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Original Article

Scoliosis After Liver Transplantation in Pediatric Patients

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ABSTRACT

Objective: Little is known about the development of scoliosis after pediatric liver transplantation. In this study, we aimed to evaluate the frequency of scoliosis and its relationship with potential risk factors in children after liver transplantation.

Methods: Pediatric liver transplantations (under of age 18) performed between January 2009 and December 2017 at Malatya İnönü University Institute of Liver Transplantation were scanned retrospectively. In the spinal axis, >10° lateral deviations were accepted as scoliosis. The curve patterns were classified according to the Lenke classification.

Results: Among 287 pediatric liver transplantationss, 17 of them were scoliosis (6%). Nine patients were females and eight were males. The median Cobb angle was 12° at the time of diagnosis and then 17° at the last follow-up. According to the Lenke classification, 11 patients had type 5 curve pattern. During the follow-up period (ranging from 1 to 11 years), scoliosis progression was slow and no patient requiring surgical treatment was detected.

Conclusion: We found that the prevalence of scoliosis increased after pediatric liver transplantation, but we do not have any definite information about the cause. Comparable new studies with more patients are needed to make a definitive conclusion in this regard.

Keywords: Liver transplantation, musculoskeletal system, pediatric, scoliosis

INTRODUCTION

Liver transplantation (LT) is the only curative treatment for acute liver failure, and end-stage liver disease.[1] However, in pediatric patients, mortality and morbidity rates after LT are higher than those in adults.[1,2] The surgical techniques and immunosuppressive medication developed in recent years provide satisfactory results. Increasing the quality of life of transplant patients and avoiding the side effects of immunosuppressive drugs have become important issues.[3,4]

During childhood, growth and development are affected by many factors. Rapid development makes muscle and bone tissue more sensitive to external effects. In pediatric cases where the patient's life expectancy is considered, the effects of an organ transplant and immunosuppressive drugs on the musculoskeletal system should be understood and closely monitored.[5] A decrease in bone mineral density may occur due to medical treatment, immobilization, and metabolic bone disease after LT. Additionally, musculoskeletal system pathologies including developmental retardation, osteoporosis, atraumatic fractures, and spinal deformity may occur.[6,7]

Scoliosis is the lateral curvature of the spine in the coronal plane.[8] It is divided into 2 types: structural and non-structural scoliosis. Idiopathic scoliosis is structural scoliosis and is the most common type. Other causes of structural scoliosis are neuromuscular, congenital, trauma, infection, and tumors. Non-structural scoliosis includes scoliosis caused by posture, nerve root irritation, inflammation (such as appendicitis), and lower limb asymmetry.[9,10] There is a strong relationship between congenital heart disease, thoracotomy/sternotomy, and scoliosis. In most cases, scoliosis can be seen in the vertebral column without morphological abnormalities.[11] However, only few studies have been conducted on the development of scoliosis after pediatric LT and the factors that may affect it. Sharing the experiences of high-volume centers will contribute to the literature. In this study, we present the relationship between probable prognostic factors by retrospectively scanning the frequency of scoliosis after pediatric LT.

METHODS

The Ethics Committee of İnönü University approved this retrospective study (Approval No: 2017/8-14). Two hundred eighty-seven patients (under of age 18) who underwent LT at

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Malatya İnönü University Liver Transplant Institute between January 2009 and December 2017 were included in this study. Age, gender, height, weight, pediatric end-stage liver disease (PELD) score (<12 years), model for end-stage liver disease (MELD) score (≥12 years), Child–Pugh score, primary liver disease, transplantation type, medical treatment information, and radiological images of the patients were scanned using the hospital automation system and archived. The inclusion criteria were radiography images for spinal evaluation and at least 1-year follow-up after LT. The exclusion criteria were spinal axis deformity in vertebral column before LT and having comorbid musculoskeletal disease. Routine triple drug immunosuppression with tacrolimus, mycophenolate mofetil, and corticosteroids was applied to pediatric liver transplant recipients in our center. In cases where calcineurin inhibitory toxicity was suspected or antiproliferative effect such as malignancy was desired, everolimus treatment was initiated by stopping or decreasing tacrolimus treatment in the first postoperative month. Vitamin D and calcium supplements were given.

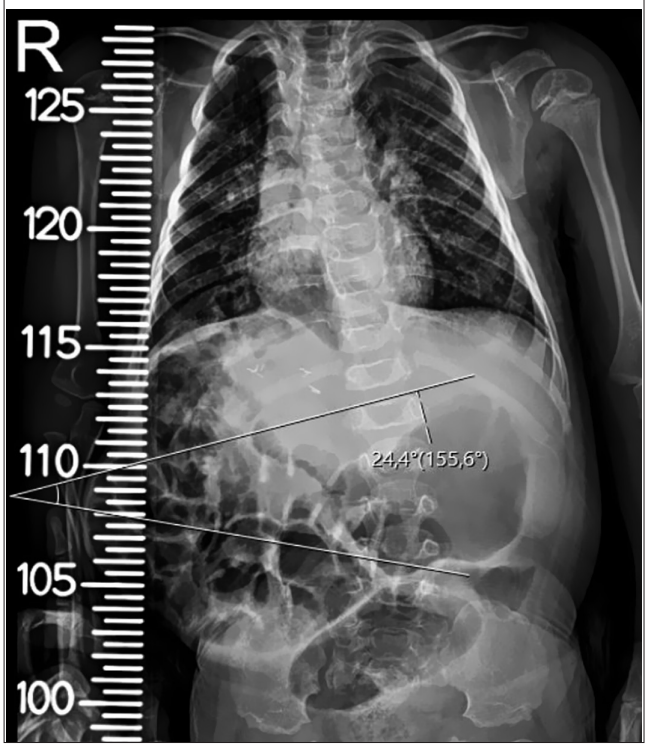
The Cobb method was used to diagnose scoliosis in this study. First, the upper and lower end vertebrae of the curvature were detected. Then, perpendicular lines were drawn to the upper end plate of the upper end vertebra and the lower end plate of the lower end vertebra. The angle formed between these lines was the Cobb angle (Figure 1). In the spinal axis, >10° lateral deviations were accepted as scoliosis.[12] The curve patterns were classified according to the Lenke classification. The main thoracic represents type 1, double thoracic type 2, main thoracic and lumbar curves type 3, triple major (proximal, main thoracic, and lumbar) type 4, thoracolumbar or lumbar type 5, and thoracolumbar/lumbar and main thoracic type 6 curves.[13] Measurements were made via radiograph and computed tomography (CT) by 2 pediatric radiologists with 5 and 10 years of experience, respectively.

Descriptive statistics were calculated and presented as number, degree and percentage. The continuous data were expressed as median (range).

RESULTS

Scoliosis was detected in 17 (6%) of the 287 patients included in the study. Nine patients were females and 8 were males. The diagnosis time for scoliosis was 0.6 years at the earliest and 1.8 years at the latest. The patients were followed up for 1 to 11.2 years after transplantation. The median Cobb angle was 12° at the time of diagnosis and then 17° at the last follow-up. In 13 patients, the angle ranged from 10° to 19°. In 4 patients, the angle was measured between 20° and 30°. According to the Lenke classification, 11 patients had type 5, 4 patients had type 1, and 2 patients had type 3 curve patterns. Liver transplantation indication was end-stage liver disease in 12 patients. Four of them had Wilson disease and 3 had neonatal cholestasis. In 5 patients, LT indication was fulminant hepatitis. Of the LTs performed, 13 were living donor liver transplantation and 4 were deceased donor liver transplantation. The median age was 4.4 years when LT was performed and 47% of the patients (8/17) were in the 0-3 age range. The median PELD score of 12 patients under the age of 12 was 31. The median MELD score of the other 5 patients was 20. The median Child–Pugh score was 10 (n = 17). When scoliosis was detected, 9 patients had incisional hernias (Figure 2). Routine immunosuppression medications were prescribed in 14 patients after LT. In 3 patients, tacrolimus was stopped and everolimus treatment was started. The patients' demographic and scoliosis characteristics are summarized in Table 1.

Figure 1. In a standing posterior–anterior radiograph, Cobb angle was measured at 24° in a 9-year-old male patient.



Main Points

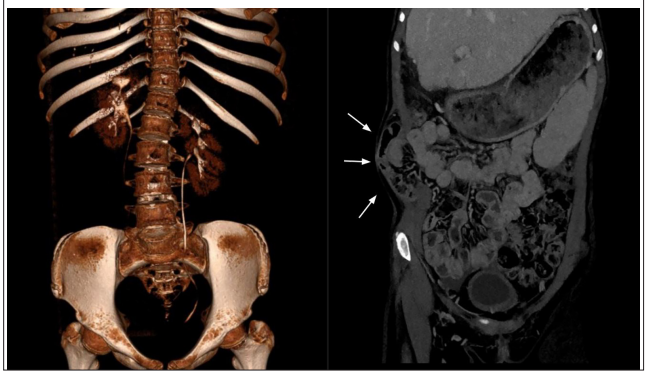
- Liver transplantation (LT) is the only curative treatment for acute liver failure, and end-stage liver disease.
- Musculoskeletal pathologies such as growth retardation, osteoporosis, atraumatic fractures, and spinal deformity may occur after LT.
- It should be kept in mind that scoliosis may develop in pediatric patients after LT, and the patient should be evaluated in this respect.

DISCUSSION

In our study, we found that the frequency of scoliosis increased after pediatric LT. Early age and growth-developmental retardation were noteworthy among possible risk factors. However, scoliosis progression was slow in the follow-up, and no patient requiring surgical treatment was detected.

Scoliosis prevalence in children is 1-3% worldwide.[9] In a study conducted in Turkey, this rate was reported as 2.3%.[14] Structural

Figure 2. A 10-year-old male patient had left-facing scoliosis at the lumbar level on volume-rendered CT image, and on coronal plane CT image, incisional hernia (white arrows) was observed. CT, computed tomography.



scoliosis is more common than non-structural scoliosis. It occurs most often in the adolescent period, and the vast majority of cases are idiopathic. Non-structural scoliosis is rarely seen.[15] The rib cage plays an important role in keeping the spine upright and balanced.[16] Large surgical procedures in this area can lead to unstructured scoliosis. Some studies report the development of scoliosis in children who underwent a thoracotomy/sternotomy.[11]

Little is known about the development of scoliosis after pediatric LT. One study demonstrated that the prevalence of scoliosis increased after a solid organ (heart, liver, kidney) transplantation. The study found that scoliosis after LT did not reach serious degrees. The results of the present study were similar. However, we do not have certain information about why scoliosis increased after pediatric LT. Factors leading to this condition may be impaired liver function, immunosuppressive therapy, or growth hormone therapy (GHT). Additionally, incisional hernia and pain can lead to posture disorder, causing scoliosis. Rapid growth and development during childhood makes bone tissue vulnerable.[17] Therefore, even the smallest risk factors can lead to pathological consequences.

Pre-LT, fat-soluble vitamin levels are generally low in children with end-stage liver disease. This is often caused by intestinal absorption disorders due to bile deficiency. Also, the activation of vitamin D in the liver is impaired. For these reasons, musculoskeletal system problems such as growth-development retardation, bone quality deterioration, and sarcopenia can be seen. The intrinsic support structures of the spine are the vertebrae, discs, and intraspinal-erector spinal muscles. Impairment in liver function negatively affects these spinal support structures. The therapeutic effect of LT can usually take 2 to 3 years.[7,18,19] All these problems may lead to an increase in the frequency of scoliosis after LT. Additionally, scoliosis was detected in all patients within the first 2 years after LT. This demonstrates that scoliosis develops before the therapeutic effect of LT is complete. Children receive long-term immunosuppressive therapy after LT.

Table 1. Patients' Demographic and Scoliosis Characteristics

Variables (n=17)	Number/Degree (Percentile/Range)
Age (at transplantation), median, year	4.4 (0.8–15.5)
0–4 years	9 (54%)
5–12 years	4 (23%)
13–18 years	4 (23%)
Gender	
Female	9 (53%)
Male	8 (47%)
Height, median, cm	88 (58–163)
Weight, median, kg	12 (5–60)
Height percentiles < 5th	10 (59%)
Weight percentiles < 5th	9 (53%)
PELD score, median (n=12)	31 (13–44)
MELD score, median (n=5)	20 (10–21)
Child–Pugh score, median	10 (7–13)
Primary liver disease:	
Fulminant hepatitis	5 (29%)
Wilson's disease	4 (23%)
Neonatal cholestasis	3 (18%)
Biliary atresia	2 (12%)
Cryptogenic hepatitis	2 (12%)
Autoimmune hepatitis	1 (6%)
Type of transplant:	
LDLT	13 (77%)
DDLT	4 (23%)
Cobb angle (last), median	17° (12°–29°)
10°–19°	13 (77%)
≥20°	4 (23%)
Lenke type	
Type 5	11 (65%)
Type 1	4 (23%)
Type 3	2 (12%)
Time to diagnosis after LT, median, year	1 (0.6–1.8)
Follow-up after LT, median, year	5 (1.0–11.2)

PELD, pediatric end-stage liver disease; MELD, model for end-stage liver disease; LDLT, living donor liver transplantation; DDLT, deceased donor liver transplantation; LT, liver transplantation.

Immunosuppressive agents, especially glucocorticoids, have many side effects on the skeletal system that negatively affect quality of life, including osteoporosis and fractures.[6] Glucocorticoids affect calcium absorption–excretion, parathormone level, and skeletal growth factors, directly reducing bone formation and increasing destruction. Tacrolimus, another immunosuppressive agent, prevents osteoclast formation and causes

osteoporosis.[20,21] These results suggest that immunosuppressive therapy is a factor that can cause scoliosis after LT. Therefore, the dosage and duration of the use of these drugs should be closely monitored. A more careful physical examination of the vertebral column should be performed to detect the possible development of scoliosis.

Incisional hernia is a frequent complication seen in 4-20% of patients after LT. Immunosuppression with end-stage liver disease, corticosteroid, and mycophenolate mofetil or sirolimus have significant effects on the development of incisional hernia.[22] In our study, 9 of the 17 patients with scoliosis had incisional hernias. The development of an incisional hernia may have caused a postural disorder in pediatric patients, leading to the development of co-sided scoliosis. Additionally, pain control after surgery is an important issue. The pain in the operation area may have triggered the formation of scoliosis with a similar posture disorder. Therefore, postoperative wound care and pain control should be performed carefully.

Physical examination for scoliosis should be performed with the patient completely naked in a bright room. The posture should be carefully examined from the front and side. The findings vary according to the severity of the deformity. The symmetry of the shoulders and nipples should be examined.[16] The basic imaging method in the diagnosis and evaluation of scoliosis is a standing radiograph. When considering a bone or neurological cause for scoliosis, CT or magnetic resonance imaging is used. It can also be used in planning, before CT scoliosis surgery.[23] In post-LT follow-up, CT is frequently performed, with different indications. In CT images, the spine and intra-abdominal organs can be evaluated. However, in the supine position, spinal rotation can be corrected spontaneously up to 30%.[24,25] Therefore, especially in cases with a low Cobb angle, false results may occur. Diagnosis and follow-up of patients with suspected scoliosis should be done by standing radiograph.

There were some limitations in our study, the most important being that we could not include physical examination findings of patients because this was a retrospective study. Additionally, as the side radiographs of all patients were not available, kyphosis evaluation could not be performed. In future prospective studies, it would be more appropriate to handle scoliosis in all aspects, clinically and radiologically. Another limitation was that our study was based on a single-center experience and a relatively small sample size.

CONCLUSION

In conclusion, although we could not find any specific risk factor for scoliosis development, we found that the prevalence of scoliosis after pediatric LT was higher than that in the general population. When following up with pediatric LT patients, caution should be exercised in terms of scoliosis, and a standing posterior–anterior radiograph should be taken when necessary. More patients are needed to make an exact conclusion in order to evaluate with comparable studies.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of İnönü University (Decision No: 2017/8-14).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

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