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Surgical correction of spinal deformities after solid organ transplantation in childhood

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Abstract A review of the current literature reveals no systematic analyses of the results of surgical correction of spinal deformity after pediatric organ transplantation. We therefore evaluated clinical and radiographic outcomes of spinal deformity correction after solid organ transplantation in childhood and adolescence. All 211 cases of heart, liver, and kidney transplantations performed in children in our country were reviewed. Six patients had undergone surgical correction of spinal deformity at a mean age 14.6 (range 12–17) years. Clinical data of the patients were evaluated. Radiographs of the whole spine were taken preoperatively, immediately after, at 2-year, and final follow-up visits. The Scoliosis Research Society (SRS) questionnaire was completed and a physical examination was performed at the final follow-up visit. The mean follow-up after spinal surgery was 4.9 years (range 2–7.6 years). Four patients developed scoliosis after organ transplantation without any evidence of scoliosis prior to organ transplantation. One patient with congenital scoliosis was operated on after kidney transplantation. One boy had osteoporosis and severe local kyphosis due to vertebral compression fractures. Four patients underwent

anterior and posterior surgery, two posterior only. The mean preoperative Cobb angle of the thoracic curve was 54° (range 42–69°) in the patients with scoliosis. The postoperative values were 30° (26–38°) immediately after instrumentation and 39° (34–42°) at the final follow-up visit. The patient with vertebral compression fractures and progressive kyphosis had 70° curve before surgery, 23° immediately after the operation, and 60° at the final check up. The mean total score on the SRS questionnaire was 95.5 (range 90–101). There is a relatively high incidence (2.8%) of spinal deformities needing operative treatment after solid organ transplantation. Possible etiologies for spinal deformities are growth disturbance and muscle weakness due to the basic disease. The other important factors are related to immunosuppressive medication, especially glucocorticoids needed after transplantation. Primary correction of these deformities was satisfactory, but during follow-up, a certain amount of recurrence of the curves was evident. Poor bone quality may explain some of the loss of correction.

Keywords Spinal deformity · Solid organ transplantation · Spinal surgery

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Introduction

Organ transplantation is an accepted therapeutic modality for children and adolescents with end-stage organ failure. More than 2,000 pediatric transplantations are performed each year worldwide. Improvements in surgical techniques, peri- and postoperative care, immunosuppressive medication, and diagnosis and treatment of rejections and infections have contributed to the current high rate of patient and graft survivals [3, 22, 32]. Quality of life and avoidance of the side effects of the medication have become major issues in the management of these patients.

There are a number of factors which may compromise bone quality in children undergoing transplantation: metabolic bone disease especially in kidney and liver patients, immunosuppression, and immobilization [11]. The incidence of fractures after transplantation is not well documented in children [11]. An association between congenital heart disease and scoliosis is well established, and most of these cases involve idiopathic scoliosis without any morphological abnormality in the vertebral column [2, 4, 6, 13, 28]. These curves usually develop quite early and are very severe, requiring surgical treatment [4].

A review of the current literature reveals no systematic evaluation of the results of surgical correction of spinal deformity after organ transplantation in childhood. There are two case reports of spinal deformity correction after solid organ transplantation. Dunn and Aiona [14] described instrumentation and spondylodesis in a case with idiopathic scoliosis after kidney transplantation, and Ceroni et al. [9] a similar case after heart transplantation.

The aim of the present study is to describe the results of surgical correction for spinal deformities in pediatric transplant patients with different etiologies: One case with osteoporotic vertebral fractures due to immunosuppressive medication, one with congenital scoliosis, and four related to basic disease and organ transplantation without any previous evidence for scoliosis.

Materials and methods

Patients and medication

During the period of 1986–2002, 211 children and adolescents (age below 18 years at the time of transplantation) had survived after kidney, liver, or heart transplantations in Finland. The operations and all posttransplant surgical treatments were performed at the Hospital for Children and Adolescents, University of Helsinki, Helsinki, Finland. Retrospective review of the patient records revealed that six children with a mean age of 14.8 (12–17) years had undergone surgical

correction of spinal deformity (Table 1). None of the six children had been treated conservatively with a brace prior to surgical treatment. The mean follow-up time after spinal surgery was 4.9 (2–7.6) years. Of all 211 transplanted children, 196 (93%) have been screened for rib hump, and those with clinically significant hump (over 6°) underwent standing posteroanterior radiograph of the spine. Forty three (21.9%) of the patients had scoliosis greater than 10°, and 21 (10.7%) of them had curves greater than 20° [21].

After transplantation, all patients received triple drug immunosuppression with cyclosporine (CsA), methylprednisolone (MP), and azathioprine [31]. CsA dosing was based on the trough blood concentrations. The goal was 300–400 µg/l during the first weeks. The doses were then slowly reduced to attain trough levels of around 100 µg/l at 1 year and thereafter. MP was first given 3 mg/kg/day and was then tapered to 0.25 mg/kg at 1 month, and to 0.37 mg/kg every other day after 3 months (kidney transplantation) or after 6 months (liver and heart transplantation). After the first year, MP was given every other day with a dose of 0.1–0.3 mg/kg. Azathioprine was first given 2 mg/kg/day and was reduced to 1 mg/kg/day after 2 weeks, and increased to 1.4 mg/kg/day at 3 months (kidney TX) or 6 months (liver and heart TX). All patients received calcium supplementation (500 mg/day) after transplantation, but none had received bisphosphonates or calcitonin before or during follow-up period.

Study design

The study design was a retrospective follow-up study. Age, sex, body mass index, diseases leading to transplantation, number of acute rejections, timing of transplantation, and immunosuppressive medications were recorded from patients' clinical files. Follow-up physical examinations were performed by an independent observer (I.H.). Standing posteroanterior and lateral radiographs of the whole spine were taken preoperatively, immediately after surgery, 2 years postoperatively, and at the final follow-up visit. Bending X-rays were obtained preoperatively to evaluate the curve stiffness. The Scoliosis Research Society (SRS) questionnaire [16] was mailed to the patients with the exception of patient no. 5 at the same time as the invitation to participate in the study.

Operative technique and postoperative treatment

'One-stage posterior correction of the deformity and instrumentation was performed in two patients.

Table 1 Demographic data, radiologic data, instrumentation, and follow-up period

Patient no.	Age/sex	Transplantation (basic disease)	Deformity	Treatment	Deformity postop/follow-up	Follow-up (yrs)
1	16/F	Heart (dilated cardiomyopathy, congenital muscle disease)	Scoliosis (major thoracic 69°, minor lumbar 51°)	Anterior release, discectomy Th V–Th XI; posterior instrumentation and spondylodesis (Colorado)	Thoracic 38°/38°, lumbar 37°/31°	6.5
2	17/M	Heart (restrictive cardiomyopathy, congenital muscle disease)	Scoliosis (major thoracic 59°, minor lumbar 44°)	Anterior release, discectomy, spondylodesis Th VIII–Th XII; posterior instrumentation Th III–L III and spondylodesis (Colorado)	Thoracic 26°/42°, lumbar 33°/45°	5.4
3	12/M	Heart (restrictive cardiomyopathy, Noonan syndrome)	Scoliosis (major thoracic 46°)	Anterior release, discectomy, spondylodesis Th VI–Th XI; posterior instrumentation Th II–Th XII and spondylodesis (USS pediatric)	Thoracic 26°/38°	4.0
4	12/M	Liver (bile duct atresia, two liver grafts)	Scoliosis (major, left thoracic 56°, minor lumbar 27°)	Anterior release, discectomy spondylodesis Th VI–Th XI; posterior instrumentation Th III–Th XII (Harrington–Luque)	Thoracic 28°/41°, lumbar 15°/22°	7.6
5	13/M	Kidney (polycystic kidneys, spastic diplegia, diastematomyelia)	Congenital scoliosis (upper thoracic 42°, lower thoracic 38°, lumbar 26°)	Posterior instrumentation Th II–LI and spondylodesis (Colorado)	Upper thoracic 30°/34°, lower thoracic 30°/37°, lumbar 15°/29°	2.0
6	16/M	Kidney (Prune-Belly)	Kyphosis 70° (fractures of Th XI–Th XII)	Posterior decancellation osteotomy instrumentation Th IX–LI and spondylodesis (Colorado)	Kyphosis 23°/60°	4.0

Anterior and posterior surgery was carried out in four. Anterior operation included multilevel discectomies, cutting the anterior longitudinal ligament, and intercorporeal spondylodesis with autologous rib bone grafts. Correction of scoliosis was performed with two Harrington distraction and compression rods with sublaminar wires in one patient. Instrumentation with selective distraction and compression was used in four patients (Colorado in three cases, USS pediatric in one) (Figs. 1, 2, 3). One patient underwent posterior subtraction osteotomy at the apex of the kyphosis with transpedicular fixation and spondylodesis (Figs. 5, 6, 7). Posterior arthrodesis included decortication of laminae, opening of facet joints, and use of autologous bone grafts from spinous processes and allogeneous morselized bone grafting. During the operations, somatosensory or motor evoked potential monitoring, or wake-up test was used. To diminish allogeneic blood transfusion, cell saver was used.

The patients were treated in ICU for 1–2 days postoperatively. All patients with scoliosis were allowed to walk on the third or fourth postoperative day. The mean stay in hospital was 18 (12–22) days. The patient with severe thoracic kyphosis wore an extension brace (TLSO) for 3 months postoperatively. All patients received intravenous prophylactic antibiotics (cefuroxime

Fig. 1 Right thoracic scoliosis (69°) with left compensatory lumbar curve (51°) in a 16-year-old female 3.5 years after cardiac transplantation (patient no. 1 in Table 1)

Fig. 2 Immediate postoperative radiograph after anterior discectomy, release, spondylodesis, and posterior instrumentation shows a correction of 49% for thoracic and 35% for lumbar curve

or clindamycin) preoperatively. Immunosuppressive medication was given intravenously during the immediate perioperative period.

Physical examination

At final follow-up, a systematic physical examination including neurological examination of the lower extremities was performed. Leg length discrepancy was evaluated clinically and if necessary by radiographs. Waist asymmetry was assessed subjectively: yes or no. The degree of rib hump was measured with a scoliometer [8].

Radiographic evaluation

Standard standing posteroanterior and lateral radiographs of the entire spine were obtained. The thoracic and lumbar curves were measured using the Cobb technique [10]. Spinal balance was determined as the

horizontal distance of the spinous process of C7 from the center sacral line measured in millimeters. Thoracic kyphosis and lumbar lordosis were measured from the lateral views [10]. The stability of the instrumentation hardware was evaluated too. Pseudarthrosis, vertebral subluxation (posterior, anterior, or lateral) as well as degenerative changes of the discs and facet joints of the free vertebrae were recorded.

Questionnaire

The SRS questionnaire [16] was translated into Finnish and was mailed to all patients except patient no.5. This translated questionnaire has been previously validated in Finnish, and we have evaluated the subjective outcome

Fig. 3 A period of 6.5 years after primary procedure shows no loss of correction and a good balance

of over 400 young patients operated for scoliosis or spondylolisthesis using this questionnaire [17, 18, 20, 30]. The 24 questions give a maximum score of 120, meaning a highly satisfied and asymptomatic patient. The questionnaire was completed by the patients at home and returned at the follow-up visit. The answers were verified during the physical examination.

Definitions

Subluxation of lumbar vertebrae was defined as displacement of the vertebral body in the sagittal or coronal plane by more than 2 mm [12]. Lower extremity length discrepancy was recorded when it exceeded 5 mm. Narrowing of a disc space was noted when it was less than 50% of an adjacent normal disc space [34]. Spinal imbalance was recorded when the horizontal distance of the spinous process of C7 from the center sacral line exceeded 20 mm.

Ethical aspects

The written informed consent of all participants was obtained. The study was approved by the Ethics Committee of the hospital where it was conducted.

Results

Four cases developed scoliosis after organ transplantation without earlier history of spine problems. Two of them had congenital muscle disease with cardiomyopathy (patients 1 and 2 in Table 1). One had Noonan syndrome with restrictive cardiomyopathy

(patient 3). The fourth patient had had two liver transplantations due to congenital biliary atresia (patient 4). He had received large amounts of MP due to chronic rejection of the first liver graft. One boy developed severe osteoporosis and local kyphosis due to vertebral compression fractures at the level of Th XI–Th XII. He had Prune-Belly syndrome with renal dysplasia and muscular defect of the abdominal wall (patient 6). His lumbar spine (L1–L4) bone mineral density was 0.953 g/cm² (Hologic 4500A scanner, Waltham, MA), and respective age and gender specific z-score −1.7 at the time of deformity correction. He did not receive bisphosphonates, because his bone mineral density values were within normal limits. One patient with congenital scoliosis due to Th V hemivertebra was operated on after kidney transplantation (patient 5). He had also diastematomyelia and paraparesis, and neurosurgical liberation of the filum terminale was carried out prior to scoliosis surgery.

The type of the scoliosis was considered as idiopathic in three patients (nos. 1, 2, and 4 in Table 1), one had congenital deformity (patient 5), and the curve of the patient no. 3 resembled neurogenic type of scoliosis. The neuromuscular component of the disease was mild in all patients and was associated with cardiomyopathy in patients 1 and 2 (Table 1).

Four patients had anterior and posterior spinal surgery, and two patients posterior only (Table 1). Patients with idiopathic-like scoliosis (patients nos. 1–4) underwent bending radiographs preoperatively. In them, the major curve reduced from a mean of 58° (range, 46–69°) to a mean of 46° (31–55°).

The mean blood loss during the operations was 1,900 ml. Because of the osteoporotic bone, and to avoid loosening of the implants, maximal correction of the deformities during instrumentation was not done.

Fig. 4 Mean scoliosis curve magnitude pre- and postoperatively. *Closed circles* indicate thoracic curve and *open circles* lumbar curve. 1 preoperatively, 2 primary correction, 3 at 2-year follow-up, and 4 at final check

Fig. 5 a, b Severe local kyphosis (70°) due to Th XI and XII vertebral compression fractures 4 years after kidney transplantation in a 16-year-old boy with Prune-Belly syndrome (patient no. 6 in Table 1)

Radiographic results

Individual deformities, Cobb angles and instrumentations used are shown in Table 1. The mean (range) correction of the major curve in bending radiographs was 25% (7–33%). The mean Cobb angle of the instrumented thoracic curve was 54° (range 42 – 69°) before surgery, 30° (26– 38°) immediately after, 34° (31– 38°) at the 2-year follow-up, and 39° (34– 42°) at the final follow-up visit in the five patients with scoliosis (Table 1, Figs. 1, 2, 3). The mean lumbar curve was 30° (0– 51°) preoperatively, 20° (0– 37°) immediately after operation, 26° (0– 59°) at the 2-year follow-up, and 25° (0– 45°) at the final follow-up (Fig. 4). The mean number of the instrumented vertebrae was 11.8 (range 10–13). The patient with vertebral fractures had a thoracic kyphosis of 70° before surgery, 23° immediately after, 45° at the 2-year follow-up, and 60° at the final follow-up visit. Junctional kyphosis and loss of correction occurred in this patient (Figs. 5, 6, 7).

The mean thoracic kyphosis in patients with scoliosis was 28° (4– 52°) preoperatively and 33° (21– 50°) at the final follow-up visit. Similarly, the lumbar lordosis averaged 53° (44– 69°) preoperatively and 46° (35– 58°) at the final follow-up. None of the patients had radiographic

evidence of spinal imbalance, lateral subluxation, or degenerative changes at the final follow-up visit.

Clinical results

Three patients had waist asymmetry and two leg length discrepancy of 15 and 20 mm, respectively. The mean magnitude of the thoracic rib hump measured with scoliometer at the final follow-up was 12° (6– 16°) in patients with scoliosis. Neurological examination of the lower extremities was abnormal in one patient with congenital scoliosis and paraparesis, which status was already noted after the neurosurgical operation.

SRS questionnaire

The mean total SRS questionnaire score averaged 95.5 (range 90–101). None of the patients reported back pain often or very often (SRS #6). Four patients were satisfied with the results of surgery (SRS #22), and all would choose surgery definitely or probably again with the same diagnosis (SRS #24).

Fig. 6 Immediate postoperative radiograph after Th XI posterior decancellation osteotomy and posterior instrumentation shows a correction of 67%

Complications

All wounds healed *ppi* and no infections were recorded. There were no cardiovascular complications either.

Discussion

Spinal problems in patients after solid organ transplantation have not been studied in depth. Scoliosis requiring operative treatment represented 2.8% of the whole pediatric transplant population in our series. The occurrence of spinal deformities needing operative treatment is relatively high if compared with previously published data from our normal population [25]. Scoliosis was associated with the basic disease in four patients who have had muscular disease from birth, two patients with probable mitochondrial disease, one Prune-Belly syndrome, and one Noonan syndrome. Myopathy is not a typical sign of this disorder but abnormal histopathological changes in striated musculature have been reported in individual cases of Noonan syndrome [7]. One patient had congenital scoliosis. The sixth patient had biliary tract atresia with no known muscular involvement. In his case, high doses of MP and growth disturbance may have enhanced the

Fig. 7 A period of 4.0 years after primary correction shows development of junctional kyphosis and loss of correction to a 60° kyphosis

development of scoliosis. Whether the spinal deformity is mainly related to the underlying disease or the factors associated with the organ transplantation is not fully known. It has been shown that growth disturbances occur in patients who have had solid organ transplantation [31]. On the other hand, abnormal growth is also due to the medication in these patients.

In spite of the improvements in surgical techniques and spinal instrumentations, corrective surgery for spinal deformities remains difficult and has the potential for serious complications. In children with organ transplants these risks are even higher. The patients need their daily immunosuppressive medication also perioperatively [11, 14], which may result in delayed wound healing and increased risk of postoperative infections [9]. In our series, these problems, however, were not observed. Most transplant patients receive small doses of glucocorticoids which can cause osteoporosis that weakens the bone quality and hence complicate the fixation. Osteoporotic bone increases the risk of perioperative fractures and thus bleeding. The mean blood loss during posterior surgery was 1,900 ml, which was slightly higher than in spinal deformity surgery in our hospital on average (data not published).

It has been suggested that an anterior approach is contraindicated to avoid re-entering the previously operated pleural cavity in patients with heart transplant [9]. Coran et al. [13] reviewed the results of spinal fusion in patients with congenital heart disease. In their series

of 74 patients, anterior approach did not increase the risk of peri- or postoperative complications. In this series, both anterior and posterior surgery was performed in all three heart transplant patients. The indications for anterior approach were rigid curves in bending radiographs in two patients, and prevention of crankshaft phenomenon in one skeletally immature patient. Although pleural adhesions can be encountered, we think that this approach does not increase the frequency of complications.

Progressive spinal deformities can lead to significant problems for patients with underlying cardiovascular disease [13]. Primiano et al. [27] observed elevated pulmonary artery pressure, right ventricular dysfunction, and even cor pulmonale in patients with severe idiopathic scoliosis. An inverse correlation exists between the degree of spinal curvature and pulmonary function [15, 29, 33]. Therefore, spinal fusion has been recommended for patients with compromised cardiovascular or pulmonary status associated with progressive spinal deformities [13, 33].

In heart transplant patients, the denervated graft poses special requirements for the anesthesia. The graft lacks the ability to respond acutely to hypovolemia or hypotension with reflex tachycardia. It responds to stress primarily by an increased stroke volume. In addition, there is a lag period in the hemodynamic response because the increased output is secondary to humoral reflexes and not to neural reflexes [23].

Ceroni et al. [9] received 54% curve correction after a short 17 month follow-up on their heart transplant patient using posterior surgery. Dunn and Aiona [14] reported 40% after posterior surgery in a kidney transplant patient. In the current series, the primary correction of the thoracic curve was 49% for patients with idiopathic scoliosis, but during a mean of 4 years follow-up, some of this correction was lost leaving a final correction of 29%. We did not see crankshaft phenomenon. Some of the low primary correction can be

explained by poor bone quality, which prevented full primary correction to avoid pull-out of the instrumentations. In addition, the curves appeared quite rigid in the bending radiographs, which is typical of idiopathic scoliosis in males [19]. Several authors have reported loss of correction mainly during the first postoperative year in patients with idiopathic scoliosis [1, 5, 17, 24, 26]. Loss of correction in our series occurred even after 2-year follow-up.

This may partly be due to poor bone quality and diminished capacity for bony fusion in our patients. Recurrence of the spinal deformity occurred also due to junctional scoliosis or kyphosis. In the patient no. 6, clear recurrence of the kyphosis and loss of correction occurred probably due to several factors: too short instrumentation, weak abdominal muscles (Prune-Belly syndrome), and progression of the deformity because of the underlying metabolic disease and poor bone quality. In general, the distal fusion level was chosen to be in stable sacral zone in patients with scoliosis. In the case of kyphosis, the end vertebrae of the kyphosis were chosen, but this selection of fusion level turned out to be too short. In this particular patient, one additional level above and below the end vertebrae could have been a more appropriate solution. It may be that using apical pedicle screws and longer fusions, some of the loss of correction could have been avoided.

In conclusion, there exists a relatively high incidence of spinal deformities needing operative treatment in patients with solid organ transplantation. Therefore regular assessment of the spine is important in these patients during growth. Instrumented spinal fusion prevented further progression of the curves in these patients. Combined anterior and posterior surgery did not increase complications, but made moderate correction of the curves possible. Loss of correction decreased the final results, which may indicate longer instrumentation with apical pedicle screws to prevent junctional deformity postoperatively.

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