Journal of Clinical Densitometry: Assessment & Management of Musculoskeletal Health, vol. 20, no. 2, 180–187, 2017
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1094-6950/20:180–187/$36.00
http://dx.doi.org/10.1016/j.jocd.2016.08.010

Review Article

The Use of the Fracture Risk Assessment (FRAX®) Tool in Predicting Risk of Fractures in Patients With Inflammatory Bowel Disease: A Systematic Review

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Abstract

Inflammatory bowel disease (IBD), which includes Crohn's disease and ulcerative colitis, is associated with an increased prevalence of osteoporosis and osteopenia. We aim to evaluate the use of the World Health Organization Fracture Risk Assessment (FRAX®) tool in these patients to assess 10-yr risk of fracture. Electronic searches were performed with key words relating to IBD and FRAX in the MEDLINE, EMBASE, and SCOPUS databases. Summary estimates were calculated. A fixed or random-effects model was used depending on heterogeneity (I^2). The search yielded 146 references; 7 that included research carried out in adult patients, were used in the systematic review and quantitative summary. No significant publication bias was noted according to the Harbord test. The 10-yr probability of hip and major osteoporotic fracture in adult IBD patients was 1.03% (95% confidence interval [CI]: 0.37%–2%; I^2 = 0%) and 4.05% (95% CI: 2.61%–5.79%; I^2 = 49%), respectively. In those patients with Crohn's disease, hip and major osteoporotic fractures calculated with FRAX increased to 1.74% (95% CI: 0.42%–3.93%; I^2 = 37.5%) and 6.65% (95% CI: 2.97%–11.66%; I^2 = 8.7%), respectively. Risks of fracture in adults with ulcerative colitis were provided by a single study only. The FRAX tool has been limitedly used in patients with IBD; however, the evidence currently available only shows a modest increase in the 10-yr risks of bone fracture and does not support unequivocally the need for specific interventions. Further well-designed studies are needed to confirm the results obtained from this systematic review.

Key Words: Bone fracture; Crohn's disease, ulcerative colitis; FRAX; inflammatory bowel disease; risk.

Introduction

The development of bone fracture is the most clinically relevant complication of a reduced bone mineral density (BMD) *(1)*. People with inflammatory bowel disease (IBD) exhibit a higher risk of bone loss than the general population. Chronic inflammation causes a reduction in BMD that leads to osteopenia and osteoporosis *(2)*. Cross-sectional studies have reported a highly variable prevalence of ostepenia and osteoporosis that ranges from 22% to 77% and and from 17% to 41%, respectively *(3)*, depending on the study population, location, and design *(4)*. As a result, IBD patients are at increased risk of major osteoporotic fractures, comprising of fractures of the hip, vertebra, distal radius, or humerus.

However, BMD alone indicated only a modest increase in the risk of fracture *(5–7)*, and as such the routine screening with dual-energy X-ray absorptiometry (DXA) scans of IBD patients was not justified, according to the British Society of Gastroenterology and American Gastroenterological Association guidelines *(8,9)*. Although a low BMD constitutes a major determinant of the

Received 03/25/16; Accepted 08/16/16.
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risk of osteoporosis and a subsequent bone fracture, several other factors also have influence on the development of the latter, including exposure to systemic steroids, smoking, age, and gender.

The Fracture Risk Assessment (FRAX®) tool *(10)* is a risk-assessment survey developed by the World Health Organization (WHO) that calculates the 10-yr probability of hip fracture and major osteoporosis-related fracture (including clinical spine, forearm, hip, or proximal humerus fracture). The WHO FRAX score utilizes age, sex, body mass index, clinical risk factors, and femoral neck BMD to estimate the 10-yr probability (of hip fracture and major osteoporosis-related fracture). It is composed of 11 variables: age, sex, weight, height, previous fracture as an adult, parental hip fracture, current cigarette smoking, current (or 3 months prior) use of glucocorticoids, diagnosis of rheumatoid arthritis, consumption of ≥3 units of alcohol daily, and secondary osteoporosis. It can be used with or without the addition of the BMD-derived T-score at the femoral neck, but conflicting results have been provided regarding the reliability of FRAX estimation without BMD measurements *(11,12)*.

FRAX has been revealed as 1 of the most accurate methods for assessing the risk of fractures in different populations *(13–15)*. However, the use of the FRAX tool in patients with IBD who have been recognized as presenting an increased prevalence of osteoporosis *(6,7,16)* and in the risk of osteoporotic fractures, has not been well assessed in literature. As a consequence, it is unclear whether IBD predicts major osteoporosis-related fractures or hip fractures independent of FRAX; whether the increased fracture risk seen in IBD patients is accounted for in the component variables of the FRAX score; or whether the IBD subtype—Crohn's Disease vs ulcerative colitis—has differential effects on the risk of fracture.

Our research aims to conduct a systematic review to assess the 10-yr risk of fracture as determined by the FRAX tool in patients with IBD to provide an up-to-date summary of the available evidence on the utility of this tool in the prediction of bone fracture risk among these patients.

Methods

This systematic review has been registered in the PROSPERO International prospective register of systematic reviews (www.crd.york.ac.uk/PROSPERO; register no. CRD42014015539), and has been reported in accordance with the PRISMA statements *(17)*.

Selection of Studies

A systematic literature search of 3 major bibliographic databases (PubMed, EMBASE, and Scopus) was performed independently by 2 researchers (BS-M and AA) for the period up to January 24, 2016. The search was not restricted with regard to date or language of publication. The researchers used a predetermined protocol in accordance with the quality standards for reporting meta-analyses of observational studies in epidemiology *(18)*.

Comprehensive search criteria were used to identify articles dealing with the risk of fracture in patients with IBD, both children and adults. The following search strategy was used to consult the thesauri for MEDLINE (MESH) and EMBASE (EMTREE): ("inflammatory bowel disease*" OR "ulcerative colitis" OR "Crohn's disease") AND (fracture risk assessment tool OR frax) AND ("bone mineral density" OR "osteoporosis" OR "osteopenia" OR "bone diseases, metabolic" OR "fractures, bone" OR "bone diseases" OR "bone disease, metabolic" OR "bone density"). For the Scopus database, only free-text searches with truncations were carried out. We also examined the reference lists from retrieved articles and abstracts of conference proceedings (these were taken from abstract books from the annual Digestive Diseases Week, American College of Gastroenterology Meetings, the United European Gastroenterology Week, and the European Crohn's and Colitis Organization meetings for the period between 2005 and 2015) to identify additional, relevant studies. Three reviewers (BS-M, ABF-R, and AA) independently screened the database search for titles and abstracts. If any of the reviewers felt that a title or abstract met the study eligibility criteria, the full text of the study was retrieved.

Inclusion Criteria

The following are the inclusion criteria: (1) a diagnosis of IBD was made according to standard clinical, endoscopic, histological, and radiological criteria *(19–21)*, independently of its clinical type (Crohn's disease and ulcerative colitis), location, and behavior; (2) original data on the risk of fracture among recruited patients were provided; and (3) the risk of bone fracture was estimated by using the WHO fracture risk assessment tool FRAX.

Exclusion Criteria

Our analysis excluded clinical guidelines; consensus documents and reviews that did not provide original data. We also excluded studies not carried out on humans; papers providing duplicated information (i.e., repeated abstracts presented at different congresses or abstracts subsequently published as a full paper); studies using subsets of patient cohorts from previously published research by the same group of authors; and research not based on the use of FRAX.

Risk of Bias Assessment

Retrieved documents were evaluated for risk of bias only if the article described all the patients' demographic data, the diagnostic criteria used for IBD, and the reported risk of fracture. Risk of bias assessment was checked with a specific evaluation form for observational studies developed by our group and based on the STROBE statements *(22)* and critical appraisal tools from the Critical Appraisal Skill Program. A study was considered to be at low risk of bias

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if each of the bias items could be categorized as low risk. On the contrary, studies were judged to have a high risk of bias if even 1 of the items was deemed high risk. Two investigators (BS-M and AJL) independently gave each eligible study an overall risk of bias rating of high, low, or unclear; if disagreements arose, a third reviewer (AA) was consulted.

Data Extraction

Three reviewers (BS-M, ABF-R, and AJL) independently extracted relevant information from each eligible study using a standardized data extraction sheet and then proceeded to cross-check the results. The extracted data included the last name of the first author, year of publication, study period, type of IBD, location and extension if available, age and gender of study participants, sample size (total as well as by sex), and reported 10-yr risk of fracture according to the FRAX tool.

Methodological design and risk of bias assessment for all included studies were also extracted. Disagreements between reviewers regarding data extraction were resolved through discussion.

Statistical Analysis

Estimations of the 10-yr risk of fracture were carried out with the aid of a fixed or random-effects meta-analysis weighted for inverse variance following DerSimonian and Laird's method. Summary estimates, along with their 95% confidence intervals (CIs), were calculated for IBD and its subtypes, if possible.

Heterogeneity between studies was assessed with a chi-square test (Cochran Q statistic) and quantified with the I^2 statistic. Generally, I^2 was used to evaluate the level of heterogeneity, assigning the categories of low, moderate, and high to I^2 values of 25%, 50%, and 75%, respectively *(23)*. Publication bias was evaluated with the aid of the Harbord test *(24)*.

For the primary outcome, planned subgroup analyses were performed based on the type of IBD (i.e., Crohn's disease and ulcerative colitis), patients' age (adults vs children), patients' gender (male vs female), and study dates (before 2001 vs after 2001). Estimations were made through fixed-effects meta-analysis.

Subgroup analyses were planned with regard to risk of bias and type of document (full-length article vs abstract presented at conference proceedings), whenever possible. All calculations were made with StatsDirect statistical software version 2.7.9 (StatsDirect Ltd, Cheshire, UK).

Results

Literature Search

The search strategy yielded 146 references; 129 were excluded on the basis of the specific article type (letter, review, and guidelines) or after reviewing the abstract. Of the remaining 17 studies, 10 were excluded for the reasons listed in Fig. 1. This left 7 documents: Table 1 summarizes the characteristics of the 7 studies included in the final systematic review, including 4 full-text papers *(12,25–27)* and 3 abstracts *(28–30)*.

Of the 7 documents mentioned above, 5 were conducted in European countries *(12,26,28–30)*, 1 in Canada *(27)*, and the last 1 was an international research paper including patients from Europe and North America *(25)*. All the studies involved adult patients with IBD, and were carried out between 1997 and 2012. Individual patient age was not given in the retrieved studies, but 2 included subject aged over 50 years *(25,27)*.

Overall, data from 1436 patients with IBD (including 373 males, 776 females, and 287 subjects with gender not specified) were reported. Among them, 360 presented Crohn's disease, 142 ulcerative colitis, and the remaining 934 patients had not reported their type of disease. Data on the location or extension of Crohn's disease and ulcerative colitis were only reported in 2 studies *(12,26)*. An additional study did not provide data on the number of IBD patients recruited or the type of disease the patients presented *(25)*.

IBD and Hip Fracture Risk

In the 7 studies extracted from which the 10-yr risk of fracture in IBD was estimated with the FRAX tool, only 1 provided separate data for Crohn's disease and ulcerative colitis *(28)*; another single research paper only considered data for Crohn's disease patients *(29)*, and 4 studies provided data for overall IBD *(25,27,29,30)*.

The 10-yr overall risk of hip fracture in adult patients with IBD was estimated from 3 studies (1.03%; 95% CI: 0.37%–2%) (Fig. 2A). When only patients with Crohn's disease were considered, the hip fracture risk was calculated in 1.74% (95% CI: 0.42%–3.93%) (Fig. 3A). A low to moderate heterogeneity, according to I^2 statistic, was found.

Specific risks of fracture in patients with ulcerative colitis were exclusively provided by a single study, resulting in a 10-yr probability of 0.4% ± 0.7%, so results could not be meta-analyzed.

IBD and Major Osteoporotic Fracture Risk

A 10-yr probability of major osteoporotic fracture of 4.05% (95% CI: 2.61%–5.79%) was estimated in IBD patients overall (Fig. 2B); this risk was higher when only patients with Crohn's disease were considered (6.65%; 95% CI: 2.97%–11.66%) (Fig. 3B). Summary estimates in ulcerative colitis patients could not be calculated because risk of fracture was separately provided in a single study, in which the 10-yr probability of major osteoporotic fracture was 2.5% ± 2.4%. Intrastudy heterogeneity (I^2) also gave low to moderate results.

The limited number of studies retrieved prevented us from developing further subgroup analysis based on study design or quality, type of disease, and the effect of gender on the risk of bone fractures.

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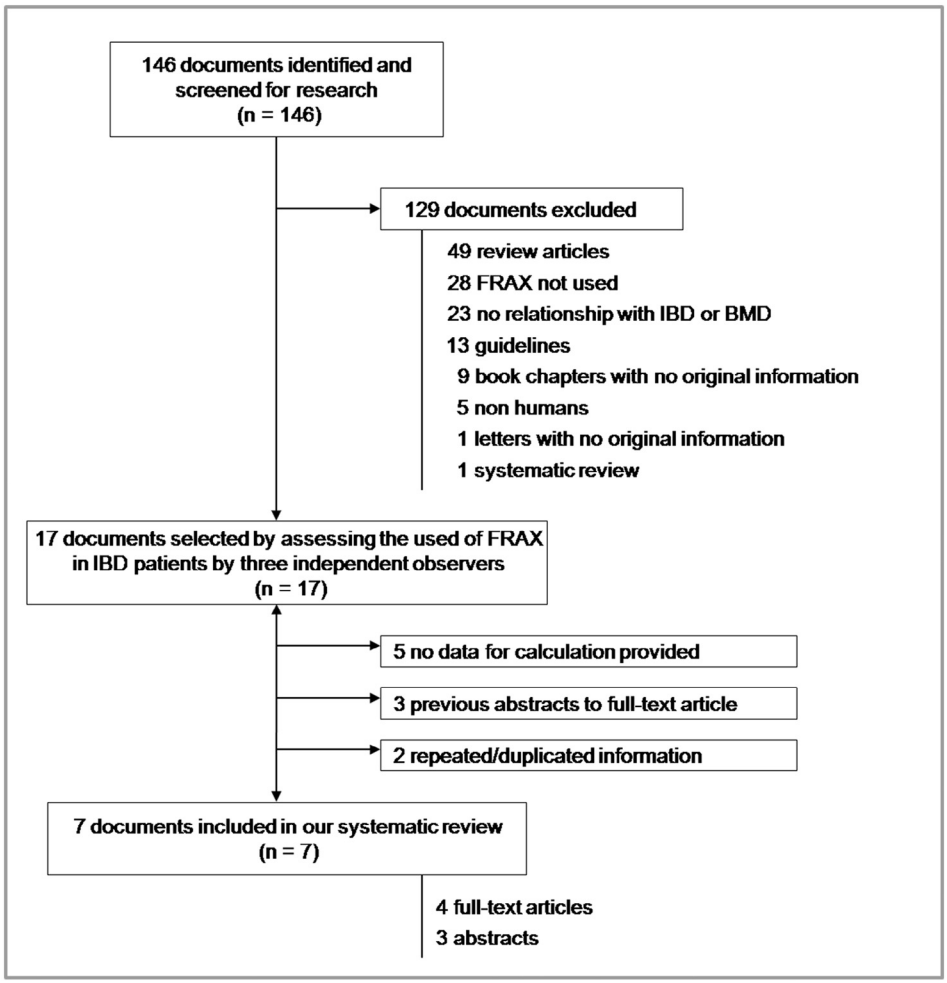

Fig. 1. Flowchart for the process of identifying studies included in and excluded from the systematic review.

Publication Bias Assessment

Statistical analysis revealed no significant publication bias according to Harbord test (p value being 0.766 for hip fracture risk, and $p = 0.899$ for major osteoporotic fracture).

Discussion

This systematic review shows that, despite the fact that increased risk of osteoporosis and bone fracture among IBD patients is well known, the WHO FRAX tool has been used in a very limited way with this specific population. After an exhaustive literature search, only 7 documents, 3 of them being abstracts only, have reported on the use of the FRAX tool to estimate the 10-yr probability of hip and major osteoporotic facture in patients with IBD.

IBD patients are frequently presented with several extraintestinal manifestations, among which bone loss and osteoporosis are prevalent ones. The major complication of osteoporosis is the increased risk of fracture, especially nontraumatic fractures *(27)* that have been reported as 40% greater in frequency in the general population *(6)*. Despite patients with Crohn's disease having shown a higher risk of osteoporosis than ulcerative colitis patients in some populations *(31)*, whether differences between Crohn's disease and ulcerative colitis fracture risk exist are not known *(4)*.

According to our results, summary estimates have shown a low risk of hip fracture in IBD patients (below a 4% fracture risk after 10 yr), and also a modest increase in 10-yr probability of suffering a major osteoporotic fracture (below 12%), according to upper limits of 95% CIs. These figures cannot justify routine DXA in all patients with IBD, and taking into account that the main reason for assessing BMD is to plan specific treatment for osteoporosis, and so to prevent fracture, an optimal procedure should be selecting those patients who are most at risk of fracture for scanning. However, this task is not easy because many risk factors are involved in an impaired BMD in IBD, and it is difficult to assess their relative importance and thereby to produce a reliable scoring system to select those most at risk *(8)*. Without a reliable scoring system, it has been suggested that patients' age over 50, those with very active disease or disease responding poorly to treatment, those

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Table 1
Demographics and Characteristics of Studies Included in Our Systematic Review and Meta-Analysis

Author	Country	Study period	N	Study design	Age of patients	Gender (M/F)	Type of IBD	FRAX score Hip fracture	FRAX score MO fracture
Bours et al *(30)*	Netherlands	-	287	Cross-sectional study	Adult	-	-	0.9% (0.1%–10%)	4.2% (1.5%–20%)
Goodhand et al *(12)*	UK	2005–2009	116	Retrospective chart review	Adult	51/65	CD: 81 UC: 35	Low: 42/116 Intermediate: 55/116 High: 19/116	
Dennison et al *(25)*	10 countries (Austria, Belgium, Canada, France, Germany, Italy, the Netherlands, Spain, UK, and USA)	2006–2008	-	Prospective cohort study	Adult (>50 years)	100%F	-	HR unadjusted 1.4 (1.2 – 1.8) HR age-adjusted 1.4 (1.1–1.7)	-
Lorinczy et al *(28)*	Hungary	-	169	Retrospective cohort study	Adult	81/88	CD: 128 UC: 41	0.6% ± 1.4% 0.4 ± 0.7	2.4% ± 2.7% 2.5 ± 2.4
Terzoudis et al *(26)*	Greece	2007–2012	134	Prospective cohort study	Adult	73/61	CD: 68 UC: 66	0.9% (0.2%–2.5%)	6.2% (3.7%–9.4%)
Targownik et al *(27)*	Canada	1997–2008	647	Retrospective case-control	Adult (>50 years)	127/520	-	HR: 2.14 (1.26–3.64)	HR: 1.12 (0.83–1.53)
Azzopardi and Ellul *(29)*	Malta	-	83	Retrospective case-control	Adult	41/42	83 CD	2.89% (0.1%–39%)	7.9% (2.5%–53%)

Abbr: CD, Crohn's disease; FRAX, fracture risk assessment tool; HR, hazard ratio; IBD, inflammatory bowel disease; MO, major osteoporotic; UC, ulcerative colitis.

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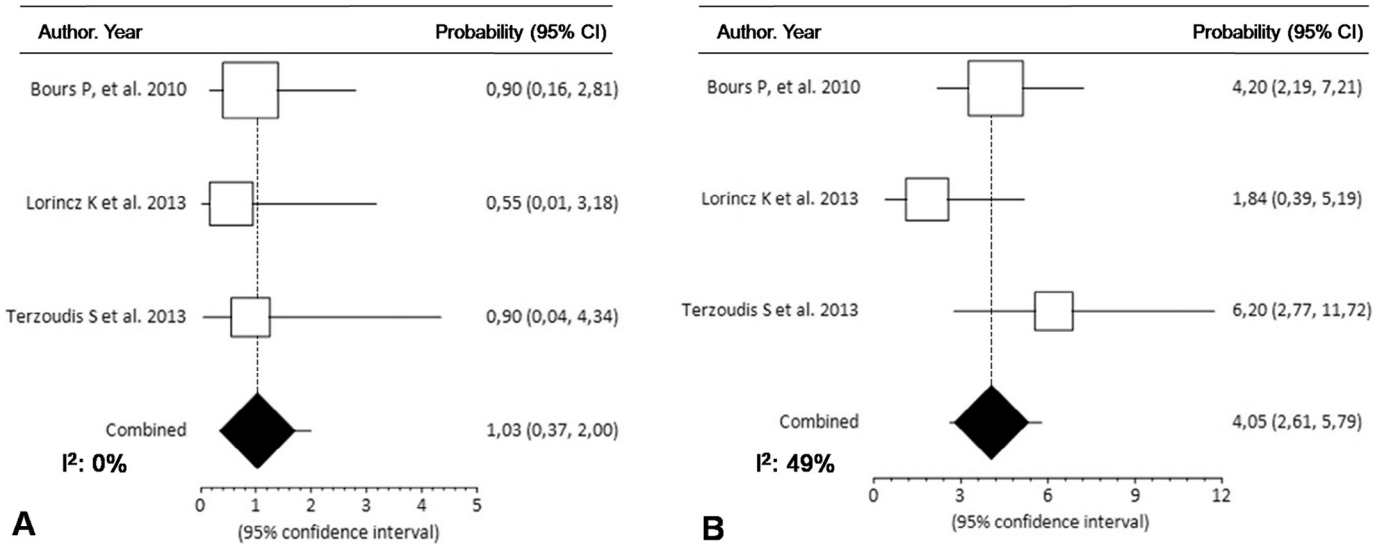

Fig. 2. Risk of fracture (estimated as 10-yr probability by World Health Organization Fracture Risk Assessment [FRAX®] tool) in adult patients with inflammatory bowel disease (IBD), including patients with both Crohn's disease and ulcerative colitis. (**A**) Hip fracture risk in IBD patients; (**B**) major osteoporotic fracture risk in patients with IBD. I^2 values indicated statistical heterogeneity, or intrastudy differences in the overall effect size. BMD, bone mineral density.

with poor nutrition or weight loss, physical inactivity and repeated used of corticosteroids, smoking habit and previous or family history of osteoporotic fracture, hypogonadism, as well as women with untreated early menopause (<45), late menarche (>15), or short fertile period (<30 years) should be considered for DXA *(6,8,32)*.

The potential advantages of using the FRAX tool with IBD patients include the fact that it allows for the assessment of additional risk factors related to the loss of bone mass and associated to IBD beyond BMD itself, including older age, postmenopausal status, smoking, malnutrition, physical inactivity, corticosteroid use for more than 3 mo, and vitamin D deficiency *(6)*. The influence of these factors on the risk of facture has been well established in postmenopausal Caucasian females; therefore, caution must be exercised when extrapolating these data for other groups *(33)*. Still, DXA scan is the current gold standard technique for the measurement of bone mass also in IBD

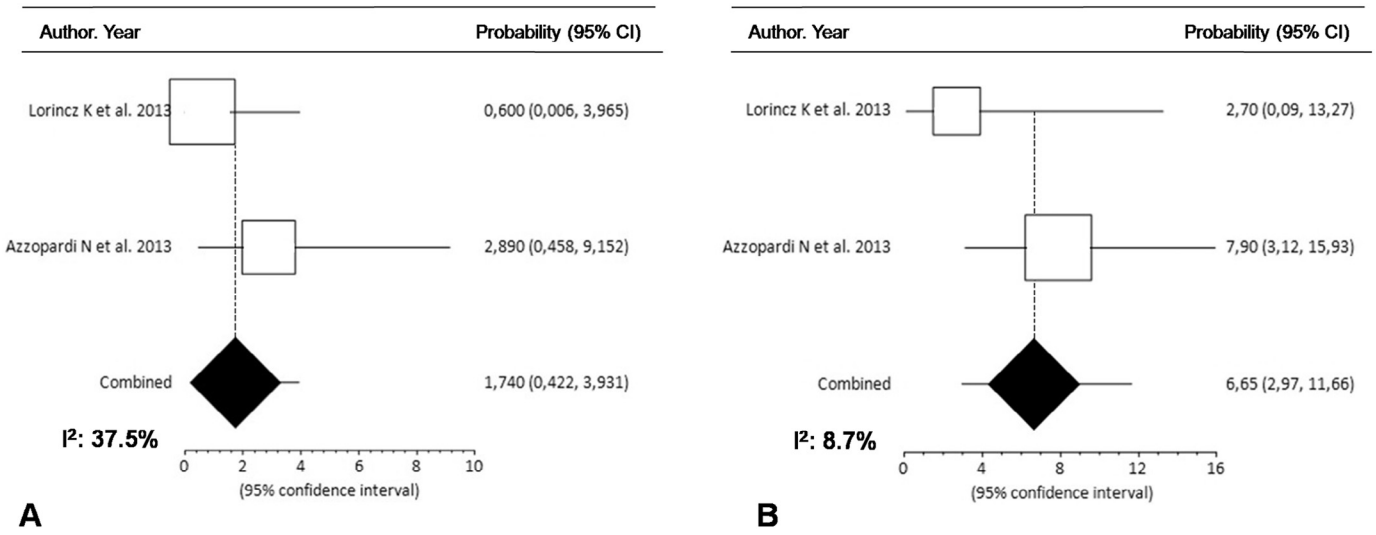

Fig. 3. Subgroup analysis of the risk of fracture (estimated as 10-yr probability by World Health Organization Fracture Risk Assessment [FRAX®] tool) in adult patients with Crohn's disease. (**A**) Hip fracture risk; (**B**) major osteoporotic fracture risk. I^2 values indicated statistical heterogeneity, or intrastudy differences in the overall effect size.

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patients, and its effect in the estimation of 10-yr fracture risk in the FRAX tool avoids an overestimation produced with the FRAX score based on clinical data *(26)*.

The scarce use of DXA scans in patients with IBD may be derived from the fact that FRAX algorithms are based on general population cohort studies undertaken in people over the age of 40 yr, and have not been validated in IBD populations. IBD frequently affects young people, and the FRAX tool calculates risk for patients under the age of 40 years using data for individuals aged 40 years *(34)*. Two of the documents summarized in our meta-analyses included IBD patients aged over 50 years *(25,27)*. Additional characteristics of IBD patients that may not have been fully represented in the FRAX tool are the dose and the duration of the exposure to corticosteroids (which greatly varies in IBD from 1 patient to the other, but is included as a dichotomous risk factor in FRAX calculation), and the fluctuations in body mass index according to disease activity over time *(12)*. The fact that gastroenterologists are less familiar with the FRAX tool compared to other medical specialists should also be taken into account.

Our results, summarizing the limited evidence available, show that the overall risk of hip fracture in IBD patients was low (1.03%; 95% CI: 0.37%–2%), and remained low in those patients suffering from Crohn's disease (1.74%; 95% CI: 0.42%–3.93%). Regarding the major osteoporotic fracture, the 10-yr risk was modestly higher (up to 6.65%; 95% CI: 2.97%–11.66%) in patients with Crohn's disease. Insufficient studies were available for ulcerative colitis to allow direct comparison. Based on the calculation of fracture risk, patients with low bone mass (T-score between –1.0 and –2.5 in the femoral neck or spine) should be treated when 10-yr chance of hip fracture is ≥3%, or a 10-yr probability of any major osteoporosis-related fracture is ≥20% (FRAX adapted to the United States). According to this recommendation, IBD patients included in our review would not need specific treatment. However, the age of a patient arises as a significant aspect to be considered when treating a reduced BMD. The age of the adult patients retrieved for our research was not complete enough for a definitive recommendation on low BMD management to be provided.

The strength of our research lies in the fact that it compiles the results of an exhaustive literature search from 3 major databases and abstract books that also retrieved relevant abstracts on this topic. Recovered studies were critically appraised according to their methodological aspects, and that different investigators independently extracted the data from the studies included. The major limitations of this systematic review include the very low number of documents retrieved and the high proportion of abstracts providing limited details on the reported research. Statistical analysis did not demonstrate a significant publication bias, but these results should be viewed cautiously due to the low number of documents included in our review.

In conclusion, the FRAX tool has been limited in its use in patients with IBD to estimate the 10-yr chance of suffering hip or major osteoporotic fractures. However, the evidence currently available shows a modest increase in such as risks that does not support unequivocally the need of specific interventions. More well-designed studies are needed to confirm the results gained from this systematic review.

References

1. Johnell O, Kanis JA, Oden A, et al. 2005 Predictive value of BMD for hip and other fractures. J Bone Miner Res 20:1185–1194.
2. Bernstein CN. 2006 Osteoporosis in patients with inflammatory bowel disease. Clin Gastroenterol Hepatol 4:152–156.
3. Ali T, Lam D, Bronze MS, Humphrey MB. 2009 Osteoporosis in inflammatory bowel disease. Am J Med 122:599–604.
4. Lima CA, Lyra AC, Rocha R, Santana GO. 2015 Risk factors for osteoporosis in inflammatory bowel disease patients. World J Gastrointest Pathophysiol 6:210–218.
5. Vestergaard P, Krogh K, Rejnmark L, et al. 2000 Fracture risk is increased in Crohn's disease, but not in ulcerative colitis. Gut 46:176–181.
6. Bernstein CN, Blanchard JF, Leslie W, et al. 2000 The incidence of fracture among patients with inflammatory bowel disease. A population-based cohort study. Ann Intern Med 133:795–799.
7. van Staa TP, Cooper C, Brusse LS, et al. 2003 Inflammatory bowel disease and the risk of fracture. Gastroenterology 125:1591–1597.
8. Lewis NR, Scott BB. 2006 Guidelines for osteoporosis in inflammatory bowel disease and coeliac disease. Available at: http://www.bsg.org.uk/images/stories/clinical/ost_coe_ibd.pdf. Accessed: February 2, 2016.
9. American Gastroenterological Association. 2003 American Gastroenterological Association medical position statement: guidelines on osteoporosis in gastrointestinal diseases. Gastroenterology 124:791–794.
10. Kanis JA, Oden A, Johansson H, et al. 2009 FRAX and its applications to clinical practice. Bone 44:734–743.
11. Camporro F, Redondo L, Bulacio E, et al. 2015 Comparison of FRAX Score without bone mineral density determination and the criteria proposed by the Argentine Osteoporosis Society for the use of antiresorptive therapy in postmenopausal women. Medicina (B Aires) 75:155–158.
12. Goodhand JR, Kamperidis N, Nguyen H, et al. 2011 Application of the WHO fracture risk assessment tool (FRAX) to predict need for DEXA scanning and treatment in patients with inflammatory bowel disease at risk of osteoporosis. Aliment Pharmacol Ther 33:551–558.
13. Schwartz AV, Vittinghoff E, Bauer DC, et al. 2011 Association of BMD and FRAX score with risk of fracture in older adults with type 2 diabetes. JAMA 305:2184–2192.
14. Bonaccorsi G, Fila E, Cervellati C, et al. 2015 Assessment of fracture risk in a population of postmenopausal Italian women: a comparison of two different tools. Calcif Tissue Int 91:50–57.
15. Azagra R, Roca G, Encabo G, et al. 2012 FRAX® tool, the WHO algorithm to predict osteoporotic fractures: the first analysis of its discriminative and predictive ability in the Spanish FRIDEX cohort. BMC Musculoskelet Disord 13:204.
16. Vestergaard P, Mosekilde L. 2002 Fracture risk in patients with celiac disease, Crohn's disease, and ulcerative colitis: a nationwide follow-up study of 16,416 patients in Denmark. Am J Epidemiol 156:1–10.

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17. Moher D, Liberati A, Tetzlaff J, et al. 2009 Preferred reporting items for systematic reviews and meta-analyses: the PRISMA Statement. J Clin Epidemiol 62:1006–1012.
18. Stroup DF, Berlin JA, Morton SC, et al. 2000 Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA 283:2008–2012.
19. Lennard-Jones JE. 1989 Classification of inflammatory bowel disease. Scand J Gastroenterol Suppl 170:2–6.
20. Van Assche G, Dignass A, Panes J, et al. 2010 European Crohn's and Colitis Organisation (ECCO). The second European evidence-based consensus on the diagnosis and management of Crohn's disease: definitions and diagnosis. J Crohns Colitis 4:7–27.
21. Dignass A, Eliakim R, Magro F, et al. 2012 Second European evidence-based consensus on the diagnosis and management of ulcerative colitis part 1: definitions and diagnosis. J Crohns Colitis 6:965–990.
22. von Elm E, Altman DG, Egger M, et al. 2007 The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Epidemiology 18:800–804.
23. Higgins JP, Thompson SG, Deeks JJ, Altman DG. 2003 Measuring inconsistency in meta-analyses. BMJ 327:557–569.
24. Harbord RM, Egger M, Sterne JA. 2006 A modified test for small-study effects in meta-analyses of controlled trials with binary endpoints. Stat Med 25:3443–3457.
25. Dennison EM, Compston JE, Flahive J, et al. 2012 Effect of co-morbidities on fracture risk: findings from the Global Longitudinal Study of Osteoporosis in Women (GLOW). Bone 50:1288–1293.
26. Terzoudis S, Zavos C, Damilakis J, et al. 2013 Increased fracture risk assessed by fracture risk assessment tool in Greek patients with Crohn's disease. Dig Dis Sci 58:216–221.
27. Targownik LE, Bernstein CN, Nugent Z, et al. 2013 Inflammatory bowel disease and the risk of fracture after controlling for FRAX. J Bone Miner Res 28:1007–1013.
28. Lorinczy K, Lakatos PL, Salamon A, et al. 2013 Is it necessary to perform X-ray absorptiometry in young IBD patients to predict the risk of fracture? Gastroenterology 144(5):S773.
29. Azzopardi N, Ellul P. 2013 Celiac and Crohn's disease as risk factors for secondary osteoporosis. J Crohns Colitis 7(Suppl 1):S122–S123.
30. Bours P, van de Wiel A, Vermeijden R. 2010 Osteoporosis screening and fracture risk assessment in patients with inflammatory bowel disease. Bone 47:S30.
31. Tsai MS, Lin CL, Tu YK, et al. 2015 Risks and predictors of osteoporosis in patients with inflammatory bowel diseases in an Asian population: a nationwide population-based cohort study. Int J Clin Pract 69:235–241.
32. Scott EM, Gaywood I, Scott BB. 2000 Guidelines for osteoporosis in coeliac disease and inflammatory bowel disease. British Society of Gastroenterology. Gut 46(Suppl 1): i1–i8.
33. 1994 Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Report of a WHO Study Group. World Health Organ Tech Rep Ser 843:1–129.
34. Lucendo AJ, Hervías D, Roncero Ó, et al. 2014 Epidemiology and temporal trends (2000–2012) of inflammatory bowel disease in adult patients in a central region of Spain. Eur J Gastroenterol Hepatol 26:1399–1407.

Descargado para Anonymous User (n/a) en Consejeria de Sanidad de Castilla y Leon(Sacyl) de ClinicalKey.es por Elsevier en febrero 07, 2018.
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