Osteoporotic VCF is a common disorder that affects 700,000 patients per year in the US alone.22 These fractures are associated with considerable morbidity and pain.22 Cases of VCF are known to occur in postmenopausal women and in elderly persons of both sexes. Other risk factors include cigarette smoking, excessive alcohol intake, sedentary lifestyle, spinal radiation therapy, and exposure to certain medications, such as phenytoin. Organ transplant recipients are also at risk for osteoporotic VCF because of their underlying disease process and because they require long-term treatment with steroid medications and other immunosuppressive drugs.

Over the last 5 years, balloon kyphoplasty has emerged as an effective treatment for VCF.9,23 Previous reports have dealt with this procedure in the context of osteoporosis associated with postmenopausal women and individuals of advanced age. To our knowledge, this operation has not been applied to VCFs in the transplant population. The purpose of this study is to report on the results of kyphoplasty treatment in six solid-organ transplant recipients.

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Preliminary results of balloon kyphoplasty for vertebral compression fractures in organ transplant recipients

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Object. Organ transplant recipients are at risk for vertebral compression fractures (VCFs). The goal of this study was to determine whether kyphoplasty is an effective treatment for VCFs that develop in this patient population.

Methods. Six consecutive patients who had undergone an organ transplant (five liver and one kidney transplant) had a total of 13 symptomatic VCFs that were treated with balloon kyphoplasty. Postprocedure follow-up duration ranged from 6 to 12 months. The mean visual analog scale pain score was 9.3 before treatment and declined to 1.8 after treatment. This improvement was highly significant (p < 0.001). Intake of narcotic drugs decreased or was eliminated in all patients, and there were no complications related to the procedure. There was one instance of clinically insig-ificant extraosseous cement extravasation. Sagittal alignment was improved by 5° in one patient and was unchanged in the remaining five. During the follow-up period, a new fracture developed adjacent to a treated level in one patient. This was successfully treated with an additional kyphoplasty procedure.

Conclusions. Kyphoplasty can be performed safely in organ transplant recipients with VCF, in whom results are just as favorable as those seen in patients with no history of organ transplantation.

Key Words • organ transplantation • vertebral compression fracture • kyphoplasty

CLINICAL MATERIAL AND METHODS

Patient Population

Six transplant recipients (five liver and one kidney transplant) in whom we found a total of 13 symptomatic VCFs were studied (Table 1). Balloon kyphoplasty was performed at all symptomatic levels. Balloons and other equipment were supplied by Kyphon, Inc. (Sunnyvale, CA). All fractures were treated within 3 months of onset. Treated levels ranged from T-7 to L-5. Postprocedure follow-up duration was 6 to 12 months.

The diagnosis of VCF was established using MR imaging, bone scans, and plain x-ray films. Balloon kyphoplasty was performed after induction of general anesthesia. Vertebral biopsy sampling was performed at all treated levels. The mean treatment time was 45 minutes per level, and patients with one or two fractures were treated in a single session. One patient had five fractures and was treated in three separate sessions. The primary clinical end point was back pain, which was measured using the VAS. Narcotic analgesic drug requirements were also assessed.

Sagittal alignment was assessed based on pre- and postprocedure standing lateral radiographs. The Cobb angle was measured at each treated level, before and after kyphoplasty.
Statistical Analysis

The pre- and posttreatment VAS results were analyzed using the Student t-test. Probability values less than 0.05 were considered statistically significant.

RESULTS

The mean VAS pain score was 9.3 before and 1.8 after treatment ($p < 0.001$). Pain relief was noticed within 24 hours of the procedure, and narcotic drug intake was decreased or eliminated in all patients. Vertebral biopsy samples were negative for malignancy in all cases. There were no infections or other complications of the procedure. There was one instance of clinically insignificant extraosseous cement extravasation. Sagittal alignment was improved by $5^\circ$ in one patient and was unchanged in the remaining five.

In one patient who was initially treated for a T-8 compression fracture, a new fracture developed at T-7 1 month after the T-8 kyphoplasty. He underwent a kyphoplasty at T-7 and has subsequently done well.

ILLUSTRATIVE CASE

This 66-year-old man underwent liver transplantation and prednisone therapy was started at that time. Seven months later, he experienced recurrent liver failure and required a second transplant. At the same time, he noted acute, severe back pain with a VAS pain score of 9. An MR image of the thoracic and lumbar spine revealed VCFs at T-11, T-12, and L-1. There was edema in the T-11 and L-1 VBs, indicating that these were acute fractures. There was no edema in the T-12 VB, indicating this was most likely a chronic fracture that would not benefit from augmentation (Fig. 1). Balloon kyphoplasty was performed at T-11 and L-1 by using a bilateral approach at each level. Methyl methacrylate volumes were 8.5 ml at T-11 and 10.5 ml at L-1. Postoperatively, the patient reported immediate pain relief, with the VAS pain score decreasing to 2. Follow-up radiographs show MMA deposition in the T-11 and L-1 VBs (Fig. 2).

DISCUSSION

Kyphoplasty Procedure

Balloon kyphoplasty is a method of vertebral augmentation that has been shown to be an effective treatment of VCF. Garfin, et al., have documented a 95% improvement in pain and a significant improvement in function after treatment with this procedure. In some cases, kyphoplasty is able to increase the height of the fractured VB and decrease kyphosis, which helps to relieve back pain by improving sagittal alignment.

This procedure is safe, but not completely risk free. There is a potential for spinal cord or nerve root compression due to extravasation of MMA, pulmonary embolism from MMA, and infection. The reported complication rate is 0.7% per fracture and 1.2% per patient. The procedure may not be technically feasible if the vertebra is compressed too severely (vertebra plana).

Findings in the Present Study

In this study we have shown that kyphoplasty can be performed safely in organ transplant recipients, with results that are just as favorable as those obtained in other patients with osteoporotic VCFs. Infection is a potential concern when an immunocompromised patient undergoes an invasive procedure that involves placement of a foreign body in the spine; however, there were no infectious complications observed in this series.

A small amount of asymptomatic cement extravasation was seen at one of 13 treated levels (7.7%). These data are consistent with the findings of Lieberman, et al., who reported a 9% incidence of cement extravasation, usually with no clinical sequelae. One patient suffered a new VCF adjacent to a previously treated level. This is not unique.

TABLE 1

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Organ Transplanted</th>
<th>Fracture Level</th>
<th>Pre-Tx VAS</th>
<th>Post-Tx VAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>64, M</td>
<td>liver</td>
<td>L1–5</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>63, F</td>
<td>kidney</td>
<td>L4</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>65, M</td>
<td>liver</td>
<td>T7–8</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>66, M</td>
<td>liver</td>
<td>T11–L1</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>68, F</td>
<td>liver</td>
<td>L3</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>56, F</td>
<td>liver</td>
<td>T12–L1</td>
<td>10</td>
<td>3</td>
</tr>
</tbody>
</table>

* Tx = treatment.
to the subgroup of transplant recipients, but rather is a known complication of kyphoplasty in the general population of patients with VCF.\textsuperscript{24}

Other investigators have reported a greater improvement in sagittal alignment than we obtained in this series. For example, Phillips, et al,\textsuperscript{17} reported that 58% of patients treated with kyphoplasty experienced a kyphosis correction of greater than 5°. The reasons for this difference are unclear. It does not appear that the anatomical characteristics of VCFs in transplant recipients are inherently different from typical osteoporotic VCFs. It may be that in our series these lesions were treated later in their clinical course or somewhat less aggressively than those in other series. Further study of this issue will be required.

Metabolic Bone Disease in Liver Transplant Recipients

Regardless of its origin, all patients with end-stage liver disease are at risk for hepatic osteodystrophy, defined as osteopenia/osteoporosis.\textsuperscript{4,8,20} The pathogenesis of this bone disease in these patients is multifactorial.\textsuperscript{21}

End-stage liver disease (especially cholestatic disease such as primary biliary cirrhosis, primary sclerosing cholangitis, and autoimmune disorders) is strongly associated with selective impairment of osteoblast (bone-forming cell) activity, predisposing patients with liver disease to a high turnover of bone metabolism and an increased loss of bone mass.\textsuperscript{11} Accelerated bone loss increases the risk for osteoporotic fractures and avascular necrosis.\textsuperscript{2} The incidence of fractures is reported to range from 24 to 65%, with the highest incidence occurring in women with primary biliary cirrhosis. The greatest risk factors for the development of bone disease posttransplantation are the bone quality and density prior to transplantation and the immunosuppressive regimens that patients must endure.

In most patients with liver disease, the combination of glucocorticoids and calcineurin phosphate inhibitors, for example, cyclosporine and tacrolimus, have marked deleterious osteoporotic effects on the skeleton. Glucocorticoids exert their deleterious effect on bone primarily by the suppression of osteoblasts and the activation of osteoclasts (bone-resorbing cells).\textsuperscript{14} Other effects of glucocorticoids that contribute to the net loss of bone include reduction of gonadal function, reduction of calcium absorption, increase in urinary calcium excretion, and an increase in parathyroid hormone. Glucocorticoid-induced bone loss is related to both dose and duration of therapy.\textsuperscript{7,16}

The most significant period of bone loss in organ recipients is within the first 6 months posttransplantation. Bone resorption and formation are usually linked so that they occur in close sequence and remain balanced. An imbalance in the bone remodeling cycle causes bone loss that eventually leads to osteoporosis and fracture risk.\textsuperscript{12}

Trabecular bone of the spine appears to be most at risk, with vertebral fractures occurring most often.\textsuperscript{20} In previous studies conducted in liver transplant recipients, the median lumbar bone mineral density was shown to decrease 4.5% during the first 3 months posttransplantation.\textsuperscript{12} Fracture rates ranged between 24 and 65% in the 1st year posttransplantation, but were especially high within the first 6 months.\textsuperscript{5-7,20}
There are limited data regarding the prevalence of bone complications in patients undergoing liver transplantation as well as the treatment of osteopenia/osteoporosis in this population. The presence of bone fractures in this population indicates substantial bone loss. Medical treatment with bisphosphonates, calcium, and vitamin D is important to prevent or at least to decrease further bone loss. New therapies are needed in this patient population to improve the rate of complications of osteoporosis, such as back pain, and to improve the overall quality of life.

CONCLUSIONS
Experience with this small group of patients indicates that balloon kyphoplasty is a safe and effective treatment for VCFs that occur in organ transplant recipients.

Disclaimer
None of the authors has a financial interest in Kyphon, Inc., or in any of the devices discussed in this report.

References

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