REVIEW

Fragility fracture risk in cirrhosis: a comparison of the fracture risk assessment tool, British Society of Gastroenterology and National Institute for Health and Clinical Excellence guidelines

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Abstract

Objective Low bone mineral density (BMD) is common in chronic liver disease and predisposes to fracture. We aimed to compare British Society of Gastroenterology (BSG) and National Institute for Health and Clinical Excellence (NICE) osteoporosis guidelines with the fracture risk assessment tool (FRAX). FRAX is a web-based algorithm used to estimate fracture risk with or without dual-emission x-ray absorptiometry (DXA). Pre-BMD FRAX categorises patients to low, intermediate or high risk according to thresholds set by the National Osteoporosis Guidelines Group (NOGG) and recommends lifestyle advice, DXA or anti-osteoporosis treatment, respectively.

Design The guidelines were applied to 132 patients with cirrhosis (91% Child–Pugh A). The number that would require DXA and be recommended treatment was determined. Using post-BMD FRAX/NOGG as a reference point, high-risk patients not recommended treatment and low-risk patients treated ‘unnecessarily’ were identified.

Results BSG guidelines were applicable to 100% of the cohort, 88% required DXA and 30% would be recommended treatment. Equivalent figures for NICE guidelines were 30%, 17% and 12%, and for FRAX/NOGG guidelines were 78%, 27% and 15%, respectively. Using BSG guidance 8% of high-risk patients were not recommended treatment and 62% of those treated were low risk, compared with NICE: 3%, 60% and FRAX/NOGG: 13%, 40%, respectively.

Conclusion For patients with Child–Pugh A cirrhosis BSG guidelines are the most inclusive, but have high cost implications in terms of DXA scanning and unnecessary treatment. Risk stratification using FRAX requires fewer DXA scans with minimal impact in terms of missing high-risk patients, and yields a modest reduction in unnecessary treatment.

Introduction

Bone disease is an important complication of chronic liver disease. Osteopenia and osteoporosis are associated with fractures resulting in significant morbidity. Severity rather than aetiology of liver disease correlates with (lower) bone mineral density (BMD).^{1–3} Patients with alcohol-related cirrhosis tend to sustain more non-vertebral fractures than other patients with cirrhosis.⁴

Prospective studies have shown that the risk of fracture in cirrhosis increases progressively with decreasing BMD, such that the risk of fracture is two to three-fold for each SD decrease in BMD.⁵ However, BMD has a low sensitivity for fracture and other factors such as personal or family history of fragility fracture and smoking are important.

Bone loss in chronic liver disease is predominantly caused by decreased bone formation.^{1 6} Increased bone turnover

also contributes.⁷ The clinical risk factors (CRF) often present in patients with cirrhosis are low body mass index (BMI), excess alcohol, hypogonadism and occasionally steroid use.

British Society of Gastroenterology (BSG) guidelines (published in 2002)⁸ recommend that all patients with cirrhosis should be assessed with dual x-ray absorptiometry (DXA). National Institute for Health and Clinical Excellence (NICE) guidelines (technology appraisal guidance 160,⁹ 161¹⁰ and 204¹¹) exist to guide treatment in the general population and apply to postmenopausal women (table 1).

General population cohorts have been used to generate the fracture risk assessment tool (FRAX),¹² which integrates individual CRF as well as the presence of secondary causes of osteoporosis, including chronic liver disease. This web-based tool¹³ allows the calculation of an individual's 10-year fracture risk for major osteoporotic fractures and osteoporotic hip fractures. The National Osteoporosis Guidelines Group (NOGG)¹⁴ have set thresholds to categorise patients into low and high-risk groups, recommending lifestyle advice and anti-osteoporotic treatment, respectively. Risk can be estimated using CRF alone or refined with DXA. If used without DXA (pre-BMD FRAX) an intermediate risk may result, prompting BMD measurement and recalculation of the FRAX score (figures 1 and 2).

In a small UK-based survey (Ayres, unpublished data, 2011) very few clinical hepatologists were aware of FRAX, and although most hepatologists are aware of BSG guidelines, less than half follow a specific protocol.

FRAX has recently been applied to a cohort of patients with inflammatory bowel disease.¹⁵ The authors concluded that pre-BMD FRAX accurately predicts the risk of osteoporotic fracture when compared with post-BMD FRAX and reduces the need for DXA scans and unnecessary treatment.

The aims of this study were to apply three guideline approaches (BSG, NICE and FRAX/NOGG) to a cohort of patients with liver cirrhosis and compare outcomes with respect to the number of patients that would require DXA scans and be recommended anti-osteoporosis treatment.

Methods

Subjects were identified from a clinical database of patients with cirrhosis screened for osteoporosis between April 2001 and April 2011.

Eligibility criteria:

1. Cirrhosis
2. DXA within 10 years
3. Age greater than 40 years
4. Data available to calculate FRAX score.

Patients with cirrhosis

Patients attending our outpatient service with a histological or clinical/radiological diagnosis of cirrhosis

Table 1 Summary of guidelines

Guideline	Inclusion/exclusion	Investigation	Treatment*
BSG	All patients with cirrhosis or severe cholestasis (bilirubin >3 times upper limit of normal for 6 months)	DXA (unless previous fracture) Thyroid function Bone profile Oestradiol/FSH/LH Testosterone ±spine x-rays	Treat if osteoporosis, or empirical treatment if previous fracture First line: treatment of hypogonadism if present Second line: bisphosphonates Reassess with DXA after 2 years
NICE TAG 160/204 (primary prevention)	Postmenopausal women not on steroids without previous fracture Men excluded	Empirical treatment if age >75 years and indicator of low BMD or ≥2 CRFs for fracture DXA if: 70–75 years and ≥1 CRF or indicator of low BMD 65–69 years and ≥1 CRF <65 years and ≥1 CRF and indicator of low BMD	Bisphosphonates First line: alendronate Second line: risendronate and etidronate (different age, CRF combinations apply) Third line: Denosumab (TAG 204) or Strontium (different age, CRF combinations apply)
NICE TAG 161/204 (secondary prevention)	Postmenopausal women not on steroids with previous fracture Men excluded	Empirical treatment if age >75 years DXA if: <75 years	Treat if osteoporosis or empirically if >75 years Bisphosphonates First line: alendronate Second line: risendronate and etidronate (different age, CRF combinations apply) Third line: Denosumab (TAG 204) or Strontium (different age, CRF combinations apply)
FRAX/NOGG	Applies to postmenopausal women and men aged >50 years	Treat if previous fracture in postmenopausal women Calculate FRAX score and treat if high risk, lifestyle advice if low risk DXA if intermediate risk and recalculate risk	Bisphosphonates

*All recommend adequate intake of calcium and vitamin D.
BMD, bone mineral density; BSG, British Society of Gastroenterology; CRF, clinical risk factor; DXA, dual-emission x-ray absorptiometry; FRAX, fracture risk assessment tool; FSH, follicle-stimulating hormone; LH, luteinising hormone; NICE, National Institute for Health and Clinical Excellence; NOGG, National Osteoporosis Guidelines Group.

Figure 1 National Osteoporosis Guidelines Group management algorithm for patients at risk of fracture, adapted from Kanis *et al.*¹⁴ BSG, British Society of Gastroenterology; NICE, National Institute for Health and Clinical Excellence; FRAX, fracture risk assessment tool; DXA, dual-emission x-ray absorptiometry.

aged greater than 40 years were included (the FRAX score age limits are 40–90 years). Electronic case note review was performed and data were collected on DXA scan, serum vitamin D level, age, gender, height, weight, previous fractures (self-reported), smoking status, history of rheumatoid arthritis, parental hip fracture, steroid use, alcohol intake, menopausal status and parameters to calculate the Child–Pugh score (all data relate to when the patient's DXA scan was performed). Any information not available in the case notes was obtained by telephone interview.

BMD measurement

Patients were scanned using one of two General Electric Hologic (Lunar Prodigy and Lunar DPX;

Figure 2 Age-specific risk of fracture with treatment recommendations, adapted from Kanis *et al.*¹⁴ BMD, bone mineral density.

General Electric Fairfield, Connecticut) scanners. WHO definitions of osteopenia (T-score between -1 and -2.5) and osteoporosis (T-score <-2.5) were used. When patients had more than one scan the most recent was used (age and CRF at the second scan were used). T-scores, Z-score and BMD for both total hips, both femoral necks and lumbar spine were obtained. If the T-score was less than -2.5 at any site the overall result was categorised as osteoporosis.

FRAX score

The FRAX score was calculated retrospectively using age and other variables at the time of DXA scanning. This requires 12 fields: age, gender, weight (kg), height (cm), previous (fragility) fracture, parental hip fracture, current smoking, steroids (currently or previously exposed to oral steroids for >3 months of prednisolone 5 mg daily or more, or equivalent doses of other steroids), rheumatoid arthritis, secondary osteoporosis (including chronic liver disease), alcohol (three or more units a day currently) and femoral neck BMD (g/cm^2). Pre and post-BMD FRAX scores were calculated and the patients' corresponding NOGG recommendations were recorded.

Guideline interpretation

For consistency, when possible patients were allocated to empirical treatment without recourse to DXA: BSG recommend that patients with previous low-impact fracture are treated empirically, in comparison with NOGG, which recommend this only for postmenopausal women. NICE recommend empirical treatment for women aged over 75 years with previous fracture; without previous fracture there must be an indicator of low BMD or two or more CRF.

Statistical methods

Statistical analyses were carried out using SPSS V.16.0. Univariate analysis of baseline characteristics was carried out comparing those with normal and those with low BMD. *p* values less than 0.05 were considered significant.

Each guideline was used to establish the number of patients to whom it could be applied; the numbers eligible for DXA scanning and treatment; and the proportion of high-risk patients untreated and low-risk patients 'unnecessarily' treated, using post-BMD FRAX (and the NOGG treatment threshold) as a reference point.

Spearman's coefficient was calculated to assess the correlation of pre and post-BMD FRAX in categorising patients (with and without previous fracture) to lifestyle advice or treatment, assuming that intermediate-risk patients would be re-scored following DXA.

We were retrospectively evaluating hypothetical outcomes using various guidelines applied to this cohort who had already been investigated. Therefore formal

Table 2 Baseline characteristics by BMD

	Normal BMD (n=43)	Low BMD (n=89)	p Value
Gender			
Women	20 (46.5)	36 (40.4)	0.317 (Fisher's exact)
Men	23 (53.5)	53 (59.6)	
Age (SD)	56.4 (9.5)	60.7 (9.9)	0.02 (unpaired t test)
BMI (SD)	29.3 (6.0)	27.9 (5.8)	0.07 (unpaired t test)
Aetiology (%)			
AIH	0 (0)	1 (1.1)	0.35 (χ^2)
AIH/PBC	0 (0)	1 (1.1)	
ALC	20 (46.5)	52 (58.4)	
ALC/NASH	1 (2.3)	0 (0)	
CRY	0 (0)	2 (2.2)	
HBV	2 (4.7)	4 (4.5)	
HCV	14 (32.6)	17 (19.1)	
NASH	5 (11.6)	6 (6.7)	
PBC	1 (2.3)	6 (6.7)	
Child–Pugh Score (%)			
A	39 (92.9)	81 (94.2)	0.82 (χ^2)
B	3 (7.1)	4 (4.7)	
C	0 (0)	1 (1.2)	
Total vitamin D serum level	58.6 (29.2)	58.9 (35.2)	0.96 (unpaired t test)
Positive smoking history (%)	18 (41.9)	45 (50.6)	0.46 (Fisher's exact)
Previous corticosteroid use (%)	0 (0)	3 (3.4)	0.55 (Fisher's exact)
History of rheumatoid arthritis (%)	0 (0)	1 (1.1)	1.00 (Fisher's exact)
Menopause (n=56) (%)	11 (57.9)	33 (89.2)	0.01 (Fisher's exact)

AIH, autoimmune hepatitis; ALC, alcohol; BMD, bone mineral density; BMI, body mass index; CRY, cryptogenic; HBV, hepatitis B virus; HCV, hepatitis C virus; NASH, non-alcoholic steatohepatitis; PBC, primary biliary cirrhosis.

ethical approval was not required according to the UK National Research Ethics Service.¹⁶

Results

Demographics and BMD

We identified 237 patients with cirrhosis in our database; 105 were excluded (six < 40 years, 89 had not had a DXA scan (22 of these patients were deceased), eight were not contactable and two DXA results were unavailable (performed at another hospital)). Therefore, 132 patients were included. Of these, 58% (76) were men, 32.5% (43) had normal BMD, 47.0% (62) had osteopaenia and 20.5% (27) had osteoporosis. Previous fragility fracture was reported in 12.1% (16) of the cohort; the true incidence may be higher due to asymptomatic fractures. The cause of liver disease was alcohol 62.1% (82), primary biliary cirrhosis 5.3% (seven), non-alcoholic steatohepatitis (NASH) 8.3% (11), hepatitis C virus 15.9% (21), hepatitis B virus 4.5% (six), cryptogenic 1.5% (two), autoimmune hepatitis 1.5% (two) and alcohol/NASH 0.7% (one). Most patients had Child–Pugh A disease: 90.9% (120), B 5.3% (seven), C 0.7% (one). In 3.0% (four) there was insufficient data to calculate disease severity.

Those with low BMD were significantly older: 60.7 years versus 56.4 years ($p=0.02$), were more likely to be postmenopausal ($p=0.01$) and tended to

have lower BMI, but this was not statistically significant. There was no difference in the gender distribution or aetiology of cirrhosis, nor the severity of disease, although the majority (90.9%) of patients in our cohort had well compensated, Child–Pugh A disease (table 2).

Vitamin D levels taken at the time of DXA showed no correlation with femoral neck T-scores ($r=-0.001$), pre-BMD FRAX ($r=0.064$) or post-BMD FRAX ($r=0.047$).

Clinical risk factors

All patients had at least one CRF, ie, chronic liver disease. Forty-one per cent of both men and women had a single CRF. Forty-six per cent of men and 45% of women had two CRF, 12% and 14%, respectively, had three CRF and only one (1.3%) man had four CRF (table 3).

Outcome according to guideline

Table 4 shows outcomes according to each guideline. The key differences between guidelines were: (1) NICE was applicable to the least number (30% compared with BSG 100% and FRAX/NOGG 78%); (2) BSG required a high proportion of DXA scans (88% compared with NICE 17% and FRAX 27%) and recommended treatment in the largest proportion of patients (30%); (3)

Table 3 CRF prevalence

Clinical risk factors	Men n=76 (%)	Women n=56 (%)
0	0	0
1	31 (41)	23 (41)
2	35 (46)	25 (45)
3	9 (12)	8 (14)
4	1 (1.3)	0

CRF, clinical risk factor.

using post-BMD FRAX to stratify risk, all three guidelines recommended treatment to a large number of patients who were in fact low risk; however, FRAX/NOGG resulted in the lowest proportion (40% compared with BSG 62% and NICE 60%). All guidelines resulted in broadly similar proportions of high-risk patients not recommended treatment (figure 3).

Comparison of pre and post-BMD FRAX scores and NOGG recommendations

This comparison was made in 95 (72%) cases as FRAX is only applicable to postmenopausal women and men aged over 50 years. Comparison also excluded eight postmenopausal women with previous fracture because they would be treated empirically under NOGG. According to pre-BMD FRAX, 64 were low risk, 28 intermediate and three high risk. Following the inclusion of BMD, the intermediate group was stratified to low (24/28) and high risk (4/28), producing a final outcome of lifestyle advice in 88/95 and treatment in seven of 95 (table 5). Of 88 patients assigned to lifestyle advice, post-BMD FRAX demonstrates that 10 were high risk.

Pre and post-BMD FRAX scores correlate well ($r=0.76$) and comparison of treatment outcomes for patients with and without previous fracture ($n=103$) yields a sensitivity of 60%, specificity of 100%, positive predictive value of 100% and negative predictive value of 89%.

Of eight women with previous fracture treated empirically under NOGG and BSG, six (75%) are low risk according to post-BMD FRAX and one had normal BMD. Of eight men with previous fracture, four (50%) were low risk and two had normal BMD. Seven (88%) men and four (50%) women had alcohol-induced cirrhosis in this subgroup.

Comparison of high-risk and low-risk patients with respect to BMD

Patients with a high risk of major fracture as determined by post-BMD FRAX had significantly lower femoral neck T-scores (-2.6 vs -1.0 , $p<0.0001$) compared with the low-risk group. There was no significant difference in lumbar spine T-scores between the high and low-risk groups (-1.4 vs -0.6 , $p=0.10$) (table 6).

Discussion

The prevalence of osteoporosis in our cohort (18.9%) is broadly similar to other series of patients with cirrhosis of mixed aetiology (12–43%).^{1–3} The prevalence of low impact cross-sectional fractures (12.1%) is also similar (12–18%).⁶

We have demonstrated that different guidelines have a degree of overlap, particularly BSG and FRAX/NOGG with respect to patients treated (figure 4), but differ significantly in applicability and DXA requirements in this cohort of patients with predominantly Child–Pugh A cirrhosis.

According to BSG guidelines 30% (39) of patients should be treated. Of these 62% (24/39) have a relatively low 10-year risk of fracture. A high proportion of those recommended treatment under BSG guidance have osteoporosis, but according to post-BMD FRAX many have a low estimated risk of fracture. This apparent contradiction is possible because the NOGG treatment threshold is age specific. Therefore, older patients who may have osteoporosis, and have a raised absolute fracture risk compared with younger patients, may still not be recommended treatment if their risk relative to others of their own age is relatively low. Using a risk-based approach allows treatment to be directed to those who are relatively high risk. Osteoporosis is, after all, an arbitrary definition and BMD is a single factor among many that contribute to fracture risk.

Using FRAX/NOGG results in significantly fewer scans and a smaller proportion of those treated were low risk (40%, 6/15) according to post-BMD FRAX. These six patients were all postmenopausal women who reported previous low impact fractures and would also be treated empirically under BSG guidance.

NICE guidelines have a good performance in terms of directing treatment to high-risk patients and using

Table 4 Outcomes according to guideline

Guideline	Applicable to	DXA	Treatment recommended	High risk not recommended treatment	Low risk unnecessarily treated
BSG	100% (132)	88% (116)	30% (39)	8% (7/93)	62% (24/39)
NICE	30% (40)	17% (7)	12% (5)	3% (1/35)	60% (3/5)
FRAX/NOGG	78% (103)	27% (28)	15% (15)	13% (11/88)	40% (6/15)

BSG, British Society of Gastroenterology; DXA, dual-emission x-ray absorptiometry; FRAX, fracture risk assessment tool; NICE, National Institute for Health and Clinical Excellence; NOGG, National Osteoporosis Guidelines Group.

Figure 3 Treated and untreated patients categorised by post-bone mineral density fracture risk assessment tool (FRAX) risk category and guideline. DXA, dual-emission x-ray absorptiometry.

the smallest relative proportion of DXA scans, but are not practical to use in chronic liver disease by virtue of excluding men, premenopausal women ($n=17$, 30%) and postmenopausal women exposed to steroids ($n=3$, 7.5%). They are also the most complex in that two guidelines must be used in parallel, with the option of using a third (TAG 204)¹¹ if patients cannot tolerate bisphosphonates (table 6).

Analysis of the patients populating the 'low-risk treated unnecessarily' category for each guideline reveals them generally to consist of postmenopausal women with previous fracture. Six out of eight of these women had low computed risk according to post-BMD FRAX. This discrepancy between the generally accepted high risk of this group and the low estimated risk explains why all guidelines appear to have performed relatively poorly in this respect. It is possible that some fractures were not truly low impact, and thus some patients genuinely are low risk (one in eight had normal BMD). Excluding these patients alters the proportion of patients treated unnecessarily (BSG 46% (18/39), NICE 20% (one of five), FRAX/NOGG 0% (none of 15)) improving performance for all guidelines particularly FRAX/NOGG.

Table 5 Comparison of risk stratification between pre and post-BMD FRAX (not including patients with previous fracture)

Pre-BMD FRAX		Post-BMD FRAX	
		Low risk	High risk
Low risk	64	54	10
Intermediate risk	28	24	4
High risk	3	0	3
Total	95	78	17

BMD, bone mineral density; FRAX, fracture risk assessment tool.

This highlights the fact that the measure used in this study to judge guidelines is imperfect. One could argue that the weighting assigned to previous fracture is not high enough in the FRAX algorithm, indeed this is acknowledged on the FRAX website.

Vitamin D did not appear to be protective and had no correlation with FRAX score or BMD. Vitamin D deficiency is common in patients with cirrhosis, but osteomalacia is rarely encountered. Other groups have noted that high serum vitamin D does not lower the fracture rate or influence BMD,⁴ but treatment with vitamin D supplementation has been shown to improve BMD in alcohol-induced cirrhosis.¹⁷

To our knowledge this is the first instance in which the FRAX algorithm has been applied to a group of patients with cirrhosis. FRAX has not been validated in patients with cirrhosis and it is important to state that the individual scores are computed fracture risks over 10 years. This study cannot validate the score, which would take many more patients and a follow-up period of several decades to generate a meaningful number of fractures to assess the accuracy.

It is relatively common that at first presentation patients already exhibit complications of cirrhosis including ascites and malnutrition. DXA scanning is not a priority in the acute situation and is usually performed on an outpatient basis, often once nutritional status has improved. The FRAX score is based on current rather than historic BMI and alcohol consumption. These are factors that differentiate this

Table 6 Comparison of guidelines

Guideline	Advantage	Disadvantage
BSG	Simple approach to investigation and treatment	High frequency of DXA Potential to overtreat
NICE	Low cost of investigation and treatment	Applies to post menopausal women not taking steroids only Complex Treatment generally restricted to osteoporosis only
FRAX/NOGG	Reproducible assessment of risk Potential to limit DXA costs	Applies to postmenopausal women and men >50 years Approximately 10% incorrectly risk stratified when compared to post-BMD FRAX/NOGG Internet access essential May underestimate risk when lumbar spine <femoral neck BMD by >1 SD

BMD, bone mineral density; BSG, British Society of Gastroenterology; DXA, dual-emission x-ray absorptiometry; FRAX, fracture risk assessment tool; NICE, National Institute for Health and Clinical Excellence; NOGG, National Osteoporosis Guidelines Group.

Figure 4 Euler diagram of treated patients and overlap between guidelines. BSG, British Society of Gastroenterology; FRAX, fracture risk assessment tool; NICE, National Institute for Health and Clinical Excellence; NOGG, National Osteoporosis Guidelines Group.

group from the general population and are likely to operate through lower BMD. This may explain why 11 patients assigned to lifestyle advice under FRAX/NOGG who were in fact high risk according to post-BMD FRAX, were predominantly men with normal BMI with alcohol-induced cirrhosis.

Although FRAX incorporates 'chronic liver disease' as a cause of secondary osteoporosis, it is a catch-all term and does not differentiate between chronic liver disease and cirrhosis, nor between the various degrees of cirrhosis. As such, fracture risk is likely to be underestimated in those with advanced cirrhosis and overestimated in mild chronic liver disease unless BMD is included in the assessment. Although pre and post-BMD FRAX outcomes were identical for Child-Pugh B and C cirrhosis in this study, meaningful comparison of the performance of FRAX between early and advanced cirrhosis is not possible due to the small number of patients with Child-Pugh B/C disease ($n=6$). Advice given on the FRAX website addresses this theme and encourages the clinician to take into account clinical risks that have a dose-response relationship, and thus use clinical judgement in interpreting the overall risk.

A final factor specific to liver disease that may hinder risk assessment in FRAX is the presence of ascites. Large volume ascites falsely lowers BMD but does not have a clinically relevant effect on femoral neck BMD and will not affect the FRAX score.¹⁸ In contrast, fluctuations in weight and thus BMI mean that patients with large volume ascites will tend to have their risk underestimated by FRAX. In practice, this is not likely to be relevant; in most scenarios assessment of bone disease occurs once other

complications of liver disease have been addressed (in the present study only three patients had significant ascites when DXA scanning took place).

An initial concern of ours was that because FRAX uses femoral neck BMD there would be a proportion of patients in whom risk is underestimated by virtue of their having disproportionately low lumbar spine BMD, particularly as vertebral fractures are the most frequently encountered type of fracture in liver disease.⁴⁻⁹ A recent paper has addressed spine-hip discordancy and offers a validated calculation for these cases in which lumbar spine BMD is more than 1 SD below femoral neck BMD.¹⁹ Approximately one quarter of those with an offset greater than 1 SD changed risk classification.

A further limitation of FRAX is that age ranges below 40 years generate a risk calculated for a patient aged 40 years. Individuals below this cut-off are likely to have their individual risk overestimated. This may become more important as the incidence of younger patients with cirrhosis caused by alcohol rises.

Post-BMD FRAX was selected as a reference point to estimate risk as it incorporates BMD with other objective parameters and is internationally recognised. This selection may bias towards a better performance for pre-BMD FRAX, which will correlate well as it includes all parameters except BMD. The treatment outcomes of pre and post-BMD FRAX/NOGG were similar and yielded a sensitivity of 60% for 'correctly' risk stratifying patients. In other series¹⁵⁻²⁰ the sensitivity is approximately 50%.

In contrast to other studies, we did not find that the Child-Pugh score correlated with low BMD. This is probably explained by the small proportion ($n=6$, 4.5%) of patients with Child-Pugh B or C liver disease in the present study. DXA is often arranged for stable patients once ascites and synthetic liver function has improved, potentially down-scoring patients. Other patients with advanced disease may die before DXA scanning has been arranged, and thus there is probably a bias towards not including those with more severe disease. Furthermore, a high proportion of patients had alcohol-induced cirrhosis, which, combined with the negligible proportion of patients with Child-Pugh B/C cirrhosis, may not make these results generalisable to all units, patients with advanced liver disease or those awaiting transplant.

Conclusions

Predicting fracture risk will inevitably be an imperfect process and leads to varying degrees of under and over-treatment depending on the guideline or approach used. Published guidelines to identify fracture risk vary in their applicability to patients with cirrhosis. For patients with Child-Pugh A cirrhosis BSG guidelines are the most inclusive but have high cost implications; proportionally, BSG requires the most DXA scans and recommends treatment to more patients at low risk of

fracture. Risk stratification using FRAX reduces the number of scans required with minimal impact in terms of missing high-risk patients but offers a modest reduction in unnecessary treatment.

FRAX/NOGG shows promise in providing a standardised, risk-based approach to fracture prevention, but without BMD appears to underestimate the risk for male smokers with alcohol-induced cirrhosis.

A combination of risk stratification plus DXA is likely to be the most cost-effective way of using resources to direct treatments to those most at risk of fracture, but this needs to be validated prospectively.

Key messages

What is already known on this topic

- ▶ Osteoporosis and fragility fracture are common in chronic liver disease.
- ▶ Severity, rather than aetiology of liver disease correlates with low BMD.
- ▶ Clinical risks (especially previous fracture) are important in predicting the risk of future fracture.

What this study adds

- ▶ FRAX/NOGG can reduce the need for DXA scans and the frequency of unnecessary treatment in low-risk patients.
- ▶ Pre-BMD and post-BMD FRAX correlate well, as such offering accurate risk assessment in areas with poor access to DXA.
- ▶ FRAX score without BMD appears to underestimate fracture risk in men with alcohol-induced cirrhosis.

How might it impact on clinical practice in the foreseeable future

- ▶ FRAX provides an objective, reproducible assessment of fracture risk, which emphasises the importance of CRF in generating treatment decisions.
- ▶ FRAX is gaining widespread use and should be considered for incorporation into national guidelines on osteoporosis in liver disease when they are due for review.

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