doi: 10.1016/S0140-6736(21)01548-8
5. Anatone AJ, Danford NC, Jang ES, et al. Risk Factors for Surgical Site Infection in Orthopaedic Oncology. J Am Acad Orthop Surg. 2020;15;28(20):e923-e928. doi: 10.5435/JAAOS-D-19-00582
6. Miwa S, Shirai T, Yamamoto N, et al. Risk factors for surgical site infection after malignant bone tumor resection and reconstruction. BMC Cancer. 2019;19(1):33. doi: 10.1186/s12885-019-5270-8
7. Brasil. Agência Nacional de Vigilância Sanitária (ANVISA). NOTA TÉCNICA GVIMS/GGTES/ANVISA nº 02/2021 - Critérios Diagnósticos das Infecções Relacionadas à Assistência à Saúde – 2021. https://www.gov.br/anvisa/pt-br/centraisdeconteudo/publicacoes/servicosdesaude/notas-tecnicas/nt-022021-revisada-criterios-diagnosticos-de-iras-050521.pdf
8. Piednoir E, Robert-Yap J, Baillet P, Lermite E, Christou N. The Socioeconomic Impact of Surgical Site Infections. Front Public Health. 2021; 9:712461. doi: 10.3389/fpubh.2021.712461
9. Prates CG, Stadñik, CMB, Bagatini, A, et al. Comparação das taxas de infecção cirúrgica após implantação do checklist de segurança. Acta Paulista de Enfermagem. 2018;31,2,116-122. doi: 10.1590/1982-0194201800018
10. Houdek MT, Hevesi M, Griffin AM, et al. Morbid Obesity Is

Associated With an Increased Risk of Wound Complications and Infection After Lower Extremity Soft-tissue Sarcoma Resection. J Am Acad Orthop Surg. 2019;1;27(21):807-815. doi: 10.5435/JAAOS-D-18-00536

11. Zheng S, Wang Z, Qin S, Chen JT. Usefulness of inflammatory markers and clinical manifestation for an earlier method to diagnosis surgical site infection after spinal surgery. Int Orthop. 2020;44(11):2211-2219. doi: 10.1007/s00264-020-04567-0
12. Su J, Cao X. Risk factors for wound infection after open reduction and internal fixation of calcaneal fractures. Medicine (Baltimore). 2017; 96(44):e8411. doi: 10.1097/MD.0000000000008411
13. Higgins RM, Helm MC, Kindel TL, et al. Perioperative blood transfusion increases risk of surgical site infection after bariatric surgery. Surg Obes Relat Dis. 2019(4):582-587. doi: 10.1016/j.soard.2019.01.023
14. Al-Harbi SA, Alkhayal N, Alsehali A, Alshaya S, Bin Obaid W, Althubaiti A, van Onselen RE, Al Annany M, Arifi AA. Impact of blood transfusion on major infection after isolated coronary artery bypass surgery: Incidence and risk factors. J Saudi Heart Assoc. 2019;31(4):254-260. doi: 10.1016/j.jsha.2019.06.005
15. Brock-Utne JG, Ward JT, Jaffe RA. Potential sources of operating room air contamination: a preliminary study. J Hosp Infect. 2021;113:59-64. doi: 10.1016/j.jhin.2021.04.020
16. Carvalho RLR, Campos CC, Franco LMC, et al. Incidence and risk factors for surgical site infection in general surgeries. Rev. Latino-Am. Enfermagem 2017, 25:e2848. doi: 10.1590/1518-8345.1502.2848
17. Pirisi L, Pennestrì F, Viganò M, Banfi G. Prevalence and burden of orthopaedic implantable-device infections in Italy: a hospital-based national study. BMC Infect Dis. 2020;20(1):337. doi: 10.1186/s12879-020-05065-9
18. Nolan MB, Martin DP, Thompson R, et al. Association Between Smoking Status, Preoperative Exhaled Carbon Monoxide Levels, and Postoperative Surgical Site Infection in Patients Undergoing Elective Surgery. JAMA Surg. 2017;1;152(5):476-483. doi: 10.1001/jamasurg.2016.5704 Erratum in: JAMA Surg. 2017;152(5):508.
19. Nagano S, Yokouchi M, Setoguchi T, Sasaki H, Shimada H, Kawamura I, Ishidou Y, Kamizono J, Yamamoto T, Kawamura H, Komiya S. Analysis of surgical site infection after musculoskeletal tumor surgery: risk assessment using a new scoring system. Sarcoma. 2014;2014:645496. doi: 10.1155/2014/645496
20. De Gori M, Gasparini G, Capanna R. Risk Factors for Perimegaprosthetic Infections After Tumor Resection. Orthopedics. 2017;40(1):e11-e16. doi: 10.3928/01477447-20161128-01
21. Akiboye F, Rayman G. Management of Hyperglycemia and Diabetes in Orthopedic Surgery. Curr Diab Rep. 2017;17(2):13. doi: 10.1007/s11892-017-0839-6
22. Novato TF, Wilk MMGS, Araújo LT, et al. Perfil de infecções em artroplastia de quadril: uma revisão integrativa, HRJ. 2021;2(10). doi: 10.51723/hrj.v2i10.145
23. Plat VD, Voeten DM, Daams F, van der Peet DL, Straatman J. C-reactive protein after major abdominal surgery in daily practice. Surgery. 2021;170(4):1131-1139. doi: 10.1016/j.surg.2021.04.025
24. Bi X, Li Y, Lin J, Li C, Li J, Cao Y. Concentration standardization improves the capacity of drainage CRP and IL-6 to predict surgical site infections. Exp Biol Med (Maywood). 2020;245(16):1513-1517. doi: 10.1177/1535370220945290
25. Hajong R, Newme K, Nath CK, Moirangthem T, Dhal MR, Pala S. Role of serum C-reactive protein and interleukin-6 as a predictor of intra-abdominal and surgical site infections after elective abdominal surgery. J Family Med Prim Care. 2021;10(1):403-406. doi: 10.4103/jfmpc.jfmpc_1191_20

AUTHORS' CONTRIBUTIONS:

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