

# Management of Stabil Vertebra Fractures in Patients Underwent Liver Transplantation

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## Abstract

**Objective:** Bone mineral density decreases after liver transplantation, and the incidence of vertebral fracture concerning this increase. Vertebral fractures due to bone mineral density increase mortality due to pain, spinal deformity, neurological deficit, and immobility. This study discussed the patients with a vertebral fracture who underwent liver transplantation and received kyphoplasty and conservative treatments to reference clinical treatments.

**Methods:** Among the 2200 patients who underwent liver transplantation between 2002-2020, 65 of the 110 patients underwent spinal Magnetic Resonance Imaging (MRI), and computed tomography (CT) due to back and low back pain had vertebral fractures. Of these 65 patients, 48 were unstable, and 17 were stable vertebral fractures. Patients with stable vertebral fractures were grouped as conservative (n=9) and balloon kyphoplasty (n=8), as these groups compared the following parameters: age, sex, bone densitometry, laboratory findings (Ca, P), vertebral fracture levels, cigarette, high blood pressure, alcohol use, pre-operation, and post-operation 20th-day Visual Analogue Scale scores.

**Results:** While there were no significant differences between the VAS score and the VAS score after 20 days in the patients who received conservative treatment, a significant difference was found between the VAS score and the VAS score after 20 days in the patients who received kyphoplasty.

**Conclusion:** It disrupts patient compliance in treating the primary disease due to pain and immobilization in patients who received organ transplantation, and increases the complications due to immobilization. Therefore, performing kyphoplasty is recommended in symptomatic vertebral fractures that do not require stabilization after organ transplantation regardless of the VAS score.

**Key words:** Liver Transplantation, Osteoporosis, Kyphoplasty, VAS score

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## Introduction

The incidence of vertebral fractures observed in patients who need liver transplantation is higher in the post-transplantation period than the pre-transplantation period. The bone mineral density decreases in the first three months after transplantation in patients who underwent liver transplantation, and it reaches the pre-transplantation level after two years. Thus, fractures after liver transplantation are generally observed within the first two years. Although fractures are observed at different patients' levels, the fractures are often occurred together at more than one vertebrae and rib levels. The incidence of this unification is between 15-27% (1-3).

Although age, sex, type of liver disease, and menopause in female patients are regarded as risk factors for the increase in fractures observed after liver transplantation, no consensus is reached (4). The presence of cirrhosis in diseases requiring liver transplantation increases the risk of osteoporosis two times; thus, the osteoporosis prevalence in cirrhotic patients in the 6th and 7th decades is observed between 12-55% (4, 5). Monegal et al. investigated 58 patients with cirrhosis due to viral hepatitis and reported that the risk of osteoporosis highly increased (6).

Vertebral fractures developed after liver transplantation cause severe pain in patients regardless of etiologic reasons and disrupt the compliance and comfort of the patient in the treatment of the primary disease, with additional complications emerging due to immobilization performed on the follow-up and treatment periods (7). Vertebral fractures due to bone mineral density increase mortality due to pain, spinal deformity, neurological deficit, and immobility. Kyphoplasty and nonsurgical treatments are used in these types of fractures. However, there are differences regarding which treatment to apply. The number of studies on these treatments in patients who underwent organ transplantation is limited. The triple column theory, defined by Denis in 1983, is used in practice in vertebral fractures. Front column; 2/3 anterior part of the vertebral body, middle; the back 1/3 of the vertebral body, the back column contains the other bone structures of the spine. It is considered stable only if there is a fracture in the anterior and posterior column and unstable if there is a middle column fracture with one of these fractures (8). In diagnosis, the presence of hyperintensity in the T2 stir sequence in Magnetic Resonance Imaging (MRI) and the evaluation of the vertebral bone structure in computed tomography (CT) (Figure 1).

This study discussed the patients with stable vertebral fractures who were consulted at the neurosurgery clinic after liver transplantation at the İnönü University Organ Transplant Institute and received kyphoplasty and/or conservative treatment in line with the literature and aimed to be a reference for clinical treatment

## Methods

Among 2200 patients who underwent liver transplantation in the Inonu University Liver Transplantation Institute between 01.01.2002-01.01.2020, 65 of 110 patients underwent T2 stir sequence MRI (Siemens Magneto 3 tesla MRI) and spinal CT (Toshiba Astetion 4 CT) due to back and back pain detected vertebral fractures were. According to Denis' triple column theory, 48 of these 65 patients were diagnosed with an unstable fracture, tumor metastasis, and spinal infection and were not included in the study. Conservative treatment was applied to 9 patients with a Visual Analogue Scale (VAS) score below 5 five among 17 patients with stable vertebral fracture included in the study, and balloon kyphoplasty was applied to 8 patients VAS score above 5.

Patients with stable vertebral fractures were grouped as conservative (n=9) and balloon kyphoplasty (n=8), as these groups compared the following parameters: age, sex, bone densitometry, laboratory findings (Ca, P), vertebral fracture levels, cigarette, high blood pressure, alcohol use, pre-operation, and post-operation 20th-day Visual Analogue Scale scores.

## Statistical analysis

Quantitative data were given as median (min-max) or mean (standard deviation), while qualitative data were given as numbers (percentage). The suitability to normal distribution was assessed using the Shapiro-Wilk test. Mann-Whitney U test, Fisher's exact chi-square, and Wilcoxon paired samples tests were used in the statistical analyses. The statistical significance level was  $p < 0.05$ . IBM SPSS Statistics 26.0 program was used in the analyses.

## Results

The total number of vertebral fractures was 65 (3%). The number of patients with stable vertebral fractures was 17 (0.77%). The number of patients with a stable vertebral fracture who received conservative treatment was 9 (52.9%), while the number of patients who received balloon kyphoplasty (average 4-5 ml cement application was made) was 8 (47.1%). Of the 17 patients, five were female

(29.4%), and 12 were male (70.6%). Of the patients, 13 (76.5%) smoked, and 4 (23.5%) did not smoke. Of them, 11 (64.7%) had a history of DM, and 6 (35.3%) did not. Among the patients, 4 (23.5%) had HT, and 13 (76.5%) did not. The number of patients who used alcohol was 10 (58.8%), and 7 (41.2%) patients did not use alcohol (Table 1).

While the variables of age, DEXA, the lowest CA value, the lowest P-value, and VAS score after 20 days showed normal distribution (Shapiro-Wilk;  $p > 0.05$ ), the variable of VAS score in the first examination did not. The mean age of 17 patients was  $61.00 \pm 9.09$  years, and the mean age of the females was  $60.60 \pm 12.52$  years, and the mean age of the males was  $61.17 \pm 7.94$  years. The mean DEXA was  $-3.19 \pm 0.93$ ; the mean lowest CA value was  $6.74 \pm 0.74$ ; the mean lowest P-value was  $14.59 \pm 7.12$ , and the mean VAS score after 20 days was  $3.82 \pm 2.04$ , and the median (min-max) VAS score in the first examination was 5.00 (4.00-9.00) (Table 2).

Of the patients, 2 (11.7%) had a thoracic vertebral fracture, 9 (52%) had a lumbar vertebral fracture, 6 (35%) had a thoracolumbar vertebral fracture, and 9 (52%) had multiple level vertebral fractures. No costa fractures were detected. 6 (75%) of the patients who received balloon kyphoplasty had multiple level fractures. Six of the patients who were followed up

had a single-level vertebral fracture. No complications occurred in the patients who received kyphoplasty.

No statistical differences were found between the patients who received conservative treatment and/or kyphoplasty in terms of age, DEXA, the lowest CA value, the lowest P-value, and VAS score after 20 days (Mann-Whitney U test;  $p > 0.05$ ) while there was a significant difference in terms of VAS score (Mann-Whitney U test;  $p = 0.001$ ) (Table 3).

No significant differences were found between the patients who received conservative treatment and kyphoplasty in terms of the history of smoking, DM, HT, and alcohol use (Fisher's Exact Chi-Square Test;  $p > 0.05$ ).

While there were no significant differences between the VAS score and the VAS score after 20 days in the patients who received conservative treatment (Wilcoxon Paired Two Sampling test;  $p = 0.472$ ), a significant difference was found between the VAS score and the VAS score after 20 days in the patients who received kyphoplasty (Wilcoxon Paired Two Sampling test;  $p = 0.011$ ).

**Table 1.** Distribution of sex, cigarette, DM, HT, alcohol

Variable	Variable Categories	n	%
Condition	Conservative treatment	9	52.9
	Receiving Kyphoplasty	8	47.1
Sex	Female	5	29.4
	Male	12	70.6
History of Smoking	No	4	23.5
	Yes	13	76.5
History of DM	No	11	64.7
	Yes	6	35.3
History of HT	No	13	76.5
	Yes	4	23.5
Alcohol use	No	7	41.2
	Yes	10	58.8

**Table 2.** Age, DEXA, CA, P, VAS Scores of All Patients

Variables	Mean ± Standard Deviation [Median (Min-Max)]
Age	$61.00 \pm 9.09$ [62.00 (40.00-77.00)]
DEXA	$-3.19 \pm 0.93$ [-3.30 (-4.90--1.40)]
Lowest CA Value	$6.74 \pm 0.74$ [6.80 (5.70-8.00)]
Lowest P Value	$1.62 \pm 0.54$ [1.70 (0.70-2.50)]
VAS Score in the first examination	$6.06 \pm 1.68$ [5.00 (4.00-9.00)]
VAS Score after 20 days	$3.82 \pm 2.04$ [4.00 (0.00-7.00)]

**Table 3.** Age, DEXA, Ca, P, VAS scores between the two groups

Variable	Conservative Treatment Median (min-max) (n=9)	Receiving Kyphoplasty Median (min-max) (n=8)	p*
Age	62 (40-77)	61 (47-69)	0.562
DEXA	-3.6 (-4.2--2)	-2.9 (-4.9--1.4)	0.175
Lowest CA Value	6.8 (5.7-8)	6.85 (5.7-7.1)	0.287
Lowest P Value	1.7 (0.9-2.4)	1.7 (0.7-2.5)	1.000
VAS Score in the first examination	5 (4-6)	7.5 (5-9)	0.001
VAS Score after 20 days	4 (3-7)	4 (3-5)	0.766

\*: Mann-Whitney U test



**Figure 1:** sagittal whole spinal CT on the right, sagittal T2 streak sequence MRI on the left



**Figure 2:** AP and Lateral scoliosis radiographs after kyphoplasty procedure

**Discussion**

The osteoporosis prevalence in cirrhotic patients in the sixth and seventh decades who need liver transplantation is known to be between 12-55% (4, 5).

In line with the literature, the mean age of all patients in the present study was 61.00±9.09, of the patients who received conservative treatment was 62 and of the patients who received kyphoplasty was 61. It is known that chronic liver diseases cause bone loss, and it was revealed that female sex, menopause, long-term alcohol use, cigarette, chronic diseases, immobilization, malnutrition, and low body mass index cause osteoporosis (4, 9). Butin S. et al. conducted a study on 115 patients and found that the risk of vertebral fracture was higher after transplantation (10). The trabecular bone score calculated in DEXA measurements reflects the trabecular structure of the vertebrates. Bone densitometer performed on various patient groups such as low T scores gives information about pre- and post-menopausal kidney disease, diabetes mellitus gives information about the trabecular structure. The lumbar vertebra and thigh bone densitometry screenings are recommended in patients with hepatic cirrhosis regardless of the cause and severity of the disease (11-15). In the present study, the results of T score in bone densitometry were found to be severe osteoporosis (-2.95> T) and are in line with the literature. In our series, the results obtained after age, alcohol, and cigarette use in patients with vertebral fractures are parallel with the literature, and there are no differences between the groups. Female sex is at the forefront in the sex-based evaluation but there is no similar opinion in the literature (4). Male sex is at the forefront of our series. The occurrence of severe osteoporosis explains the multiple levels of fractures. According to Leidig-Bruckner et al., vertebral fractures after transplantation are observed in the lower thoracic and lumbar regions. Vertebral fractures are usually seen at multiple levels and with rib fractures (1-3). Vertebral fractures were most often in the thoracolumbar region in the present study, and the incidence rate of multiple level fractures was 52%, but there was no rib fracture unity.

When considering the vertebral corpus, a 4-6 ml cement application was regarded as fit (16, 17). Approximately 4-5 ml cement application was performed in 8 patients who received balloon kyphoplasty (Figure 2). The treatment protocols applied in the osteoporotic vertebral fractures are resting, analgesia, corset, and kyphoplasty. Studies reported that patients with osteoporotic vertebral fractures did not benefit much from analgesics and that the treatment duration was long. Balloon kyphoplasty performed on these patients is a minimally invasive procedure, and it is an effective method preventing the development of deformity due to providing rapid analgesia and achieving normal vertebral corpus height (18-21).

On the other hand, some studies report that balloon kyphoplasty provided better results only in the first month in the one-year follow-up of the patients and that there is no significant difference in the change in the VAS score at the end of the year compared to the patients who received conservative treatment. Therefore, instead of emergency balloon kyphoplasty, balloon kyphoplasty is recommended in patients who did not benefit from conservative treatment after three weeks (20). The presence of pain due to vertebral fractures and facet degeneration in elderly patients creates difficulties in evaluating pain scales.

It is the reason why the pain is reduced but does not pass completely after kyphoplasty (22). Most of the literature studies present the comparative results of the treatments on osteoporotic vertebral fractures; however, the number of studies on vertebral fractures and organ transplantation is limited. While no significant differences were found between the VAS score and VAS score after 20 days of the patients who received conservative treatment, there was a significant decrease in the post-operative 20th day VAS score of the patients who received balloon kyphoplasty compared to the pre-operation VAS score. This indicates that the pain experienced by the patients who received kyphoplasty significantly decreased

### Conclusions

Osteoporotic vertebral fractures in patients who underwent liver transplantation are limited. Therefore, the management of these vertebra fractures is still controversial. Conservative treatment in patients who received liver transplantation disrupts patient compliance in treating the primary disease due to pain and immobilization and increases the complications due to long-term immobilization. Therefore, we recommend performing balloon

kyphoplasty in the presence of symptomatic vertebral fractures that do not require stabilization after organ transplantation regardless of the VAS score.

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