Vertebral augmentation in the treatment of pathologic compression fractures in 792 patients with multiple myeloma

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Multiple myeloma is the most common form of neoplasm affecting or involving the bone, accounts for 1% of all cancer types with a lifetime risk of 0.62%, and new cases are now estimated at 21 700 adults in the United States per year. This plasma cell dyscrasia is characterized by clonal proliferation of neoplastic plasma cells producing osteoclast-activating and osteoblast-inhibiting factors. Clinical symptoms result from pathological fractures at the site of osteolytic lesions or profound osteoporosis, often resulting in hypercalcemia. Symptomatic fractures are most commonly seen in the vertebral bodies centered in the thoracolumbar region. These types of compression fractures result in significant pain, decreased activity levels, disability and increased morbidity. We describe the fracture distribution and the efficacy of vertebral augmentation (vertebroplasty or kyphoplasty) in 792 consecutive patients with myeloma-related symptomatic compression fractures, who underwent 2693 vertebral augmentations at the University of Arkansas for Medical Sciences between January 2001 to May 2007. Information was collected on type of augmentation (vertebroplasty or kyphoplasty), patient vitals, magnetic resonance imaging, computed tomography (CT) and Positron emission tomography–CT for vertebral fracture location. All of the patients were on cancer therapy or about to receive therapy. Pre- and post-procedure pain, medication and activity level were assessed by survey in a subset of 361 subjects. When the participants were not in hospital to complete the survey, surveys were mailed to patient-reported addresses, which were often not reflective of their current living situation, as most patients (80%) had relocated to the local area for treatment. Efficacy was assessed by changes in pain with the Visual Acuity Scale (VAS), analgesic usage and activity level pre-procedure and 1 month post procedure by chart documentation and patient survey. All patients received 1 g Cefazolin (Ancef) pre-procedure. Institutional Review Board approval was obtained for this study.

RESULTS

Of the 792 patients who underwent vertebroplasty or kyphoplasty, the median age was 63 years (range, 16–99) with 76 (10%) patients being 80 years and older, and 56% of patients were males. These patients underwent a total of 1072 sessions; the majority of patients (75%) had one vertebral augmentation session, 18% of patients had two vertebral augmentation sessions, 7% had three to six sessions. The number of repairs varied per session with the median being 2 (interquartile range (IQR) 1–3) repairs per session with 23% of sessions involving four to nine augmentations. The majority (83%) of the 2693 levels treated were repaired with vertebroplasty. The distribution of vertebroplasty repairs was 37% for T1–T10, 39% for T11–L2 and 24% for L3–sacrum (Figure 1a). Overall, 68% of all sessions involved repair on ≥ 2 vertebra, and a similar distribution across levels was seen for patients with kyphoplasty. Two complications (0.3%) required antibiotics. No neurological deficits were observed.

Pre- and post-assessments

For the outcomes study, 361 participants provided both pre- and post-assessments (1 month) for 447 sessions for at least one of the three outcomes (VAS, analgesics, or activity level assessments). Of these participants, 82% had assessments for one session only, 15% for two sessions and 4% for three or four sessions. Patients participating in the outcomes study were significantly more likely to be younger (median, 60 vs 65), male (63 vs 50%) and from out of state (66 vs 36%) than those who were non-participants (Table 1). Most patients were from out of state and relocated to the area for treatment. The number of levels repaired did not differ significantly with the median being 2 (IQR, 1–3) for both participants and non-participants.

STATISTICAL METHODS

As many of the subjects participating in the outcomes study underwent multiple sessions, clustering of sessions within subjects was addressed by using mixed models with a random effect for subject for analyzing change in pain score, and generalized mixed models with a fixed effect for time and a random effect for subject for pain medication and physical activity.
Reduction in pain

Using the 0-10 VAS scale, 351 subjects provided pre- and 1-month post-procedure assessments of their pain for 428 sessions (Figure 1b). From a baseline pain assessment score of 6.9 to a post score of 2.7, there was an average reduction of 4.2 points (95% confidence interval [CI] 4.0-4.5) that was significant (P<0.001).

Reduction in analgesic medication

Pain medication usage pre- and post-procedure was available for 437 sessions in n = 355 patients. Across all sessions, 12% of sessions had subjects reporting zero pain medications pre-procedure as compared with 34% post-procedure. Patients were taking narcotics for 70% of sessions pre-procedure compared to 48% post-procedure (Figure 1c). Accounting for clustering, the odds of good activity (score of 0–1) was 4.2 (95% CI, 3.1–5.8) times higher post-procedure as compared to pre-procedure (P<0.001).

There were no significant differences in improvements between the type of procedure performed (kyphoplasty vs vertebroplasty or kyphoplasty + vertebroplasty) for pain relief, decreased narcotics usage or improvement in activity (all P>0.05), after adjusting for age, gender, session, number of augmentations and baseline scores or medication. The smaller sample sizes should be kept in mind of this comparison, as 74% of sessions with outcome data involved vertebroplasty only, 13% kyphoplasty only and 13% both procedures. For the subset with repairs confined to a single region (T1–T10, T11–L2 and L3–sacrum), there was no difference detected in pain reduction, medication usage and activity according to region (all P>0.05, n = 197–203 patients).

Our analyses found that vertebral augmentation (vertebroplasty or kyphoplasty) therapy significantly decreased the VAS level of pain, decreased narcotic usage and increased activity levels in multiple myeloma patients with multiple and single repairs (Figure 1b–d). Only two (0.3%) patients required antibiotics for local infections, and no neurological deficits were observed. From a baseline VAS of 6.9, average pain scores decreased to 2.7 (Figure 1b) following vertebral augmentation. Other recent studies have noted in cancer and osteoporotic patients that vertebral

Improve in activity

Activity assessments were provided by 354 subjects across 430 sessions. Across sessions, pre-procedure 28% of subjects scored 0–1 (that is, no limitations or walking without assistance) as compared to 59% post-procedure (Figure 1d). Accounting
augmentation provided significant pain relief and minimal complications. Myeloma patients who are severely limited by pain to only reclining or sitting ideally benefit from vertebral augmentation.

Multiple augmentation procedures or performing multiple levels at one session may be a necessary and appropriate resolution for pain. Hussein et al.8 state that repair of three to four vertebrae per augmentation is reasonable. We also reported up to 16 repairs in one patient in the same paper (Figure 1e). While the majority (75%) of the 792 patients in this study required a single vertebral augmentation session, the median number of repairs was consistent with other studies at two per session. Augmentation repairs have been noted in levels up to the cervical area, and percutaneous repairs in the T3–L5 levels are considered safe and effective.5,8 Others have differed in size requirements to augment vertebral collapse and placed upper limits on the number of augmentations per session for vertebral augmentation, vertebroplasty and kyphoplasty and number of augmentations per session for n = 792 subjects.

Table 1. Distribution of compression fractures (CF) among both types of vertebral augmentation, vertebroplasty and kyphoplasty and number of augmentations per session for n = 792 subjects

| Procedure/CF vertebrae | N (%)* | CF treated |
|------------------------|--------|------------|
| Vertebroplasty (n = 2223) |        |            |
| T1–T10 | 816 (37) |            |
| T11–L2 | 871 (39) |            |
| L3–acrum | 536 (24) |            |
| Kyphoplasty (n = 470) |        |            |
| T1–T10 | 165 (35) |            |
| T11–L2 | 187 (40) |            |
| L3–sacrum | 118 (25) |            |
| Total repairs | 2693 |            |

| Number of augmentations/session | N (%) sessions |
|---------------------------------|----------------|
| 1 | 337 (32) |
| 2 | 258 (24) |
| 3 | 227 (21) |
| 4 | 134 (13) |
| 5 | 66 (6) |
| 6–9 | 47 (4) |
| Total sessions | 1072 |

*Percentages based on totals for the respective procedure.

Conclusions

The authors declare no conflict of interest.

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Letters to the Editor

Prognostic impact and landscape of NOTCH1 mutations in chronic lymphocytic leukemia (CLL): a study on 852 patients

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Chronic lymphocytic leukemia (CLL) is the most common leukemia in adults. Recently, recurrent activating mutations of NOTCH1 have been reported in up to 12% of CLL patients, underlining the relevance of NOTCH1 mutations (NOTCH1mut) as an independent negative prognostic marker.1–3 NOTCH1mut in CLL are known to be located predominantly within the C-terminal PEST domain, frequently resulting in a truncated protein that is more stable than the wild-type one and activates the NOTCH1 signaling pathway.2

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