Osteoporos Int (2016) 27:1115–1121
DOI 10.1007/s00198-015-3424-3

ORIGINAL ARTICLE

Trabecular bone score in kidney transplant recipients

K. L. Naylor[1,2] · L. M. Lix[3] · D. Hans[4] · A. X. Garg[1,5,6] · D. N. Rush[3] · A. B. Hodsman[6] · W. D. Leslie[3]

Received: 25 August 2015 / Accepted: 12 November 2015 / Published online: 25 November 2015

Abstract
Summary It is uncertain whether bone mineral density (BMD) can accurately predict fracture in kidney transplant recipients. Trabecular bone score (TBS) provides information independent of BMD. Kidney transplant recipients had abnormal bone texture as measured by lumbar spine TBS, and a lower TBS was associated with incident fractures in recipients.
Introduction Trabecular bone score (TBS) is a texture measure derived from dual energy X-ray absorptiometry (DXA) lumbar spine images, providing information independent of bone mineral density. We assessed characteristics associated with TBS and fracture outcomes in kidney transplant recipients.
Methods We included 327 kidney transplant recipients from Manitoba, Canada, who received a post-transplant DXA (median 106 days post-transplant). We matched each kidney transplant recipient (mean age 45 years, 39 % men) to three controls from the general population (matched on age, sex, and DXA date). Lumbar spine (L1-L4) DXA images were used to derive TBS. Non-traumatic incident fracture (excluding hand, foot, and craniofacial) (n=31) was assessed during a mean follow-up of 6.6 years. We used multivariable linear regression models to test predictors of TBS, and multivariable Cox proportional hazard regression was used to estimate hazard ratios (HRs) per standard deviation decrease in TBS to express the gradient of risk.
Results Compared to the general population, kidney transplant recipients had a significantly lower lumbar spine TBS (1.365±0.129 versus 1.406±0.125, P<0.001). Multivariable linear regression revealed that receipt of a kidney transplant was associated with a significantly lower mean TBS compared to controls (−0.0369, 95 % confidence interval [95 % CI] −0.0537 to −0.0202). TBS was associated with fractures independent of the Fracture Risk Assessment score including BMD (adjusted HR per standard deviation decrease in TBS 1.64, 95 % CI 1.15–2.36).
Conclusion Kidney transplant recipients had abnormal bone texture as assessed by TBS and a lower lumbar spine TBS was associated with fractures in recipients.

Keywords Bone mineral density · Fracture · Kidney transplant recipient · Trabecular bone score

✉ W. D. Leslie
BLESLIE@sbgh.mb.ca

1 Institute for Clinical Evaluative Sciences (ICES), London, ON, Canada

2 Institute of Health Policy, Management, and Evaluation, University of Toronto, Toronto, ON, Canada

3 Department of Medicine, University of Manitoba, Winnipeg, ON, Canada

4 Centre for Bone Diseases, Lausanne University Hospital, Lausanne, Switzerland

5 Department of Epidemiology & Biostatistics, Western University, London, ON, Canada

6 Division of Nephrology, Western University, London, ON, Canada

Introduction

Kidney transplant recipients are at increased fracture risk compared to the general population [1–9]. Potential reasons include presence of chronic kidney disease-mineral and bone disorder (CKD-MBD) and glucocorticoid administration post-transplant [10]. The best way to examine skeletal changes and identify kidney transplant recipients at high fracture risk is not well established. In the general population, low bone mineral density (BMD) is strongly predictive of fracture

[11–14]; however, conflicting results have been found in the kidney transplant population [15–17]. BMD effectively measures bone mass but may not reflect bone quality (i.e., microarchitecture); however, bone quality may also be adversely affected in kidney transplant recipients, particularly in recipients with CKD-MBD [10]. Recognizing the limitations of BMD, the Kidney Disease Improving Global Outcomes (KDIGO) guidelines suggest a bone biopsy and biochemical measures, instead of BMD, guide treatment decisions in kidney transplant recipients with adynamic bone disease (i.e., low turnover bone disease), more advanced kidney disease (i.e., stage 4 and 5 CKD), and/or CKD-MBD [10]. Although a bone biopsy provides information on bone quality, this is an invasive test and few centers have the resources to perform it.

Trabecular bone score (TBS) is a novel, noninvasive, and inexpensive skeletal measure derived from lumbar spine dual energy X-ray absorptiometry (DXA) images [18]. TBS is a gray-level textural metric which yields information independent of BMD [19, 20]; a higher TBS value is indicative of better bone structure (e.g., dense trabecular bone network) and a lower TBS value is associated with worse bone structure. TBS has been found to be associated with fracture in the general population [21–24] and in some special populations where BMD has limited utility (e.g., diabetes, rheumatoid arthritis, and glucocorticoid-treated individuals) [25–28]. To our knowledge, no previous studies have assessed TBS in kidney transplant recipients. Therefore, we compared TBS in kidney transplant recipients with matched individuals from the general population, determined predictors of low TBS, and examined the association between TBS and incident fractures in kidney transplant recipients.

Materials and methods

Data sources

We used healthcare databases from the province of Manitoba, Canada, to conduct this population-based cohort study. Residents of Manitoba, Canada, are provided with universal access to healthcare (population 1.2 million) [29]. We obtained information on relevant covariates through Manitoba Health's computerized databases on physician billing claims and hospital discharge abstracts [30]. These databases contain diagnoses recorded using the International Classification of Diseases (ICD). To obtain information on BMD, we used Manitoba's BMD database. We used Manitoba's provincial retail pharmacy database to obtain drug information [31]. BMD measurements were linked to administrative healthcare databases though anonymous personal identifiers. Approval for this study was obtained from the University of Manitoba Research Ethics Board.

Cohort

We included adult kidney transplant recipients (≥18 years) who received their transplant in Manitoba and received a post-transplant DXA exam during the years 1999–2011; DXA examinations have been routinely administered to virtually all kidney transplant recipients at our transplant center since 1997 [32]. We matched each kidney transplant recipient on age (±2 years), sex, and DXA examination date (±2 years) to three controls from the general population. We defined the cohort entry date as the date of the first DXA examination, which was required to be administered within the first 5 years of transplantation. We only included the first DXA measurement for individuals with multiple measurements.

Bone mineral density and trabecular bone score

We used a single fan-beam scanner configuration (Prodigy, GE Healthcare) to perform and analyze all DXA scans. BMD was measured at the femoral neck and lumbar spine (L1-L4). We used the National Health and Nutrition Examination Survey to calculate hip T-scores and the US manufacturer's reference values were used to calculate lumbar spine T-scores [33]. T-scores were calculated relative to young white healthy females. TBS values were obtained from anonymized spine DXA files sent to the Bone Disease Center at the Lausanne University Hospital, Switzerland. All TBS measurements were performed blinded to clinical outcomes using the TBS iNsight® Software (version 2.1; Medimaps, Merignac, France). The TBS calculation was done over the same region as the anteroposterior spine BMD measurement. There was stable long-term phantom stability (coefficient of variation <0.5 %) for the three instruments used in this study. Mean TBS values were similar for the three DXA scanners used. Short-term reproducibility for TBS was 2.1 % based on 92 individuals who received two spine DXA scans within 28 days.

Covariates

We assessed body mass index (BMI, kg/m^2) at the time of the DXA. We assessed the following covariates prior to DXA: previous fracture (clinical vertebral, hip, forearm, and humerus fracture diagnosis, excluding those with high-trauma diagnosis codes), chronic obstructive pulmonary disease diagnosis (smoking proxy), rheumatoid arthritis diagnosis, alcohol abuse diagnosis (high alcohol use proxy), secondary osteoporosis diagnosis (which included receipt of a kidney transplant), prolonged glucocorticoid use (>3 months in the prior year), and osteoporosis therapy (≥180 days of prescription

doses filled of bisphosphonates, calcitonin, raloxifene, or systemic estrogen in the prior year). History of a parental hip fracture was only available since 2005. The Canadian Fracture Risk Assessment Tool (FRAX) (FRAX Desktop Multi-Patient Entry, version 3.7) was used to calculate the 10-year probability of major osteoporotic fracture (all individuals aged less than 40 years were entered as 40 years) [34]. Information on actual vitamin D and calcium intake was not available; however, the transplant center protocol recommends supplementation post-transplant. Regarding prednisone administration, at our center, prior to the year 2000, the average daily dose in the first year post-transplant was 12.5–15 mg and after the year 2000 was 7.5 mg. During later years, the average daily dose was 5 mg.

Incident fractures

We assessed all incident fractures in kidney transplant recipients (excluding hands, feet, and craniofacial fractures or those with high-trauma diagnosis codes) [3, 4]. Fractures were determined through diagnoses in physician billing claims and hospital discharge abstract databases using previously validated definitions [35]; it is important to note administrative databases often underestimate the number of vertebral fractures [35]. Hip and forearm fracture diagnoses were required to be accompanied by a procedural code to increase accuracy [36].

Statistical analysis

For continuous variables, we used means (±standard deviation) or medians (interquartile range [IQR]), as appropriate. For categorical variables, we used counts (percentages) to describe baseline characteristics. To compare baseline characteristics between recipients and their controls, we used the Student's *t* test for normally distributed continuous variables, Mann-Whitney test for non-normally distributed continuous variables, and the chi-square test of independence for categorical variables. We used the Kaplan-Meier method to estimate the fracture-free probability in kidney transplant recipients, and differences in fracture probability were determined using the log-rank test comparing recipients above and below the median TBS (low TBS <1.370 versus high TBS ≥1.370). We used multivariable linear regression to determine predictors of TBS. In a supplementary analysis, we also used logistic regression to determine predictors of TBS falling in the lowest tertile versus the highest tertile (referent), adjusting for all other covariates in the model. To determine the ability of TBS to discriminate between individuals with and without a fracture, we used the area under the receiver operator characteristic curve (ROC); we considered a value of 0.5 to be the null value (no discrimination). Hazard ratios per standard deviation decrease in TBS were used to express the gradient of risk for fracture using Cox proportional hazard regression (proportional hazard assumption was met), adjusting for relevant covariates. Due to a skewed distribution, the FRAX probability scores were log-transformed for all regression analyses. We performed the statistical analysis using Statistica (version 10.0, StatSoft Inc., Tulsa, OK); for the ROC analysis we used Sigmaplot for Windows (Version 10, Systat Software Inc.).

Results

Baseline characteristics

We included 327 kidney transplant recipients who received a DXA between 1999 and 2011 out of a total of 330 kidney transplant recipients during this time period. The median time from transplant to DXA examination was 106 days (IQR 74 to 207 days) with 86 % receiving a DXA within the first year after transplant (Table 1). The median time on dialysis was 2.1 years (IQR 1.0 to 4.2 years). Matching characteristics (mean age 45 years, 39 % male, and DXA year 2005) were similar between kidney transplant recipients and their controls (Table 1). Compared to the general population, kidney transplant recipients had a significantly lower mean TBS at the lumbar spine (1.365±0.129 versus 1.406±0.125, $P<0.001$), were more likely to have recently used glucocorticoids (54 versus 16 %, $P<0.001$), and had a higher fracture probability as predicted by FRAX.

Trabecular bone score

Multivariable linear regression revealed a negative association between TBS and receipt of a kidney transplant after adjusting for other covariates; recipients had a significantly lower mean TBS compared to controls (−0.0369, 95 % confidence interval [CI] −0.0537 to −0.0202) (Table 2). As well, the following factors were found to be associated with a significantly lower TBS in this analysis: older age, female sex, prior fracture, and COPD diagnosis (Table 2). When logistic regression was used to determine factors associated with a higher odds of being in the lowest TBS tertile, only older age and female sex reached statistical significance, while osteoporosis treatment was associated with a lower odds of being in the lowest TBS tertile (Table 3).

Fracture risk

Over an average of 6.6 years follow-up, 31 (9 %) kidney transplant recipients sustained one or more incident fractures (13 FRAX-defined major osteoporotic fractures, 18 other fractures), 18 (6.1 %) died, and 16 (5.4 %) were lost to follow-up. Mean TBS was significantly lower in recipients who sustained a fracture compared to recipients who did not (1.301±0.144 versus 1.372±0.125, $P=0.003$). Fracture developed in 21 of

Table 1 Baseline characteristics of kidney transplant recipients and matched controls

	Transplants (n=327)	Controls (n=981)	P value
Age	45.3±12.4	45.4±12.3	0.898
Sex (male)	126 (39 %)	378 (39 %)	1.000
Calendar year of DXA examination	2005±3	2005±3	0.958
Lumbar spine TBS (L1-L4)	1.365±0.129	1.406±0.125	<0.001
BMI (kg/m^2)	27.6±5.5	26.4±5.1	<0.001
Prior fracture	19 (6 %)	137 (14 %)	<0.001
Parental hip fracture	10 (3 %)	43 (4 %)	0.293
COPD diagnosis (smoking proxy)	9 (3 %)	60 (6 %)	0.018
Glucocorticoid use[b]	176 (54 %)	159 (16 %)	<0.001
Rheumatoid arthritis diagnosis	(<1 %)[a]	53 (5 %)	<0.001
Alcohol abuse diagnosis (high alcohol use proxy)	7 (2 %)	33 (3 %)	0.266
Secondary osteoporosis diagnosis	327 (100 %)	209 (21 %)	<0.001
Femoral neck T-score	−1.0±1.1	−0.7±1.1	<0.001
Lumbar spine T-score	−0.4±1.5	−0.7±1.5	<0.001
FRAX major fracture probability without BMD[c] (%)	4.0 (2.6–7.5)	2.6 (1.5–4.3)	<0.001
FRAX major fracture probability with BMD[c] (%)	5.0 (3.0–8.8)	3.2 (1.9–5.3)	<0.001
Osteoporosis therapy	6 (2 %)	69 (7 %)	<0.001

Data are mean±SD, median (IQR), or N (%)

BMD bone mineral density, *BMI* body mass index, *COPD* chronic obstructive pulmonary disease, *FRAX* Fracture Risk Assessment Tool, *TBS* trabecular bone score

[a] Suppressed because of small numbers ≤5

[b] Recent glucocorticoid use defined as use for ≥90 days in the year prior to the bone mineral density measurement

[c] FRAX major fracture probability expressed as a percent

163 (12.9 %) recipients with a TBS below the median (low TBS <1.370) versus 10 of 164 (6.1 %) recipients with a TBS above the median (high TBS ≥1.370) (P=0.036). Figure 1 demonstrates the Kaplan-Meier curve for fracture-free probability according to recipients who were above and below the median TBS. Kidney transplant recipients with a lower TBS were less likely to remain fracture-free (P=0.017). TBS was able to discriminate between recipients with and without a fracture (area under the curve 0.64, 95 % CI 0.53–0.74, P= 0.012). The gradient of risk for fracture was statistically significant for TBS scores even after adjustment for age and sex, and FRAX score (with and without femoral neck BMD)

Table 2 Multivariable linear regression analysis of correlates of trabecular bone score

	β	95 % CI
Age (per year)	−0.0038	−0.0030 to −0.0046
Sex (female versus male)	−0.0451	−0.0313 to −0.0590
BMI (per kg/m^2)	0.0002	−0.0011 to 0.0015
Prior fracture	−0.0240	−0.0443 to −0.0036
Parental hip fracture	0.0027	−0.0308 to 0.0363
COPD diagnosis	−0.0373	−0.0669 to −0.0076
Glucocorticoid use	−0.0150	−0.0317 to 0.0017
Rheumatoid arthritis diagnosis	0.0060	−0.0275 to 0.0394
Alcohol abuse diagnosis	0.0056	−0.0327 to 0.0439
Osteoporosis therapy	0.0257	−0.0033 to 0.0546
Transplant (versus control)	−0.0369	−0.0537 to −0.0202

BMI body mass index, *COPD* chronic obstructive pulmonary disease, *CI* confidence interval

Table 3 Odds ratios (95 % CI) for lowest versus highest lumbar spine trabecular bone score tertile

	Odds ratio	95 % CI
Age (per year)	1.08	1.06–1.10
Sex (female versus male)	1.94	1.43–2.64
BMI (per kg/m^2)	1.02	0.99–1.04
Prior fracture	1.37	0.89–2.11
Parental hip fracture	0.68	0.32–1.41
COPD diagnosis	1.24	0.65–2.38
Glucocorticoid use	1.32	0.90–1.92
Rheumatoid arthritis diagnosis	1.24	0.62–2.49
Alcohol abuse diagnosis	0.87	0.39–1.93
Osteoporosis therapy	0.50	0.26–0.97
Transplant (versus control)	2.13	1.47–3.07

Results are adjusted for all other covariates in the model

BMI body mass index, *COPD* chronic obstructive pulmonary disease, *CI* confidence interval

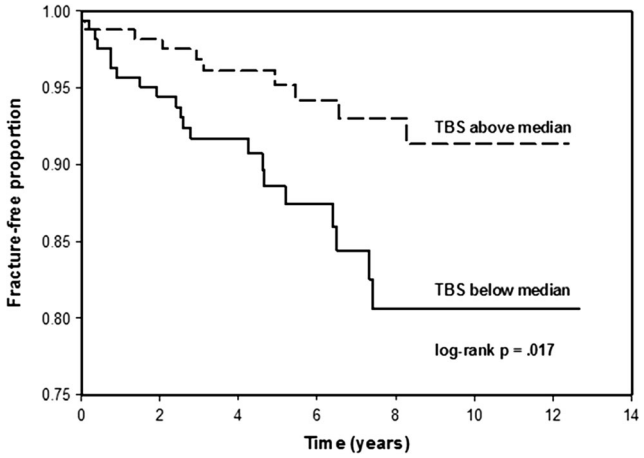

Fig. 1 Kaplan-Meier estimator for fracture in kidney transplant recipients, stratified by median trabecular bone score (*TBS*) (TBS below median <1.370; TBS above median ≥1.370)

(Table 4). Finally, lower lumbar spine TBS was associated with fracture independent of FRAX score (using femoral neck BMD) and spine BMD (adjusted hazard ratio per SD decrease 1.55, 95 % CI 1.06–2.27).

Discussion

We found that kidney transplant recipients had a significantly lower lumbar spine TBS compared to the matched general population after adjustment for relevant covariates. Lumbar spine TBS was significantly associated with fractures independent of FRAX score. These results suggest TBS may be a useful, noninvasive method to assess fracture risk in kidney transplant recipients. Aside from kidney transplantation, additional variables associated with a significantly lower TBS were older age, female sex, prior fracture, and COPD diagnosis.

In contrast to our findings which found bone health, as measured by TBS, is suboptimal in kidney transplant recipients, a previous study conducted in the same population of kidney transplant recipients found bone health as measured by BMD was average for age and sex [37]. This highlights the complexity of bone disease in kidney transplant recipients with changes in bone metabolism reflecting a variety of pathophysiologic processes (e.g., osteomalacia, adynamic bone disease, mixed bone disease) [38] which may result in kidney transplant recipients having a normal BMD but altered bone quality [10]. Bone strength is a composite of BMD and bone quality, and both contribute to a complete picture of bone health and fracture risk in kidney transplant recipients [39, 40]. This may be the reason previous studies have not consistently found that BMD can predict fractures in kidney transplant recipients [15–17]. However, our previous study found that BMD reached average values for age and sex after a mean of 8 years post-transplant [37]; therefore, if we measured TBS years after transplantation, it is plausible that TBS values would have been similar to controls.

Lumbar spine TBS was associated with fracture in kidney transplant recipients even after adjustment for age and sex, FRAX score, and FRAX score in addition to spine BMD. Similar to results of this study, TBS has shown promise in other unique populations for which BMD may not be an accurate measure of bone health. Breban et al., found that TBS in rheumatoid arthritis patients (n=185) was lower in those with a prior vertebral fracture compared to those without such a history (P<0.001), and TBS had greater discriminative ability compared to BMD (area under the curve 0.70 versus 0.62) [26]. Leslie et al., assessed TBS in women with diabetes (n= 2356) finding an association between TBS and fracture independent of BMD and other covariates (adjusted hazard ratio 1.27, 95 % CI 1.10–1.46) [25].

As demonstrated in this study, TBS may be a useful measure to assess bone health and fracture risk in kidney transplant recipients. TBS has potential advantages over other non-BMD measurements for assessing bone health and fracture risk. High-resolution peripheral quantitative computed tomography can also be used to assess bone quality but its use is limited by high costs and availability [18, 41]. A bone biopsy can also be used to assess bone quality but this is an invasive technique with limited availability [18]. In contrast, TBS can be obtained from DXA machines which are widely available. However, further research needs to be done before TBS can be routinely used in managing kidney transplant recipients. Studies with larger sample sizes are needed to assess the predictive ability of TBS for major osteoporotic fractures and hip fracture alone. Moreover, the predictive ability of TBS in recipients with and without CKD-MBD should also be assessed given the complexity of bone disease in this setting. Additionally, given the ease

Table 4 Adjusted hazard ratios for lumbar spine trabecular bone score to express the gradient of risk for incident fractures in kidney transplant recipients

Adjustment(s)	Hazard ratio	95 % CI
Age and sex	1.76	1.22–2.55
FRAX major fracture probability without BMD[a]	1.68	1.18–2.40
FRAX major fracture probability with BMD[a]	1.64	1.15–2.36
FRAX major fracture probability with BMD[a] plus spine BMD	1.55	1.06–2.27

Hazard ratio per standard deviation decrease in lumbar spine trabecular bone score

BMD bone mineral density, *CI* confidence interval, *FRAX* Fracture Risk Assessment Tool

[a] FRAX major fracture probability (log-transformed)

of obtaining TBS values, TBS could complement the use of FRAX, potentially improving its performance in kidney transplant recipients as has been observed for the general population [42, 43].

Several strengths of this study deserve mention. First, to our knowledge, this is the first study to assess TBS in kidney transplant recipients. Second, 99 % of recipients at our center received a DXA increasing the generalizability of our results. However, this study is not without limitations. First, power was limited due to the small number of fracture events and we were unable to determine whether TBS had a better predictive ability compared to BMD alone and FRAX (with and without BMD). Moreover, the small number of incident major osteoporotic fractures was insufficient for analysis alone and there were no hip fractures; therefore, we examined all non-traumatic fractures (excluding hand, foot, and craniofacial). However, others have found that the majority of fractures in kidney transplant recipients involve sites other than those designated by FRAX as major osteoporotic fractures [3, 4]. Second, it would have been of interest to assess long-term changes in TBS in recipients given that previous studies have found BMD remains stable or improves as time since transplant increases [15, 37, 44]. Last, our results may not be generalizable to other countries or ethnic groups.

In conclusion, kidney transplant recipients had reduced lumbar spine TBS compared to the general population. Lumbar spine TBS may be a useful new tool in the quest to better predict fracture risk in kidney transplant recipients. However, confirmatory studies are needed before TBS can be routinely used by clinicians in this unique patient population.

Acknowledgments Dr. Naylor is supported by the Canadian Institutes of Health Research Fellowship and the Canadian National Transplant Research Program Astellas Training Award. The authors are indebted to Manitoba Health for the provision of data (HIPC File No. 2011/2012–31). The results and conclusions are those of the authors, and no official endorsement by Manitoba Health is intended or should be inferred. This article has been reviewed and approved by the members of the Manitoba Bone Density Program Committee.

Compliance with ethical standards

Conflicts of interest Didier Hans: Co-ownership in the TBS patent. Stock options or royalties: Med-Imaps. William Leslie: Speaker bureau (paid to facility): Amgen, Eli Lily, Novartis. Research grants (paid to facility): Amgen, Genzyme. Amit Garg: Investigator-initiated grant from Astellas and Roche for a Canadian Institutes of Health Research study in living kidney donors and his institution received unrestricted research funding from Pfizer. David Rush: Advisory board member, Astellas; Grant investigator, Astellas; Speaker: Astellas, STA Communications, Pfizer. Kyla Naylor, Lisa M Lix, and Anthony B. Hodsman declare that they have no conflict of interest.

References

1. Abbott KC, Oglesby RJ, Hypolite IO, Kirk AD, Ko CW, Welch PG, Agodoa LY, Duncan WE (2001) Hospitalizations for fractures after renal transplantation in the United States. Ann Epidemiol 11:450–457
2. Conley E, Muth B, Samaniego M, Lotfi M, Voss B, Armbrust M, Pirsch J, Djamali A (2008) Bisphosphonates and bone fractures in long-term kidney transplant recipients. Transplantation 86:231–237
3. Kalker AJ, Pirsch JD, Heisey D, Sollinger HW, Beizer FO, Knechtle SJ, D'Alessandro AM (1996) Foot problems in the diabetic transplant recipient. Clin Transpl 10:503–510
4. Nikkel LE, Hollenbeak CS, Fox EJ, Uemura T, Ghahramani N (2009) Risk of fractures after renal transplantation in the United States. Transplantation 87:1846–1851
5. Ramsey-Goldman R, Dunn JE, Dunlop DD, Stuart FP, Abecassis MM, Kaufman DB, Langman CB, Salinger MH, Sprague SM (1999) Increased risk of fracture in patients receiving solid organ transplants. J Bone Miner Res 14:456–463
6. Vautour LM, Melton ILJ, Clarke BL, Achenbach SJ, Oberg AL, McCarthy JT (2004) Long-term fracture risk following renal transplantation: a population-based study. Osteoporos Int 15:160–167
7. Ball AM, Gillen DL, Sherrard D, Weiss NS, Emerson SS, Seliger SL, Kestenbaum BB, Stehman-Breen C (2002) Risk of hip fracture among dialysis and renal transplant recipients. J Am Med Assoc 288:3014–3018
8. Rizzari MD, Suszynski TM, Gillingham KJ, Dunn TB, Ibrahim HN, Payne WD, Chinnakotla S, Finger EB, Sutherland DE, Kandaswamy R, Najarian JS, Pruett TL, Kukla A, Spong R, Matas AJ (2012) Ten-year outcome after rapid discontinuation of prednisone in adult primary kidney transplantation. Clin J Am Soc Nephrol 7:494–503
9. Nikkel LE, Mohan S, Zhang A, McMahon DJ, Boutroy S, Dube G, Tanriover B, Cohen D, Ratner L, Hollenbeak CS, Leonard MB, Shane E, Nickolas TL (2012) Reduced fracture risk with early corticosteroid withdrawal after kidney transplant. Am J Transplant 12:649–659
10. Kidney Disease Imrpoving Global Outcomes (KDIGO) Work Group (2009) KDIGO clinical practice guidelines for the prevention, diagnosis, evaluation, and treatment of chronic kidney disease-mineral and bone disorder (CKD-MBD). Kidney Int Suppl 113:S1–130
11. Cummings SR, Black DM, Nevitt MC, Browner W, Cauley J, Ensrud K, Genant HK, Palermo L, Scott J, Vogt TM (1993) Bone density at various sites for prediction of hip fractures. The study of osteoporotic fractures research group. Lancet 341:72–75
12. Schott AM, Cormier C, Hans D et al (1998) How hip and whole-body bone mineral density predict hip fracture in elderly women: the EPIDOS prospective study. Osteoporos Int 8:247–254
13. Mussolino ME, Gillum RF (2008) Low bone mineral density and mortality in men and women: the third national health and nutrition examination survey linked mortality file. Ann Epidemiol 18:847–850
14. Qu X, Huang X, Jin F, Wang H, Hao Y, Tang T, Dai K (2013) Bone mineral density and all-cause, cardiovascular and stroke mortality: a meta-analysis of prospective cohort studies. Int J Cardiol 166:385–393
15. Akaberi S, Simonsen O, Lindergard B, Nyberg G (2008) Can DXA predict fractures in renal transplant patients? Am J Transplant 8:2647–2651
16. Grotz WH, Mundinger FA, Gugel B, Exner V, Kirste G, Schollmeyer PJ (1994) Bone fracture and osteodensitometry with dual energy X-ray absorptiometry in kidney transplant recipients. Transplantation 58:912–915

17. Durieux S, Mercadal L, Orcel P et al (2002) Bone mineral density and fracture prevalence in long-term kidney graft recipients. Transplantation 74:496–500
18. Silva BC, Leslie WD, Resch H, Lamy O, Lesnyak O, Binkley N, McCloskey EV, Kanis JA, Bilezikian JP (2014) Trabecular bone score: a noninvasive analytical method based upon the DXA image. J Bone Miner Res 29:518–530
19. Pothuaud L, Barthe N, Krieg MA, Mehsen N, Carceller P, Hans D (2009) Evaluation of the potential use of trabecular bone score to complement bone mineral density in the diagnosis of osteoporosis: a preliminary spine BMD-matched, case-control study. J Clin Densitom 12:170–176
20. Hans D, Barthe N, Boutroy S, Pothuaud L, Winzenrieth R, Krieg MA (2011) Correlations between trabecular bone score, measured using anteroposterior dual-energy X-ray absorptiometry acquisition, and 3-dimensional parameters of bone microarchitecture: an experimental study on human cadaver vertebrae. J Clin Densitom 14:302–312
21. Boutroy S, Hans D, Sornay-Rendu E, Vilayphiou N, Winzenrieth R, Chapurlat R (2013) Trabecular bone score improves fracture risk prediction in non-osteoporotic women: the OFELY study. Osteoporos Int 24:77–85
22. Rabier B, Heraud A, Grand-Lenoir C, Winzenrieth R, Hans D (2010) A multicentre, retrospective case-control study assessing the role of trabecular bone score (TBS) in menopausal Caucasian women with low areal bone mineral density (BMDa): analysing the odds of vertebral fracture. Bone 46:176–181
23. Hans D, Goertzen AL, Krieg MA, Leslie WD (2011) Bone microarchitecture assessed by TBS predicts osteoporotic fractures independent of bone density: the Manitoba study. J Bone Miner Res 26:2762–2769
24. Popp AW, Meer S, Krieg MA, Perrelet R, Hans D, Lippuner K (2015) Bone mineral density (BMD) and vertebral trabecular bone score (TBS) for the identification of elderly women at high risk for fracture: the SEMOF cohort study. Eur Spine J. Epub 2015 May 27.
25. Leslie WD, Aubry-Rozier B, Lamy O, Hans D (2013) TBS (trabecular bone score) and diabetes-related fracture risk. J Clin Endocrinol Metab 98:602–609
26. Breban S, Briot K, Kolta S, Paternotte S, Ghazi M, Fechtenbaum J, Roux C (2012) Identification of rheumatoid arthritis patients with vertebral fractures using bone mineral density and trabecular bone score. J Clin Densitom 15:260–266
27. Ulivieri FM, Silva BC, Sardanelli F, Hans D, Bilezikian JP, Caudarella R (2014) Utility of the trabecular bone score (TBS) in secondary osteoporosis. Endocrine 47:435–448
28. Paggiosi MA, Peel NF, Eastell R (2015) The impact of glucocorticoid therapy on trabecular bone score in older women. Osteoporos Int 26:1773–1780
29. Manitoba Health (2012) Part Two Manitoba Health Population Report. http://www.gov.mb.ca/health/population/parttwo.pdf. Accessed 27 June 2015.
30. Roos NP, Shapiro E (1999) Revisiting the manitoba centre for health policy and evaluation and its population-based health information system. Med Care 37:JS10–14
31. Kozyrskyj AL, Mustard CA (1998) Validation of an electronic, population-based prescription database. Ann Pharmacother 32: 1152–1157
32. Jeffery JR, Leslie WD, Karpinski ME, Nickerson PW, Rush DN (2003) Prevalence and treatment of decreased bone density in renal transplant recipients: a randomized prospective trial of calcitriol versus alendronate. Transplantation 76:1498–1502
33. Looker AC, Wahner HW, Dunn WL, Calvo MS, Harris TB, Heyse SP, Johnston CC Jr, Lindsay R (1998) Updated data on proximal femur bone mineral levels of US adults. Osteoporos Int 8:468–489
34. World Health Organization (2011) FRAX World Health Organization Fracture Risk Assessment Tool. http:// www.shef.ac.uk/FRAX/index.aspx. Accessed 29 June 2015.
35. Lix LM, Azimaee M, Osman BA, Caetano P, Morin S, Metge C, Goltzman D, Kreiger N, Prior J, Leslie WD (2012) Osteoporosis-related fracture case definitions for population-based administrative data. BMC Public Health 12:301
36. Tamblyn R, Reid T, Mayo N, McLeod P, Churchill-Smith M (2000) Using medical services claims to assess injuries in the elderly: sensitivity of diagnostic and procedure codes for injury ascertainment. J Clin Epidemiol 53:183–194
37. Naylor KL, Garg AX, Hodsman AB, Rush DN, Leslie WD (2014) Long-term changes in bone mineral density in kidney transplant recipients. Transplantation 98:1279–85
38. Weisinger JR, Carlini RG, Rojas E, Bellorin-Font E (2006) Bone disease after renal transplantation. Clin J Am Soc Nephrol 1:1300–1313
39. Keaveny TM, Bouxsein ML (2008) Theoretical implications of the biomechanical fracture threshold. J Bone Miner Res 23:1541–1547
40. Chesnut C, Majumdar S, Gardner J, Shields A, Newitt DC, Erickson E, Glott M, Kriegman A, Mindeholm L (2001) Assessment of bone quality, quantity, and turnover with multiple methodologies at multiple skeletal sites. Adv Exp Med Biol 496: 95–97
41. Boutroy S, Bouxsein ML, Munoz F, Delmas PD (2005) In vivo assessment of trabecular bone microarchitecture by high-resolution peripheral quantitative computed tomography. J Clin Endocrinol Metab 90:6508–6515
42. Leslie WD, Johansson H, Kanis JA, Lamy O, Oden A, McCloskey EV, Hans D (2014) Lumbar spine texture enhances 10-year fracture probability assessment. Osteoporos Int 25:2271–2277
43. McCloskey EV, Oden A, Harvey NC, Leslie WD, Hans D, Johansson H, Kanis JA (2015) Adjusting fracture probability by trabecular bone score. Calcif Tissue Int 96:500–509
44. Carlini RG, Rojas E, Weisinger JR, Lopez M, Martinis R, Arminio A, Bellorin-Font E (2000) Bone disease in patients with long-term renal transplantation and normal renal function. Am J Kidney Dis 36:160–166