Prevention of Fractures after Solid Organ Transplantation: A Meta-Analysis

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Context: Bone loss and fracture are serious sequelae of organ transplantation, particularly in the first posttransplant year. Most interventional studies have been inadequately powered to detect effects on fracture.

Objective: The objective of the study was to determine whether treatment with bisphosphonates (BP) or active vitamin D analogs (vitD) during the first year after transplantation reduces fracture risk and estimate the effect of these interventions on bone loss.

Data Sources: Sources included PUBMED, MEDLINE, Cochrane Library, and abstracts from scientific meetings (presented 2003–2010).

Study Selection: Randomized controlled clinical trials of BP or vitD in solid organ transplant recipients were included if treatment was initiated at the time of transplantation and fracture data were collected.

Data Extraction: Two investigators independently extracted data and rated study quality. Fixed effect and random-effects models were used to obtain pooled estimates.

Data Synthesis: Eleven studies of 780 transplant recipients (134 fractures) were included. Treatment with BP or vitD reduced the number of subjects with fracture [odds ratio (OR) 0.50 (0.29, 0.83)] and number of vertebral fractures, [OR 0.24 (0.07, 0.78)]. An increase in bone mineral density at the lumbar spine [2.98% (1.31, 4.64)] and femoral neck [3.05% (2.16, 3.93)] was found with treatment. When BP trials (nine studies, 625 subjects) were examined separately, there was a reduction in number of subjects with fractures [OR 0.53 (0.30, 0.91)] but no significant reduction in vertebral fractures [OR 0.34 (0.09, 1.24)].

Conclusions: Treatment with BP or vitD during the first year after solid organ transplant was associated with a reduction in the number of subjects with fractures and fewer vertebral fractures. **(*J Clin Endocrinol Metab* 96: 3457–3465, 2011)**

As the incidence of organ transplantation and survival time after transplant has increased, so have the associated complications. Bone loss and fractures, both common after organ transplantation, are associated with mortality, significant morbidity, and reduced quality of life (1, 2). These complications most frequently occur in the first year after transplantation, in which fracture rates as high as 37% have been reported (3). The rates of bone loss during the first year after transplant range from 0 to 24% at the spine and 2 to 11% at the hip (4). Estimates from recent studies are much lower than those from the 1980s (5), likely due to a decrease in glucocorticoid use.

Patients with end-stage disease involving the heart, lung, liver, and kidneys come to transplantation with very

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Abbreviations: BMD, Bone mineral density; CI, confidence interval; FEM, fixed-effect model; FN, femoral neck; LS, lumbar spine; OR, odds ratio; REM, random-effects model.

different types of underlying bone disease, relating to their disease processes and various treatment regimen (3). In contrast, the changes in bone metabolism that occur after organ transplantation are remarkably similar regardless of organ type. There is an initial period of rapid bone loss over the first 3–6 months related to increased bone resorption and uncoupling of bone turnover and a concentration of fractures within the first 2 yr after transplant (5–15).

Although many randomized clinical trials have demonstrated that initiation of bisphosphonates or active metabolites of vitamin D immediately after transplant prevents bone loss during the first year (5, 16–21), the majority have had inadequate statistical power to detect differences in fracture among treated and untreated patients. It is unlikely that a definitive clinical trial regarding fracture will be performed for many reasons, including relatively low frequency of fracture as an outcome, difficulty recruiting enough eligible patients for a trial to be sufficiently powered, and ethical concerns about placebo treatment when several medications have been shown to prevent bone loss after transplantation. Therefore, this meta-analysis was conducted to determine whether treatment with bisphosphonates or active vitamin D analogs was associated with reduced risk of fractures in the first year after transplantation. Because there are inadequate numbers of studies involving any one type of organ to provide useful data regarding fracture rates and because the changes that occur after transplantation are consistent regardless of fracture type, we included all subjects with solid organ transplantation.

Materials and Methods

Data sources and searches

We searched the PUBMED database, the MEDLINE database, and the Cochrane Controlled Clinical Trials Register to identify all trials which involved treatment with bisphosphonates or active vitamin D analogs in patients with kidney, liver, heart, or lung transplants. Key words and search terms used in the various searches included transplant, osteoporosis, bone loss, fracture, transplant and calcitriol, transplant and bisphosphonates, transplant and osteoporosis, and transplant and fracture. The reference lists of all trials included in the meta-analysis were examined for relevant article that were missed by the electronic search. We also searched for unpublished abstracts presented from 2003 to 2010 at the annual meetings of the American Society for Bone and Mineral Research, the Transplant Society, the American Society of Nephrology, the European Calcified Tissue Society, The Endocrine Society, and the International Society for Heart and Lung Transplantation. Authors of included abstracts were contacted to obtain unpublished data.

Study selection

Studies were screened and selected by all investigators on the basis of *a priori* criteria. Included studies had to be randomized clinical trials that followed patients starting at the time of transplantation, compared treatment and control groups, and included fracture assessment. Studies with historical controls were excluded. Eligible treatments included oral or iv bisphosphonates (alendronate, risedronate, pamidronate, ibandronate, zoledronic acid) or active vitamin D analogs (calcitriol, calcidiol, 1α-hydroxyvitamin D). Studies evaluating the efficacy of other treatments to prevent bone loss, including hormone replacement therapy, calcitonin, or resistance exercise, were excluded. Only trials in which all patients were older than 18 yr were included. Trials evaluating liver, heart, lung, or kidney transplants were included; studies of bone marrow transplants were excluded. There was no restriction based on sample size or specific dose of bisphosphonate or active vitamin D analog.

Data extraction and quality assessment

Two investigators independently extracted data on study design, methods, subjects, interventions, fracture, and bone mineral density (BMD) outcomes. The primary outcome was vertebral or nonvertebral fracture sustained within the first year after transplantation. Fractures were assessed using radiographs of the thoracic and lumbar spine (LS) at baseline and 12 months after transplant, except for one study [De Sévaux *et al.* (18)] in which only clinical vertebral fractures were recorded. Symptomatic and radiographically detected vertebral fractures were included and considered together because the majority of studies did not distinguish between the two. Both the proportion of patients who fractured and the total number of fractures were independently assessed.

Change in areal BMD, measured by dual-energy x-ray absorptiometry in grams per square centimeter at the LS and femoral neck (FN), was assessed across all studies as a secondary outcome measure. Both the absolute change and the percent change were noted. If only one (absolute or percent change) parameter was described in the publication, the other was calculated from the other data provided. Authors were asked to provide raw data if possible.

The quality of included trials was assessed using the guidelines of Jadad *et al.* (22). Studies were assessed based on the method of randomization, the presence or absence of double-blinding, and the description of patient dropouts and withdrawals. Studies received one point for randomization, double blinding, and description of dropouts. If methods of randomization and blinding were described in detail, an additional point was added or subtracted for each based on whether they were performed appropriately. Studies were scored between 0 and 5, with a score of 5 representing highest quality.

Data analysis

Analyses were conducted using TIBCO Spotfire S+ 8.2 (TIBCO Software Inc., Palo Alto, CA). For each study, the log odds ratio of fracture between the two groups was estimated along with its SE. A value of 0.5 was added to the 0 cell values in the odds ratio calculation. Three studies did not have specific assessment of fractures at 1 yr. Sambrook *et al.* (23) had data at 2 yr, De Sévaux *et al.* (18) at 6 months, and Schwarz *et al.* (24) at 6 months and 3 yr. For these studies the number of fractures and the number of patients with fracture at 1 yr were estimated

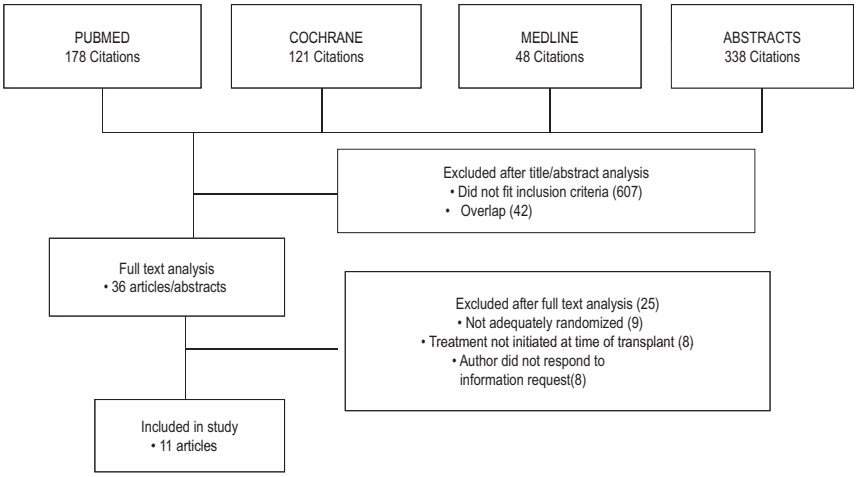

FIG. 1. Identification of randomized clinical trials for inclusion in the meta-analysis.

with the standard Poisson process. The difference of 12-month relative change of bone density from baseline between two treatment groups was calculated along with its SE. The heterogeneity of studies was examined by Cochran χ^2 tests. Both fixed-effect (FEM) and random-effects models (REM) were used in the pooling of the percentage difference and the log odds ratios. Publication bias was assessed by funnel plot and linear regression test (25).

Results

Literature search

The search identified 685 abstracts with potential for inclusion through electronic literature search and review of abstracts from annual meetings. Of these, 607 were eliminated because they did not meet all inclusion criteria, and 42 were duplicate retrievals. After abstract review of the remaining 36 titles, 28 published articles were selected for full text review and eight unpublished abstracts from annual meetings were pursued for additional experimental results and raw data. Of the 36 selected titles, nine were discovered to be not adequately randomized, eight were excluded because treatment was not initiated immediately after transplant, and eight were excluded because the authors did not respond to multiple requests for information.

Ultimately, 11 studies with a total of 780 participants were selected for inclusion in the study. A flow chart outlining the inclusion of all randomized controlled trials is presented in Fig. 1.

Included trials

The characteristics of all trials included in this meta-analysis are outlined in Table 1. Of the 11 trials chosen for this study, nine compared a bisphosphonate with a placebo or no treatment. The bisphosphonates studied were pamidronate (21, 26) zoledronic acid (16, 24, 27), ibandronate (19, 20), and alendronate (28). In eight of these trials, bisphosphonates were administered iv, albeit at variable intervals and doses. The final two trials (18, 23) compared 1α-hydroxyvitamin D or calcitriol with no treatment. In all but one study (18), subjects received calcium supplements, with or without parent vitamin D. According to the Jadad criteria, median quality score of the included trials was 3 (range 2–5). Of the 780 subjects assessed at baseline, 659 had data at the follow-up time point.

Although the immunosuppressant regimen varied by type of organ transplanted, all included prednisone. In the study by Gil-Fraguas *et al.* (28), subjects randomized to calcitonin were used as the control group. This was done because this study did not have a randomized control group and was deemed appropriate because calcitonin has not been shown to have an effect on fracture after transplant (29–31). In the majority of studies, there were no BMD criteria for study entry. Gil-Fraguas *et al.* excluded patients with normal BMD, and Kaemmerer *et al.* excluded patients with T scores below −3.0. Mean baseline T or Z-scores [provided for all but two studies (14, 28)] were greater than −2.0 at the LS and FN in all trials.

All trials assessed fractures using spine x-ray, with one study also including hip x-ray to assess for fracture (17). In the study by De Sévaux *et al.* (18), only clinical fractures were noted. In all other trials, asymptomatic vertebral compression fractures were assessed by periodic radiographs. The number of both vertebral and non-vertebral fractures, and the total number of patients who sustained fractures in each group was obtained from published data or directly from the authors if not included in the publications. Of the included trials, only Bodingbauer *et al.* and Kaemmerer *et al.* were powered to detect differences in fracture. Significant reductions in fracture were reported by four of the 11 included studies. Kaemmerer *et al.* reported a significant reduction in total number of fractures with ibandronate (eight *vs.* two). Significant reductions in vertebral fractures were reported by Bodingbauer *et al.* with zoledronic acid (11 *vs.* four), Fahrleitner-Pammer *et al.* with ibandronate (17 *vs.* two) and Sambrook *et al.* with calcitriol treatment (22 *vs.* one; assessed at 24 months in this study).

For nine of the trials, detailed data regarding changes in BMD with estimates of error were included in the manuscript or provided by the authors. Estimates of effects on LS and FN BMD were based on these publications.

TABLE 1. Characteristics of included studies

Trial	Organ	Number of subjects	Intervention	Control regimen	Immunosupression
Bisphosphonate trials					
Bodingbauer *et al.*, 2007 (27)	Liver	69	Zoledronic acid, 4 mg iv at months 1–6, 9, 12	Ca 1000 mg, Vit D 800 IU/d	CsA, Pred
Crawford *et al.*, 2006 (16)	Liver	54	Zoledronic acid, 4 mg iv at months 0, 1, 3, 6, 9	Ca 600 mg, Vit D 1000 IU/d	CsA, Pred, AZA
Fahrleitner-Pammer *et al.*, 2009 (19)	Heart	35	Ibandronate, 2 mg iv q 3 months	Ca 1000 mg, Vit D 400 IU/d	CsA, Pred, MMF
Gil Fraguas *et al.*, 2005 (28)	Heart	87	Alendronate, 10 mg daily	Calcitonin 200 IU/d	CsA, Pred, AZA
Grotz *et al.*, 2001 (20)	Kidney	72	Ibandronate, 1 mg iv month 0, 2 mg iv months 3, 6, 9	Ca 1000 mg/d	CsA, Pred, MMF
Kaemmerer *et al.*, 2010 (32)	Liver	74	Ibandronate, 2 mg iv q 3 months	Ca 1000 mg, Vit D 800–1000 IU/d	CsA, Pred, MMF
Monegal *et al.*, 2009 (26)	Liver	79	Pamidronate, 90 mg iv at months 0, 3	Ca 1000 mg/d Vit D 16,000 IU q 15 d	CsA, Pred, MMF
Schwarz *et al.*, 2004 (24)	Kidney	20	Zoledronic acid, 4 mg iv at wk 2 and month 3	Ca 1000 mg/d	CsA, Pred, MMF
Walsh *et al.*, 2009 (21)	Kidney	125	Pamidronate 1 mg/kg iv at months 0, 1, 4, 8, 12	Ca 500 mg Vit D 400 IU/d	CsA, Pred
Vitamin D trials					
De Sévaux *et al.*, 2002 (18)	Kidney	109	1α-Hydroxyvitamin D, 0.25 μg po daily	No treatment	CsA, Pred, MMF
Sambrook *et al.*, 2000 (23)	Heart and lung	65	Calcitriol, 0.25 μg po bid	Ca 600 mg/d	CsA, Pred, AZA

Vit D, Ergocalciferol or cholecalciferol; CsA, cyclosporine; AZA, azathioprine; MMF, mycophenolate mofetil; q, every; po, by mouth; bid, twice a day.

[a] Insufficient data to include in BMD analysis.

[b] Fractures reported at time points other than 1 yr. *Top number* represents estimate of fractures at 1 yr by Poisson process assumption; *bottom number in italics* is value reported at other time point.

Assessment of publication bias

Based on linear regression tests, there was not significant publication bias for any outcome, including number of subjects with fractures ($P = 0.98$), total number of fractures ($P = 0.59$), number of vertebral fractures ($P = 0.85$), LS BMD ($P = 0.45$), and FN BMD ($P = 0.53$).

Meta-analysis of bisphosphonate and vitamin D analog trials combined

The overall incidence of fracture in patients who were not treated was 24.7% over 1 yr. Treatment with either bisphosphonates or vitamin D analogs was associated with a reduction in number of subjects with fractures. There was no significant heterogeneity among studies (Q-statistic = 11.8, $df = 10$, $P = 0.15$). The pooled estimate of the odds ratio (OR) for the number of subjects with fractures was 0.50 [95% confidence interval (CI) 0.29, 0.83] by FEM (Fig. 2A). Treatment was also associated with a reduction in total number of fractures (combined vertebral and nonvertebral). There was significant heterogeneity in this outcome (Q-statistic = 40.6, $df = 10$, $P < 0.001$); OR was 0.37 (95% CI 0.22, 0.60) by REM. A reduction in number of vertebral fractures was also observed with treatment. There was significant heterogeneity in this outcome (Q-statistic = 35.6, $df = 10$, $P < 0.001$); OR 0.24, (95% CI 0.07, 0.78) by REM (Fig. 2B).

Results did not change with sensitivity analysis. The analyses were also repeated after excluding the one study in which only clinical vertebral fractures were assessed (18). The significance of the results did not change. There remained a reduction in number of subjects with fractures [OR 0.52 (95% CI 0.30, 0.90)] by FEM, total number of fractures, [OR 0.32 (95% CI 0.11, 0.92)] by REM, and number of vertebral fractures [OR 0.28 (95% CI 0.08, 0.95)] by REM.

The effects of any treatment on BMD were assessed. Control subjects had mean losses of 2.3 ± 1.3% at the LS

TABLE 1. Continued

Number of subjects with fractures		Total fractures (vertebral fractures)		LS BMD % change (SE)		FN BMD % change (SE)	
Treatment	Control	Treatment	Control	Treatment	Control	Treatment	Control
4	11	4 (4)	11 (11)	0.1 (2.2)	−2.8 (2.7)	−2.4 (2.2)	−3.9 (2.0)
2	2	2 (0)	10 (9)	4.8 (0.6)	2.8 (0.6)	−0.3 (0.5)	−3.0 (0.5)
2	9	2 (2)	17 (17)	[a]	[a]	[a]	[a]
3	7	7 (6)	15 (15)	−4.0 (0.9)	−4.9 (0.9)	−0.6 (0.7)	−4.9 (1.1)
2	2	2 (1)	2 (1)	−0.9 (1.0)	−6.5 (0.9)	0.5 (0.9)	−7.7 (1.8)
2	7	2 (1)	8 (4)	1.9 (1.1)	1.0 (1.6)	−1.1 (1.5)	−3.9 (1.3)
7	3	15 (13)	3 (2)	2.9 (0.8)	1.0 (0.8)	−3.2 (0.1)	−3.1 (1.2)
1[b] *2*	1[b] *2*	1 (1)[b] *2 (2)*	1 (1)[b] *2 (2)*	[a]	[a]	[a]	[a]
2	5	2 (0)	5 (1)	2.6 (0.8)	−6.2 (1.1)	−0.2 (1.4)	−2.6 (1.0)
0.5* *0*	4.5[b] *2*	0.5 (0.5)* *0 (0)*	12.5 (6.5)[b] *6 (6)*	−2.6 (0.6)	−5.0 (0.6)	−0.2 (0.9)	−4.0 (0.8)
1* *1*	2* *4*	1 (1)[b] *1 (1)*	11 (11)[b] *22 (22)*	−1.8 (1.2)	−2.9 (1.0)	−2.8 (1.1)	−6.6 (2.3)

and 3.6 ± 0.4% at the FN over the first year. At the LS, the χ^2 test revealed significant heterogeneity between studies (Q-statistic = 30.2, $df = 8$, $P = 0.0002$). Treatment was associated with an increase in LS BMD of 2.98% (95%CI 1.31%, 4.64%) by REM (Fig. 3A). At the FN, there was not significant heterogeneity between studies (Q-statistic = 13.0, $df = 8$, $P = 0.11$). Treatment was associated with an increase in FN BMD of 3.05%, (95% CI 2.16%, 3.93%) by FEM (Fig. 3B).

Meta-analysis of bisphosphonate trials only

Treatment with bisphosphonates (nine studies, 625 subjects) was examined separately. There was not significant heterogeneity associated with this outcome (Q-statistic = 10.1, $df = 8$, $P = 0.19$); treatment was associated with fewer subjects with fractures [OR 0.53 (95% CI 0.30, 0.91)] by FEM (Fig. 4A). The total number of fractures was not significantly reduced by treatment. There was significant heterogeneity in this outcome [Q-statistic = 32.4, $df = 8$, $P < 0.001$); OR 0.39 (95% CI 0.13, 1.15)] by REM. There was significant heterogeneity in assessment of vertebral fractures (Q-statistic = 30.1, $df = 8$, $P < 0.001$). OR for vertebral fractures was 0.41 (95% CI 0.22, 0.75) by FEM and 0.34 (95% CI 0.09, 1.24) by REM (Fig. 4B).

Bisphosphonate treatment was associated with improvement in LS and FN BMD after transplant. There was significant heterogeneity among studies for measurement of both LS (Q-statistic = 28.3, $df = 6$, $P < 0.001$) and FN BMD (Q-statistic = 12.4, $df = 6$, $P = 0.05$). Treatment was associated with an increase in LS BMD of 3.34%, (95% CI 1.10, 5.58) by REM and FN BMD of 3.04% (95% CI 1.42, 5.65) by REM.

Discussion

Treatment with bisphosphonates or active vitamin D analogs during the first year after transplantation was asso-

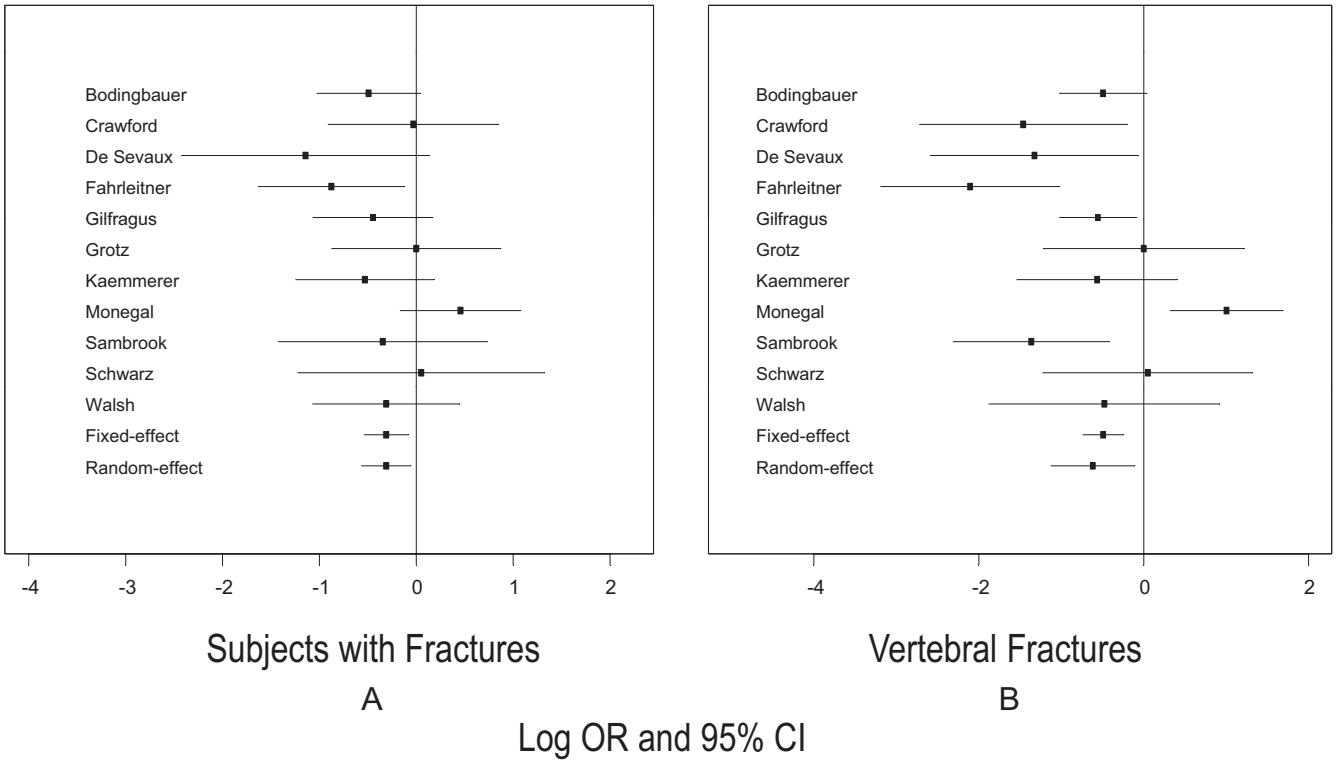

FIG. 2. Effect of treatment with bisphosphonates or vitamin D analogs after organ transplantation on number of subjects with fractures (OR 0.50, 95% CI 0.29, 0.83 by fixed effect model; A) and on number of vertebral fractures (OR 0.24, 95% CI 0.07, 0.78 by random effects model; B).

ciated with fewer fractures. With treatment, the total number of subjects with fractures, the absolute number of fractures, and number of vertebral fractures were all significantly reduced. Treatment was associated with an increase of approximately 3% in LS and FN BMD.

It was not possible to directly compare bisphosphonate and vitamin D analog treatment in our analysis because of the small number of studies using vitamin D analogs. Few studies have directly compared the two treatments (5). Bisphosphonate studies in which active vitamin D was administered to both arms were not included in this analysis. In our randomized trial of patients after cardiac transplantation (5), there was no difference in fracture incidence between the groups or when compared with an untreated reference group. In that study, we found that both alendronate and calcitriol produced similar effects on BMD, although significantly more hypercalciuria occurred in calcitriol treated patients.

It is likely that the effects of bisphosphonates alone were less significant because power was reduced in this analysis.

Although the majority of included studies were not powered to detect differences in fracture, a few did report significant differences in fracture rates. These included the studies by Kaemmerer *et al.* (32) and Bodingbauer *et al.* (27) that were specifically powered to detect differences in fracture rates. The other two studies included subjects at very high risk for fracture; the study by Sambrook *et al.* (23) included lung transplant recipients, a group at extremely high risk of fracture (10, 15, 34), and the subjects studied by Fahrleitner-Pammer *et al.* (19) received very high glucocorticoid doses, as is standard practice at that institution. These findings underscore the difficulty assessing differences in this rare outcome from single-center clinical trials.

Other meta-analyses have explored effects of treatment on bone disease in transplant patients and have found similar effects on bone loss but have not specifically focused on fractures (36–38). Palmer *et al.* (39) evaluated various treatment regimens in renal transplant recipients. They did not find a reduction in risk of fracture with bisphosphonate treatment *vs.* placebo. However, this analysis included trials of older, less potent bisphosphonates (clodronate, etidronate) and long-term transplant recipients as well. Treatment with vitamin D analogs assessed separately was not associated with a reduction in fracture, although this analysis included only two studies. Our analysis had a greater number of included subjects and therefore greater power to detect differences in fracture.

Compared with initial estimates of bone loss and fracture after transplantation, recent studies have reported lower rates and subsequently smaller treatment effects. Our estimates are similar to those reported by recent studies not included in this analysis. We found an overall in-

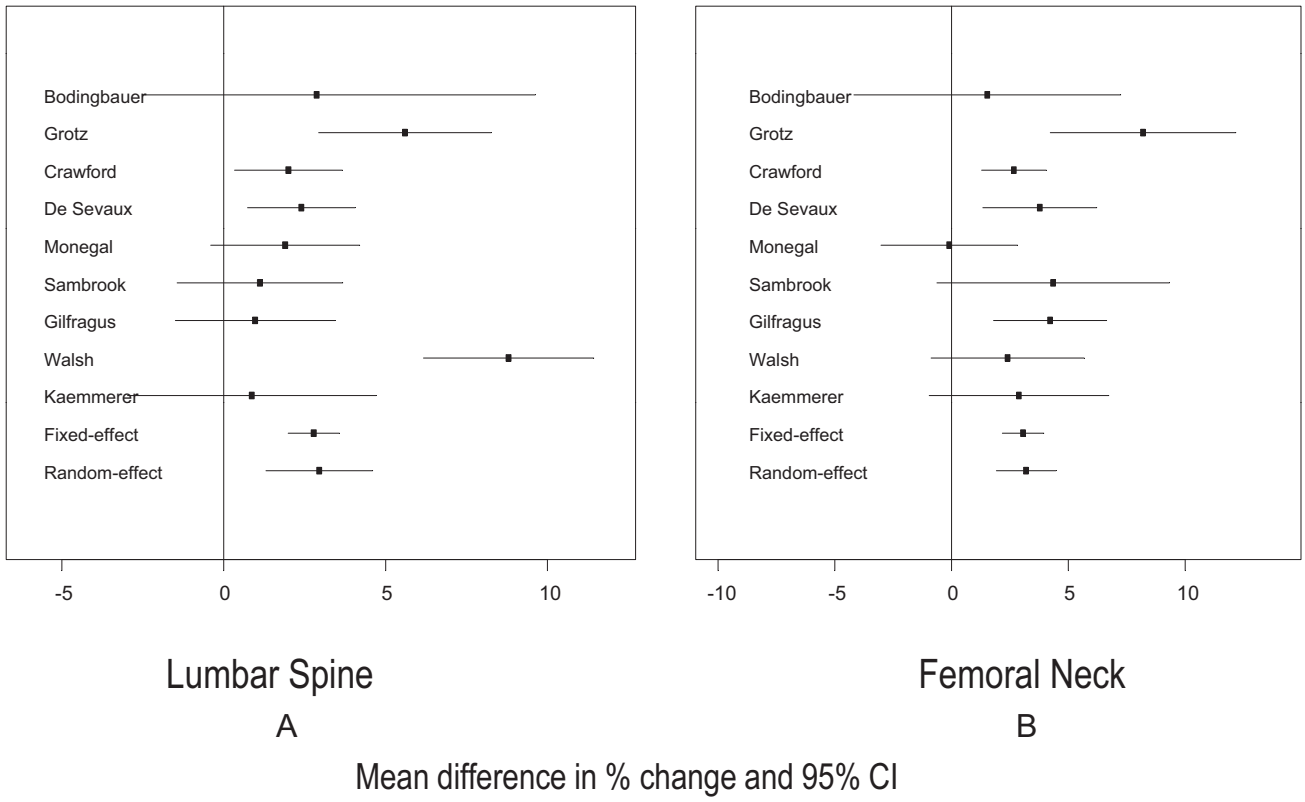

FIG. 3. Effect of treatment with bisphosphonates or vitamin D analogs on percent change in areal BMD at the LS (2.98%, 95% CI 1.31, 4.64 by random effects model; A) or FN (3.05%, 95% CI 2.16, 3.93 by fixed effects model; B) in the first year after organ transplantation.

cidence of fracture among untreated patients of 24.7%. This is in the middle range of reported estimates (5, 8–10, 13–15, 40–42), and it reflects the differential risk among subjects with various types of transplants and immunosuppressive regimens. We have previously reported losses of 3% at the LS and 6% at the FN in untreated patients during the first year after cardiac transplant (5). These rates were reduced to 0.7 and 1.7% at the LS and FN,

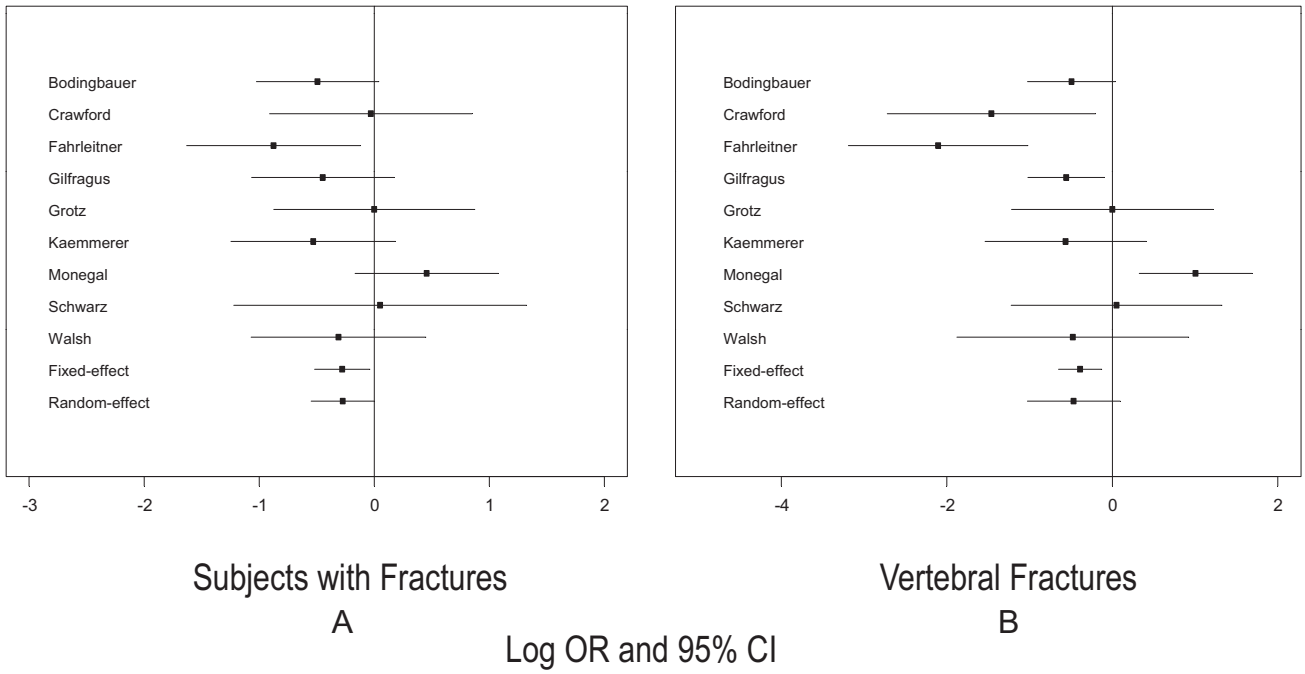

FIG. 4. Effect of bisphosphonate treatment after organ transplantation on number of subjects with fractures (OR 0.53, 95% CI 0.30, 0.91 by FEM by fixed effect model; A) and on number of vertebral fractures (OR 0.34, 95% CI 0.09, 1.24 by random effects model; B).

respectively, in subjects randomized to alendronate and 1.6% and 2.1%, respectively, at the LS and FN in subjects treated with calcitriol. In the meta-analysis by Palmer *et al.* (39), bisphosphonate treatment increased BMD by 7.7% at the LS and 7.2% at the FN. Vitamin D analogs increased LS BMD by 4.5%. These increases are greater than we observed, perhaps in part because the analysis by Palmer *et al.* included studies with a longer duration of follow-up than 12 months. These authors also reported that bisphosphonate treatment was associated with improved BMD at the LS and FN when directly compared with vitamin D analogs.

There are several limitations to our study. The number of studies included was small. There was a great deal of heterogeneity in the included trials, ranging from type of organ transplanted to type and dose of treatment and immunosuppressive regimen. However, restricting our sample further would have yielded too few studies to perform an analysis of fracture. Also, as previously mentioned, the pattern of bone loss after solid organ transplantation is similar, regardless of type of organ transplanted and underlying bone disease before transplantation (5–15). Three studies, two of vitamin D analogs and one of bisphosphonates, did not have specific follow-up of fractures at 1 yr. For these studies, the number of fractures and the number of patients with fracture at this time point were estimated, leading to a possible bias in the results. Our results were also subject to publication bias, although formal testing did not reveal significant evidence of bias. We attempted to minimize this bias by reviewing unpublished abstracts and contacting experts in the field for unpublished results. In addition, because the primary outcome for the majority of included studies was BMD and not fracture, this bias was diminished. Our results may not be applicable to those transplant patients who receive different immunosuppressive regimen. All of the regimens studied included glucocorticoids, and for kidney transplant patients, there is a trend toward regimens that are steroid free. Furthermore, none of the studies used tacrolimus, which might be associated with less bone loss than cyclosporine (33, 35) and thus could also be associated with lower fracture risk.

In summary, treatment with bisphosphonates or active vitamin D analogs during the first year after transplant was associated with fewer subjects with fractures, fewer vertebral fractures, and a 3% increase in LS and FN BMD. When considered separately, bisphosphonate treatment was associated with fewer subjects with fractures. These results suggest that in patients managed with glucocorticoids and cyclosporine A, treatment with bisphosphonates or active vitamin D analogs prevents fractures during the first year after organ transplantation.

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