Is the FRAX Score Valid in Assessing Risk of Metabolic Bone Disease in Chronic Pancreatitis?

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Background

- Chronic Pancreatitis (CP) is a long-term, inflammatory disease of the pancreas, which results in morphological changes and can cause loss of both endocrine and exocrine functions.
- Endocrine Pancreatic Insufficiency (EPI) occurs when pancreatic enzyme production/secretion is inefficient to support digestion, resulting malabsorption.
- Fat malabsorption is one of the most clinically relevant features of EPI, as it is associated with decreased up-take of fat-soluble vitamins, including vitamin D.
- Insufficient vitamin D can lead to reduced bone mineral density (BMD), and subsequent metabolic bone disease (MBD). Osteoporosis and Osteopenia are the most observed metabolic bone disease in CP and are associated with an increased risk of fragility (non-traumatic) fractures.
- FRAX is fracture risk assessment tool used to estimate a patients' 10-year probability of hip and major osteoporotic fracture (spine, wrist, humerus) by integrating eight well-defined clinical risk factors, including smoking, excessive alcohol consumption, and BMI, along with age and sex. [1] FRAX scoring places patients into low, intermediate, or high-risk categories for guidance on how to best proceed with treatment.
- FRAX guidelines suggest measuring bone mineral density for patients falling within the intermediate category, to assess whether treatment is necessary. This is done by low-dose x-ray imaging, called Dual-Energy X-Ray Absorptiometry (DEXA).

Aims, Objectives, Hypothesis

Aim: Test the clinical utility of the FRAX score in a well-defined cohort of patients with chronic pancreatitis.

Objectives: Retrospective analysis of a well-defined patient cohort to;

1. Evaluate the use of the FRAX score as a diagnostic indicator for metabolic bone disease in patients with chronic pancreatitis.
2. Evaluate the prevalence of abnormal DEXA scans within the cohort.
3. Evaluate the prevalence of patients with fragility fractures within the cohort.

Hypothesis: The FRAX score is valid for assessing risk of metabolic bone disease in patients with chronic pancreatitis.

Methods

- A retrospective analysis was undertaken at the Newcastle Upon Tyne NHS Foundation Trust. This was carried out in a well-defined cohort of CP patients to assess the clinical validity and utilization of the FRAX score in providing effective treatment of CP associated MBD.
- First, a research passport, honorary NHS trust contract and a 'Good Clinical Practice' certificate were obtained.

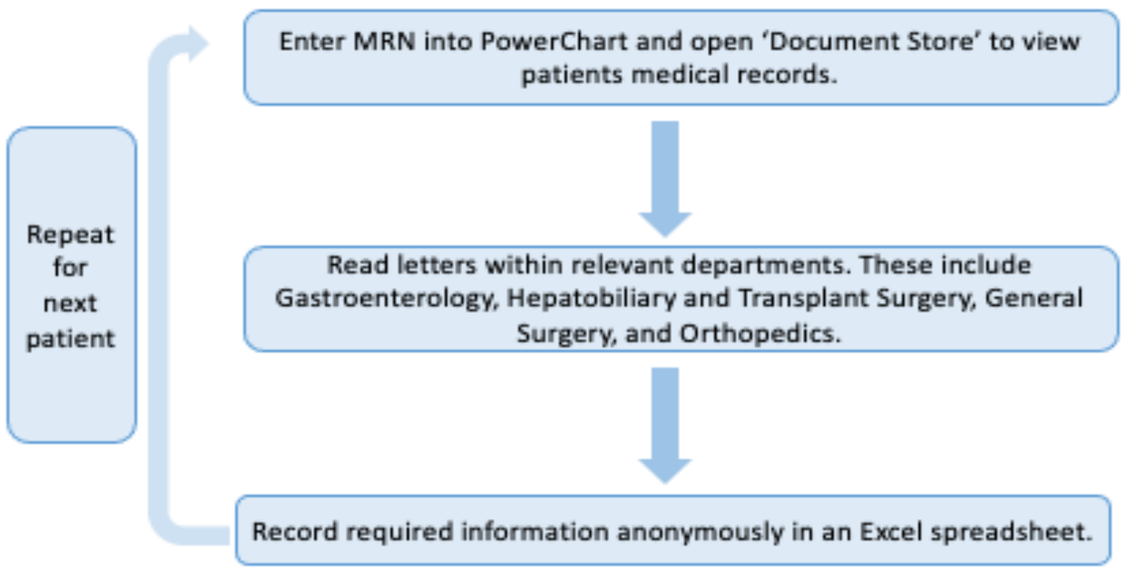

Figure 1. Method for obtaining patient data.

- Then, the relevant information from each patient was inputted into FRAX to give a score and a recommendation for therapeutic intervention based on the National Osteoporosis Guideline Group (NOGG).

References

[1] McCloskey, EV. Harvey, NC. Johansson, H. Lorentzon, M. Liu, E. Vandenput, L. Leslie, WD. Kanis, JA. 2022. Fracture Risk Assessment by the FRAX Model. *In: Climacteric*. 25(1), 22-28.
[2] 3. Fahd Rana, Noor Bekkali, Richard Charnley, Jennifer Logue, Manu Nayar, Kofi Oppong, John Leeds. Is metabolic bone disease routinely tested for in chronic pancreatitis? Gut Jun 2018, 67 (Suppl 1) A157
[3] Borgstrom, F. Karlsson, L. Ortsater, G. Norton, N. Halbout, P. Cooper, C. Lorentzon, M. McCloskey, EV. Harvey, NC. Javaid, MK. Kanis, JA. 2020. Fragility Fractures in Europe: Burden, Management and Opportunities. *For: The International Osteoporosis Foundation, in: Archives of Osteoporosis.* 15(59), pp unknown.
[4] Moran, CG. Wenn, RT. Sikand, M. Taylor, AM. 2005. Early Mortality After Hip Facture: Is Delay Before Surgery Important? *In: The Journal of Bone & Joint Surgery*. 87(3), 483-489.

Results

- Total study cohort of 257 patients, 182 men and 77 women, with a mean age of 59.9.
- 13% had at least one previous fragility fracture, 53% of this group were on medication for MBD.

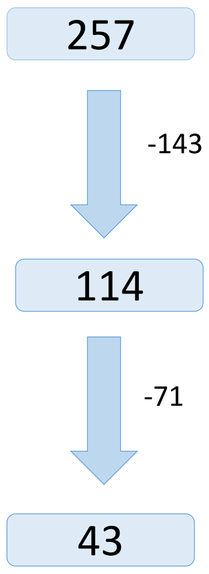

Figure 2. Exclusion criteria.
Total study cohort of 257. 143 patients were excluded due to missing information required for input into the FRAX tool, 114 remaining. A further 71 patients were excluded for lack of DEXA scan. 43 total patients with both FRAX score and BMD measurements.

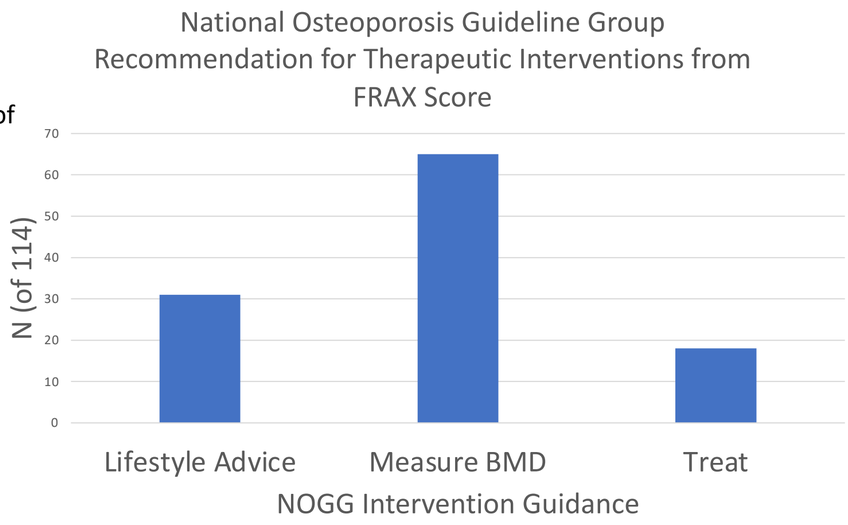

Figure 3. Graph Showing NOGG Recommendation for Therapeutic Interventions from FRAX Score.
Based on NOGG recommendations, 31 patients should be given lifestyle advice, 65 should have their BMD measured, and 18 should progress straight to treatment for Osteoporosis.

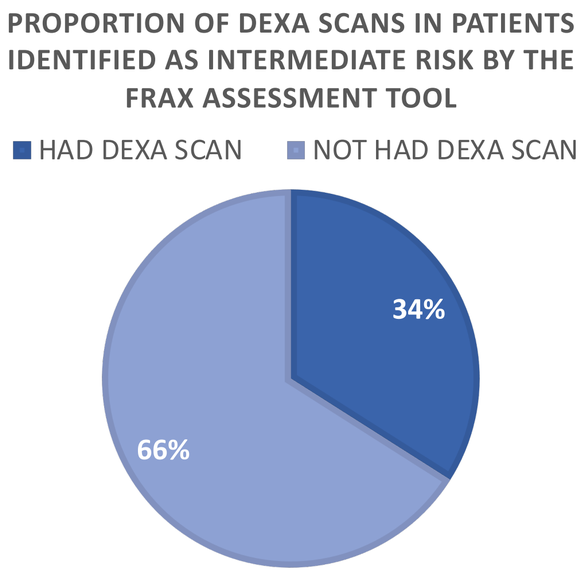

Figure 4. Actual Clinical Application of FRAX Guidelines For Measuring Bone Mineral Density.
Only 34% (22) of 65 patients recommended by FRAX for DEXA have been tested.

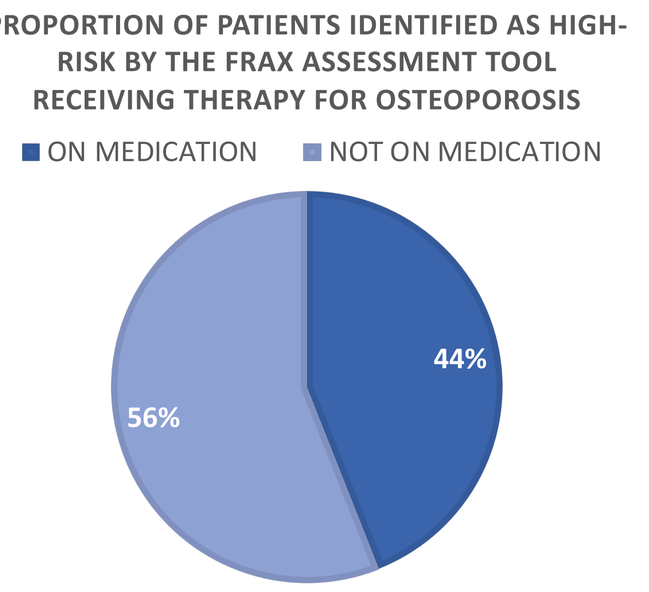

Figure 5. Actual Clinical Application of FRAX Guidelines for Treatment of Metabolic Bone Disease.
44% (8) of 18 patients recommended by FRAX for immediate treatment for MBD are currently being treated. Treatments include bisphosphonates and dietary supplements of Vitamin D.

- 66% of patients identified by FRAX as requiring DEXA scanning had not been tested.
- Only 44% of patients identified by FRAX as being high-risk for osteoporosis were being treated. Further, of the patients in this group who have had a DEXA scan, 16% had a normal BMD.
- 43% of low and intermediate-risk patients were already being treated for MBD.
- 67% of patients with available BMD measurements and described as low-risk by FRAX had either osteopenia or osteoporosis.
- Of all patients with abnormal BMD measurements (having osteopenia or osteoporosis), only 13% had been identified by FRAX as high-risk and needing treatment.
- 64% of patients with available BMD measurements and fragility fractures were identified as high-risk.

Discussion

- The FRAX score has never been validated in disease specific cohorts. This study is the first to assess the clinical validity of FRAX in CP.
- Previous study has shown a clear underutilisation of DEXA scanning in CP patients, despite the increased risk of developing osteoporosis. [2] With only 34% of intermediate-risk patients being put forward for a DEXA, this study has shown that this underutilisation is still prevalent.
- Many patients are being treated for MBD despite being identified as low or intermediate-risk by FRAX. This may increase cost burden on the NHS as patients may be being unnecessarily treated. The increased burden of taking potentially unnecessary medications may also negatively impact the patients' quality of life, and increase their risk of adverse drug effects, if they are already on several medications.
- Only 13% of the included cohort were correctly identified as high-risk and needing immediate treatment for MBD, demonstrating a clear underestimation for major fragility fracture risk. This is further supported by 46% of the cohort to have already experienced at least one fragility fracture being identified as low or intermediate-risk. The most observed fragility fracture is of the hip, requiring, on average, a 20.5-day hospitilisation [3] and incurring a huge cost to the NHS. Moreover, 10% of those admitted with hip fractures die within 1 month, and approximately 30% within the year. [4]
- Further, 70% of the underestimated group were male, demonstrating that this may disproportionately affect the male population.

Conclusion/Further Work

- Despite increased risk for MBD, there is still a clear underutilisation of DEXA scanning in patients with CP. Conduction of more DEXA scans in this population may reduce fragility fractures, and subsequent hospitilisation. This will positively affect patients' quality of life, reduce mortality and reduce cost and staffing burden on the NHS.
- FRAX may underestimate the 10-year probability of hip and major osteoporotic fracture risk in CP patients, especially in men.
- This study is limited by its retrospective analysis. Missing information resulted in many patients being unable to be inputted into the FRAX tool, therefore decreasing the power of the study. In future, providing clinicians with a check-list of information to obtain from patients will minimise the number of patients unable to be included and therefore increase the power of the study.
- A Prospective analysis study could also be carried out, wherein all the necessary information is collected from the patient throughout the course of their disease over a set time period. This would allow all the patients to be included in the analysis and therefore increase the power of the study.