












# Evaluation of biopsy results in vertebra compression fractures treated by kyphoplasty

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## Abstract

**Aim:** In the treatment of vertebral compression fractures, kyphoplasty stands out as an effective treatment method that has been performed more frequently in recent years. The etiology of compression fractures varies from patient to patient. Biopsy results taken from the patients during the procedure reflect these differences. We wanted to emphasize the importance of the biopsy procedure performed during kyphoplasty by evaluating the biopsy results.

**Materials and Methods:** The patient files, radiological images and biopsy results of the patients, who were treated with kyphoplasty due to vertebral compression fracture and who had a biopsy performed during this procedure between 2017 and 2019.

**Results:** The total number of operated patients was found to be 201, and the number of vertebrae biopsies was 269. Eighty-three of our patients were male and 118 were female. Of the 269 biopsy results in total, 18 (6.7%) had pathological findings; 3 of them were compatible with osteomyelitis, while the remaining 15 were malignant.

**Conclusion:** Since the biopsy procedure performed during the treatment of vertebral compression fractures with kyphoplasty could be performed safely and provides an opportunity for early diagnosis and treatment, a biopsy requirement for the benefit of patients would be inevitable in all kyphoplasty procedures.

**Keywords:** Biopsy; compression fracture; kyphoplasty

## INTRODUCTION

Balloon kyphoplasty (BKP), which has been frequently used in the treatment of vertebral compression fractures (VCF) in recent years, has become the most effective of surgical procedures with its good clinical results, low morbidity and mortality rates (1). The opportunity of simultaneous biopsy has made this surgical procedure even more preferable. Osteoporosis appears to be the most common cause of VCF by reducing bone mineral density. With the aging of societies, VCF is predicted to appear more frequently in the upcoming years (2). The lifelong overall risk for such fractures is 16% for European women at the age of 50 and 5% for men (3). VCF could also be caused by infection, trauma, underlying benign or malignant neoplasm or metastatic diseases (4).

While the accuracy rate of biopsies performed with BKP varies between 16-92%, this rate reaches 98% with open surgeries (4). However, the complication rate reaching 10% has been reported for open surgeries depending on the localization, whereas such a rate has not been reported for the BKP procedure (4, 5). The most common primary tumors leading to spinal metastasis are lung, breast, and prostate cancer (3). Besides, multiple myeloma was shown to be the most common primary malignant vertebral tumor and non-Hodgkin lymphoma the most common vertebral metastatic tumor (6).

In this study, we wanted to share the results of biopsies performed during BKP procedures and our clinical experience regarding spinal malignancies by presenting the biopsy results of the VCF patients treated with BKP operation in our clinic for 2 years.

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## MATERIALS and METHODS

Preoperative radiological images, patient files and pathology results of the patients who referred to our clinic between 2017 and 2019 were reviewed retrospectively. Patients who had no neurological deficit and agreed to be operated underwent the operation. Outpatient clinical control was recommended at regular intervals to the patients who did not want any surgical interventions.

Upon detecting vertebral compression fracture on the radiogram and computed tomography (CT), magnetic resonance imaging (MRI) was planned for every patient without contraindication. Patients with a hyperdense appearance on spinal imaging on fat-suppressed T1 sequence MRI and those with hypodense on T1 and T2 sequence MRI were included in the operation planning. Besides, the patients of acute trauma were operated as well after the detection of a vertebral compression fracture in spinal CT. If there was a pain complaint in the CT-compatible region taken in patients who could not have an MRI for any reason (such as a cardiac pacemaker, cardiac valve replacement), these patients were also included in the operation planning.

Spinal fractures were classified according to AO/Magerl classification (7), and minimally invasive surgery was performed to A0, A1, A2 fractures. The A3 fracture was included in the study only according to the surgeon's experience and opinion. BKP was not performed to any A4, B, or C-type fractures; those who accepted surgical intervention underwent open surgery while those who did not were recommended only rest. Written surgical consents were obtained from all patients who underwent an operation.

After 6 hours of fasting, patients were operated in the prone position with sedation and local anesthesia and with the support of fluoroscopy. All patients underwent routine minimally invasive surgical procedures (5,8). Before cement injection, a biopsy was taken from all patients by drilling and sent to the pathological examination (9). The patients were discharged within 4-24 hours after the operation and were called for outpatient control after 3 weeks.

For all statistical data, the Mann-Whitney U test and t-tests were used. P values less than 0.05 were considered statistically significant. Statistical analysis of the data was completed with SPSS for Windows, version 15.0 (IBM Corp., Armonk, New York, USA) program.

## RESULTS

In our clinic, a total of 201 patients underwent biopsy with BKP operation. Eighty-three of our patients were male (41.3%) and 118 were female (58.7%). While the mean age of our patients was  $64.4 \pm 16.3$  years, the age range varied between 16-93 years.

Of all patients, 158 cases (59.0%) had post-traumatic lumbar and back pain. One session was performed for each

patient and no more than 5 vertebrae had interventions in this single session. In total, 12 different levels of thoracolumbar vertebrae biopsies (between lumbar-5 and thoracic-6) were performed. The highest number of interventions was made to the first lumbar vertebrae (65 interventions), followed by thoracic-12 vertebrae, which was biopsied 46 times. The total number of intervened vertebrae was found to be 269 (Table 1).

**Table 1. Distribution of Treated Vertebrae**

Treated Vertebra	Procedure (n)
<b>Lumbar(159; 59.1%)</b>	
L5	9
L4	27
L3	22
L2	36
L1	65*
<b>Thoracic(110; 40.9%)</b>	
Th12	46
Th11	25
Th10	9
Th9	9
Th8	8
Th7	7
Th6	6
Total	269

\* The greatest number of interventions was performed on the first lumbar vertebrae

**Table 2. Distribution of patients according to preoperative predisposing diseases**

Predisposing disease	Patients (n)	
Steroid usage	Asthma	4
	Rheumatological disease	4
	Crohn disease	1
	Final	9(4.5%)
	Glioblastoma multiforme(GBM)	1
	Prostate adenocarcinoma	1
	Lymphoma	1
Malignancy	Lung adenocarcinoma	2*
	Breast cancer	3*
	Gynecological adenocarcinoma	3#
	Gastrointestinal adenocarcinoma	6#
	Final	17(8.5%)
Osteoporosis	38(19.0%)	
∅	137(68.0%)	

\* The initial diagnosis of lung adenocarcinoma and breast cancer biopsy was taken after kyphoplasty is performed in our patients was consistent with the first diagnosis(2/201; 0.99%).

# Biopsy results obtained after kyphoplasty in one of our patients, whose initial diagnosis was gastrointestinal adenocarcinoma and gynecological adenocarcinoma, resulted as a plasmacytoma different from their initial diagnosis (2/201; 0.99%)

While 36 (17.9%) of 201 patients admitted to our clinic were diagnosed with severe osteoporosis (Bone Mineral Density < -2.5), 9 (4.5%) had a long-term history of steroid use. Twenty-seven of our patients (13.4%) had a known malignancy before the operation. While biopsy results were compatible with the primary diagnosis in 2 of these patients, a secondary biopsy result was obtained in 2 of our patients independent of their primary diagnosis. No predisposing diseases were detected in the remaining patients (Table 2).

While 18 vertebrae underwent bilateral BKP and biopsy during the procedure, unilateral BKP was applied to the 251 vertebrae. In terms of biopsy results, there was no significant difference between bilateral and unilateral approaches (p=0.986). Afterward, a 10mm balloon was used for 1 vertebra for the BKP procedure, a 15mm balloon was used for 157 vertebrae and a 20mm balloon was used for 111 vertebrae.

Table 3. Distribution of patient and vertebra numbers according to biopsy results		
	Patient (n)	Vertebrae (n)
Osteomyelitis	3	3
Insufficient material	6	17
Plasmasitoma	4	5
Breast cancer	1	2
Malign epithelial tumor	1	1
Chondroid tumor	1	2
Malignancy		
Carcinoma metastasis	2	2
Gastrointestinal system adenocarcinoma	1	1
Lung adenocarcinoma	1	2
Final	11	15
Normal bone healing	181	234
Final	201	269

Because one level is broken in the same session kyphoplasty after biopsies 6 vertebrae, the second level fractures biopsied after kyphoplasty second vertebra, the third level fractures kyphoplasty after the biopsy was taken nine vertebrae biopsy pathological meaning a total of 17 biopsies on inadequate to be inadequate material

Due to the insufficient biopsy material collected with the drill, 17 (6.3%) vertebra biopsies could not proceed into the pathological evaluation. Biopsy results revealed findings reflecting the regular bone healing stages in 234 vertebrae (87.0%). A total of 18 biopsy results (6.7%) were evaluated as pathological (Table 3). When three patients had results compatible with an infection, their infection parameters, radiological imaging, and biopsy samples were re-examined. While the results of 2 patients changed

as the stages of bone healing, 1 patient underwent spinal fusion and debridement operation due to osteomyelitis. After appropriate antibiotherapy, the clinical treatment of the patient was completed.

According to the biopsy results, a total of 15 biopsy results (5.6%) were compatible with malignancy. While the most common malignancy was plasmacytoma with 5 patients (1.9%), it was evaluated as breast cancer (Figure 1), chondroid tumor, lung adenocarcinoma, and carcinoma metastasis in 2 cases each (0.7%). Biopsy results of malign epithelial tumor in one patient and adenocarcinoma of the gastrointestinal tract in one patient were obtained (Figure 2).

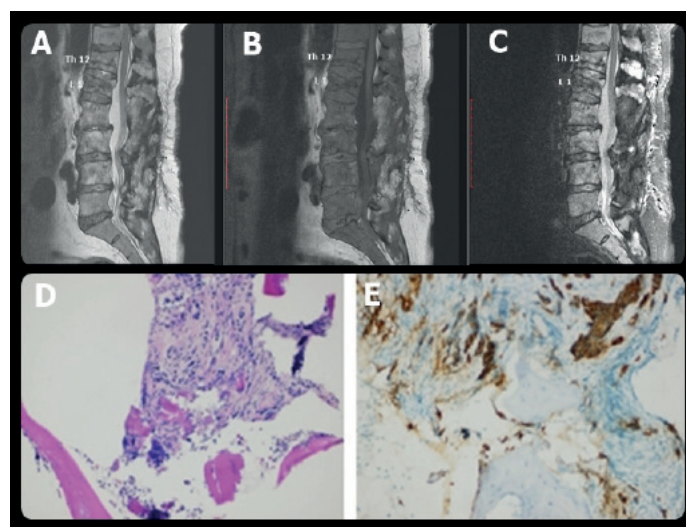


Figure 1. A, T2 sequence sagittal lumbar MRI Th12-L1 hypointense lesion. B, T1 sequence sagittal lumbar MRI Th12-L1 hypointense lesion. C, Stir sequence sagittal lumbar MRI Th12-L1 hypointense lesion. D, Epithelial cell islands in fibrotic stroma between bone trabeculae, Hematoxylin& Eosin 220X. E, Immunohistochemistry indication of primary breast origin, Mammaglobin 220X

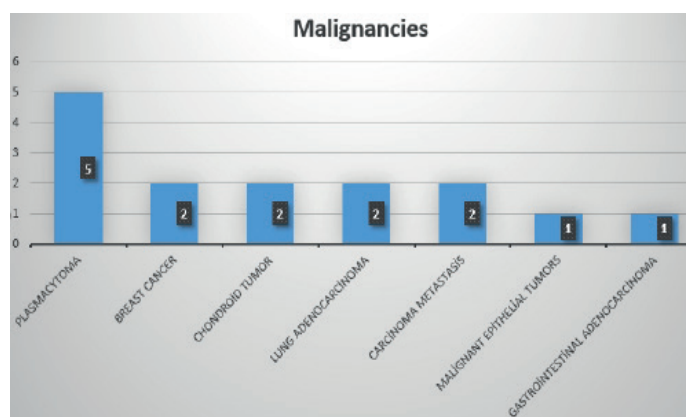


Figure 2. Malignant biopsy results

There were no neuro-motor deficits in the postoperative early and late follow-ups in any of the operated patients. The patients whose biopsy results were compatible with malignancy were referred to the oncology department and provided appropriate treatment.

## DISCUSSION

In the treatment of spinal fractures due to osteoporosis, trauma and tumor metastasis, BKP has become the most common basic surgical method in recent years. The biopsy procedure performed during the BKP stands out as an absolute method when the results are evaluated.

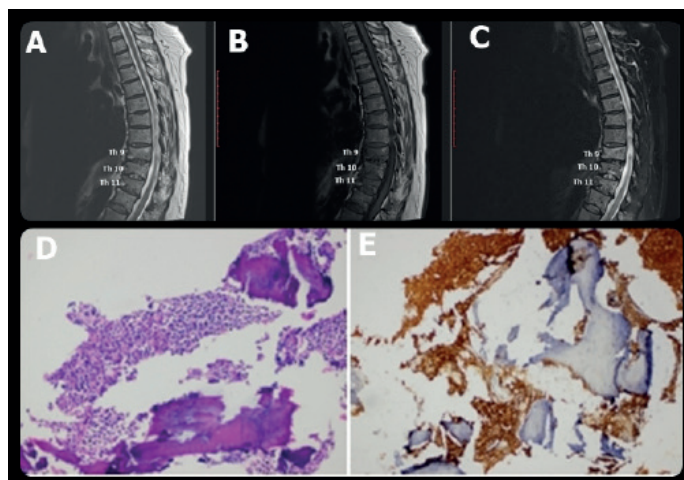
In the study of 97 biopsies performed by Nowak et al. (3), none of any specimen had a biopsy result compatible with an infection, whereas, in the study by Allen et al. (4), the first evaluation of vertebral biopsy in 13/94 (13.8%) was found to be consistent with an infection. Seven of these 13 patients had different stages of bone healing, and a total of 6/94 (6.3%) patients were evaluated as osteomyelitis in the re-evaluation. In our study, 3/269 (1.1%) biopsy results revealed osteomyelitis in the initial evaluation, but when the biopsy results were re-evaluated, 2 of these 3 patients were found to have different stages of bone healing. After the histological, radiological and infection parameters confirmed the diagnosis of osteomyelitis in the other patient (0.3%), the patient underwent a second operation and debridement and stabilization were performed. While Allen et al (4) found a rate of 53.8% for the false infections in patients; we found this rate as 66.6% in our study, similar to the literature.

Different techniques can be applied in the spine biopsies. Biopsy performed via computed tomography (CT) is among the frequently used methods. In a total of 401 biopsy series performed by Lis et al. (10), insufficient biopsy material via CT was taken in 4 cases (1.0%). The rate of insufficient biopsy material is even higher in cases treated with BKP and vertebroplasty (VP). In the literature, there were insufficient material ratios such as 9% (11) and 13.2% (9), whereas, in our study, 17 of the 269 specimens (6.3%) appeared to have insufficient material results. The reason for the low rates of insufficient material results in CT-guided cases is thought that the cases are malignant suspected and that the location of the lesion could be determined by 3D imaging and the opportunity for the biopsy to be taken with a special biopsy needle. However, in minimally invasive procedures such as BKP and VP, a biopsy is routinely performed to all patients and a drill is used for this procedure.

In the literature, there are rates of malignant biopsy results reported between 3.6% and 10.3% in biopsies performed in vertebral fractures treated with VP and BKP (2, 9, 11). In our study, this rate was found to be 5.6% (15/269). Also in the literature, the CT-guided biopsy results of patients with a malignant diagnosis are reported to result as malignant in rates ranging from 32.4% to 89.0% (10). However, in patients who underwent biopsy during treatment with minimally invasive methods due to a vertebral fracture secondary to malignancy, biopsy results corresponding to the initial malignant diagnosis ranged from 2.7% to 7.2% (3, 9, 12). In our study, this rate was found to be 1.0% (2/201), which is slightly lower than the studies in the literature.

In the study conducted by Zhang et al (2), incidental malignant biopsy results were found to be 0.4%. One of these two patients had the result of plasmacytoma and the other metastatic carcinoma. In the 196 cases of Li et al. (13), malignant biopsy results were obtained in a rate of 2.9%, while in the study of Schoenfeld et al. (14), this rate was 6.0% (3/50) and adenocarcinoma, plasmacytoma and lymphoma results were obtained in these three patients. In 78 patient-biopsy studies conducted by Muijs et al (11), 3.8% malignant biopsy results were obtained, 2 of them resulted as plasmacytoma and the other as chondrosarcoma. Ozger et al.(15) in another study performed by incidental biopsy results, it was determined as 1.49%. There was a rate of 3.5% (7/201) in incidental malignant biopsy results in our study. The results of plasmacytoma in 3 patients, carcinoma metastasis in 2 patients, chondroid tumor and malign epithelial tumor metastasis in others were obtained. Another diagnosis of malignancy was known before the operation in 2 of the patients whose biopsy results were reported as plasmacytoma (One of these patients had a diagnosis of gastrointestinal system adenocarcinoma and the other had gynecological adenocarcinoma).

The most common diagnosis is plasmacytoma in spinal metastases (6). Accordingly, in the literature, incidental plasmacytoma is determined in rates varying between 0.7% and 2.0% in biopsy results of vertebral fractures treated with minimally invasive methods (9). In our study, this rate was found to be 1.4%, similar to the literature (Figure 3).



**Figure 3.** A, T2 sequence sagittal thoracic MRI Th9-10-11 hypo-isodense lesion. B, T1 sequence sagittal thoracic MRI Th9-10-11 hypodense lesion. C, Stir sequence sagittal thoracic MRI Th9-10-11 hyperdense lesion. D, Tumoral space consisting of plasmacytoid cells between bone trabeculae, Hematoxylin& Eosin 220X. E, Plasma cell origin with CD38 stain immunohistochemically. CD38 220X

## CONCLUSION

BKP is widely used in VCF patients being the most effective and easy method. Taking a biopsy during the procedure could be applied safely as it does not affect mortality and morbidity. Simultaneously, it allows making

an early diagnosis as it reveals the unexpected and secondary malignancy diagnoses in the patients and increases survival by providing additional treatment and interventions to be started earlier. Therefore, the biopsy step is mandatory in all BKP procedures.

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