A proposed Multivariate Logistic Regression Model For Osteoporosis Patients

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ABSTRACT

Background/Aim: Osteoporosis-related diseases are associated with increased bone resorption rate and consequently, falling and fracture risks. The primary aim of this study was to construct a new proposed dietary pattern and lifestyle-based Multivariate Logistic Regression Model for femoral osteoporotic fracture risk.

Methods: This study trial was a single-center retrospective study, conducted for 206 participants who attended the rheumatology clinic between Sep 2021 and Nov 2021 at Prince Rashid Bin Al-Hasan Military Hospital under ethical approval of Ref#35, 12/2021. The results were expressed as Mean±SD and as Mean difference±SEM. The correlation strengths of binary categorical variables were also expressed as an odds ratio. FRAX score of 3% was used in our study to dichotomize the overall cohort into two cohorts. Univariate and Multiple Linear Regression Tests were conducted sequentially to abstract the significant coefficients for predicting the 10-year osteoporotic risk. Run participant's regression results were used to investigate the area under the ROC curve and to explore the optimal cut-off point.

Results: This study included a total of 206 participants who attended the rheumatology clinic between Sep 2021 and Nov 2021. 53.39% of the tested cohort (110 participants) had calculated FRAX score below 3% and so they were allocated to Group I, while the remaining 46.60% of the tested cohort (96 participants) had calculated FRAX score ≥3% and so they were grouped to the other comparative group (Group II). The overall mean age of participants was 59.88±1.673 years.

Conclusion: We revealed that the probability of 10-year osteoporosis-related fracture risk was maximally set at 2.924% as long as the minimum protein density didn't decrease below 2.5 g/100 Cal and the number of CacO3/VitD3 tablets was above 2 tablets per day in Jordanian participants who maintained regular fruits/vegetables consumption pattern and active daily lifestyle-based on the following derived multiple linear regression model.

10-Year Osteoporosis related Fracture Risk (%) =5.406-0.325×PD-0.885×FVCP-0.447*ADLS-0.169*OsCal-D.

Keywords: Osteoporosis; dual-energy X-ray absorptiometry; multivariate regression modeling; rheumatological diseases; bone density.

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INTRODUCTION

Osteoporosis is a common silent progressive orthopedic disorder in post-menopausal women and overall aged patients which is characterized by reduced bone mass and strength, and overall mineral density with a deterioration in micro-architectural structures that is commonly associated with increased skeletal fragility and consequently higher risk of fracture which remains asymptomatic till the incidence of the first fracture. [1-2]

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According to the Osteoporosis and Related Bone Diseases National Resource Center, osteoporosis is very common, with roughly 53 million people in the United States living with the condition.[3] Osteoporosis occurs in both males and females but is particularly common among women following menopause when bone turnover increases and the rate of bone resorption exceeds that of bone formation.[4] Corresponding with an aging society, the public health impact of osteoporosis is enormous, affecting 200 million individuals worldwide. The reported prevalence of osteoporosis in Caucasian women older than 50 years of age varies from 7.9% to 22.6%.[5]

Although osteoporosis is often preventable and treatable, its inaccurate and delayed diagnosis can result in substantial physical, psychosocial, and economic consequences with main clinical manifestations of chronic pain, pathological fractures, loss of height, loss of bone mineral density (BMD), spinal deformity, and ultimately osteoporotic hip or vertebral fracture.[6-7]

With the ageing population, the incidence rate of osteoporotic vertebral and non-vertebral fracture rises year by year, which has a serious impact on the life of patients, and receives increasing attention.[8] Effective treatments for osteoporosis are now available, such as bisphosphonates which are first line treatment. Thus, there is interest in identifying people at high risk who should receive targeted therapeutic interventions.[9-10] Dual-energy x-ray absorptiometry (DEXA) is the gold standard for the diagnosis of osteoporosis, but it remains expensive and is not widely available. Furthermore, studies have shown that mass screening for osteoporosis using DEXA is not cost-effective. [11-12]

A research group at the University of Sheffield developed the tool to predict the risk of fractures in a person with osteoporosis within the next 10 years, 10-year Hip Fracture Risk, or major osteoporotic fracture based on the FRAX Score. FRAX stands for Fracture Risk Assessment Tool. It has now become widespread as a clinical tool.[13] According to the Preventive Services Task Force, if a female is 65 years of age or older or is postmenopausal before the age of 50 years, she should undergo a bone mineral density (BMD) test.[14]

Clinicians will compare the results with those of a healthy young adult and give the person a T-score. If a person receives a T-score between –1.0 and –2.5, a FRAX score can help doctors determine which treatment is best.[15] A FRAX score can help doctors identify people with a high risk of fractures who may need additional support. The tool consists of questions relating to 12 factors that can increase the risk of fractures. These factors are age, weight, height, sex, smoking, history of fractures, parental history of fractures, presence of rheumatoid arthritis, and use of glucocorticoid medications, having secondary osteoporosis**,** drinking three or more units of alcohol per day, bone mineral density. [16]

Each day, in consuming a typical western diet, the human body produces approximately 1 mEq/kg of hydrogen ions which are physiologically neutralized via increasing carbon lung dioxide exhalation and acid kidney excretion.[17] Other significant acid-neutralizing mechanisms occur primarily through osteoclast-mediated loss alkaline minerals into the body fluids which will demonstrate a negative calcium balance.[18] Bone is 35 % protein and requires a supply of amino acids to be used for protein turnover.[19] Protein supplementation studies have shown an improvement in bone mineral density (BMD) or other bone indices in some studies but not in others.[20] Some associations between dietary protein and bone health will be due to confounding from dietary and lifestyle factors. The quantity of protein consumed and the adequacy of fruits/vegetables and calcium/Vit D intake may also vary between studies. These factors could explain differing results and it must be kept in mind that not all of these observational analyses are multivariate-adjusted.[21] The primary aim of this study was to construct a new proposed FRAX based multivariate linear regression model for our osteoporosis-related patients who attended the rheumatology clinic that addressed the dietary and lifestyle confounding overall bone effects.

MATERIAL AND METHODS

This study trial was a single-center, non-funded and non-sponsored retrospective study, conducted for 206 participants who attended the rheumatology clinic between Sep 2021 and Nov 2021 at Prince Rashid Bin Al-Hasan Military Hospital, Royal Medical Services, Irbid, Jordan. Ethical approval was signed by our

Institutional Review Board (Ref #35, 12/2021). An informed consent form was waived owing to the study's retrospective design. Aged male and post-menopausal Jordanian's participants were included in this study. Participants with hip or vertebral anatomy malformity, subjects with a history of renal or non-renal related metabolic osteodystrophy, secondary osteoporosis, cancer affected patients with bone metastasis, participants' history of hip or vertebral osteoporotic fracture, and prior use of any bisphosphonate were excluded from the study.

Dual-emission X-ray absorptiometry (DEXA) scans of the proximal femoral hip and anteroposterior spine participant's data were retrieved from the DEXA recorded database. Retrievable DEXA recorded database in our study included femoral Hip T-Score ($_f$HipT-Score), femoral Hip Z-Score ($_f$HipZ-Score), femoral Hip BMD in g per cm2 (f Hip BMD), Lumbar T-Score, Lumbar Z-Score, Lumbar BMD, the 10-year risk of femoral osteoporotic fracture (10-year $_f$OHF risk) FRAX score, and 10-year risk of major overall osteoporotic fracture FRAX score. A 10-year $_f$OHF risk based on a FRAX score of 3% was used in our study to dichotomize the overall cohort into two cohorts; attended rheumatological clinic patients who had assessed 10-year fOHF risk < 3% based on FRAX Score (Group I) and attended rheumatological clinic patients who had assessed 10-year Hip Fracture Risk ≥3% based on FRAX Score (Group II).

The comparative non-dichotomous variables between Group I and Group II were statistically analyzed by Independent T-Test and the results were expressed as Mean±SD and as Mean difference±SEM. While the comparative variables for the total sample were analyzed by One-Sample T-Test and the results were also expressed as Mean±SD. For dichotomous categorical data, a Chi-Square Test was used to express the analysis outcomes as Numbers (Percentages). The correlation strengths of binary categorical variables were also expressed as an odds ratio.

The FRAX score-based variables that were tested in our study include age, weight, height, sex, smoking, history of fractures, parental history of fractures, use of glucocorticoid medications, having secondary osteoporosis, drinking three or more units of alcohol per day, bone mineral density. Co-Morbidities were also tested in our study and including, rheumatoid arthritis (RA), hypertension (HTN), diabetes mellitus (DM), chronic kidney disease (CKD), peptic ulcer disease (PUD), cardiovascular disease (CVD).

In addition to FRAX score-based composite variables, dietary and lifestyle independent variables were included in our study to explore their combined interactive explanation for the prediction of our target of interest (The 10-year fOHF risk). The density of protein consumed in grams per 100 Calories (PD), the consumption pattern of fruits/vegetables (FVCP), the number of daily calcium/Vit D tablet intake (OsCal-D), and the lifestyle of daily activities (ADLs) were the 4 tested variables that were run individually into Univariate Linear Regression and collectively into Multiple Linear Regression analysis. Both the FVCP and ADLS were dichotomized into intermittent versus regular patterns and sedentary versus active lifestyles. The daily OsCal-D tablets were categorized into 1 Tab/day, 2 Tab/day, 3 Tab/day, or 4 Tab/day. Dietary PD in g/100 Cal was roughly estimated based on the attended rheumatology clinic participants' weekly average consumption quantities of foods that are mentioned in Figure 2. Also, the participants' PDs were dichotomized into either below 2.5 g/100 Cal or above 2.5 g/100 Cal.

Firstly, we conducted a Univariate Linear Regression Test for the 4 tested variables to individually explore the degree of correlation (R), how much of the total variations in the dependent variable can be explained by the independent variables and a proportion of variation accounted for by the regression model above and beyond the mean model (Coefficient of determination or R^2), how much the quality of the prediction of the dependent variable, and how the regression model is a good fit for the data (F-Ratio in the ANOVA table). Also, this test was conducted to abstract the necessary coefficients to individually predict the 10-year $_f$OHF risk. Thereafter, The Multivariate Linear Regression Test was followed to composite the predictive variables that were significantly correlated and to fit these significant explanatory variables into a proposed multiple linear regression model, after abstracting the significant coefficients, to collectively predict the 10-year $_f$OHF risk.

After the multivariable linear regression model was constructed, we ran participant composed data into this constructed proposed multivariable linear regression equation into receiver operating characteristic (ROC) and sensitivity analyses to investigate the area under the ROC curve (AUROC) and to explore the optimal cut-off point, sensitivity, specificity, positive and negative predictive values, Youden and accuracy indices, and

the negative likelihood ratio for the 10-Year Risk of f Hip OPF percentages based on our proposed multiple regression equation results. Statistical analysis was performed using Statistical Package for Social Science (SPSS) software version 23.0. Statistical significance was set at 5%.

RESULTS

This study included a total of 206 participants who attended the rheumatology clinic between Sep 2021 and Nov 2021 at Prince Rashid Bin Al-Hasan Military Hospital, Royal Medical Services, Irbid, Jordan. 53.39% of the tested cohort (110 participants) had calculated FRAX score below 3% and so they were allocated to **Group I**, while the remaining 46.60% of the tested cohort (96 participants) had calculated FRAX score ≥3% and so they were grouped to the other comparative group (**Group II**). The overall mean age of participants was 59.88±1.673 years.

Group I participants were insignificantly older than **Group II** participants [59.96±1.98 years versus 59.78±1.23 years, respectively, +0.18±0.23 years, P-value=0.436). Most of the attended rheumatological clinic participants in our study belonged to the female gender. Female to male ratio (F: M) was 5.87: 1 [176 (85.4%) versus 30 (14.6%), respectively, P-value=0.426] in which 15.5% (117 Men) and 84.5% (93 Women) belonged to **Group I** compared to 13.5% (13 Men) and 86.5% (83 Women) in **Group II**. The menopausal onset means age for female participants was 48.41±4.41 years which was also insignificantly distributed across Group I-II [48.45±4.60 years vs 48.36±4.21 years, respectively, +0.090±0.67 years, p-value=0.893].

Anthropometrically, all assessed and calculated participants' anthropometrics were insignificantly distributed between the two comparative groups. Bodyweight (BW), height, body mass index (BMI), ideal body weight (IBW), adjusted body weight (Adj_BW), and body surface area (BSA) were 76.90±7.83 Kg, 160.7±8.62 cm, 30.13±5.214 Kg/m^2, 56.37±7.29 Kg, 64.59±4.52 Kg, and 1.918±0.049 m^2 vs 76.80±7.53 Kg, 160.06±7.19 cm, 30.19±4.48 Kg/m^2, 55.83±6.25 Kg, 64.19±4.41 Kg, and 1.768±0.04 Kg, respectively, p-value>0.05.

All retrievable DEXA recorded database of f HipT-Score, f Hip Z-Score, f Hip BMD, Lumbar T-Score, Lumbar Z-Score, and Lumbar BMD were significantly higher in attended rheumatological clinic participants who had FRAX score below 3% (Group I) comparative to participants who had higher score level (**Group II**) [-1.25±0.19, -1.15±0.18, 0.78±0.023 g/cm^2, 0.676±0.578, 0.61±0.53, and 1.05±0.09 g/cm^2 versus -1.79±0.21, -1.64±0.19, 0.72±0.023 g/cm2, -0.91±0.61, -0.83±0.55, and 0.81±0.09 g/cm^2] with Mean differences±SEM of +0.54±0.03, +0.49±0.03, +0.06±0.003 g/cm^2 , +1.583±0.083, +1.439±0.075, and +0.237±0.012 g/cm^2 , respectively, p-value<0.05.

The 10-year hip fracture risk based on the FRAX score was significantly lower in Group I compared to Group II [2.25%±0.59% vs 3.86%±0.62%, -1.61%±0.084%, p-value=0.000]. Similarly, the 10-year major osteoporotic fracture (OPF) was significantly lower in Group I compared to Group II [9.77%±4.12% vs 21.04%±4.35%, -11.27%±0.59%, respectively, p-value=0.000]. Overall weekly consumption quantity of CaC03 was 2619±1138 mg/week which was significantly higher in Group I than in Group II [3297±1153 mg/week vs 1842±356 mg/week, +1455±122, respectively, p-value=0.000]. Also, 25-OH-Cholecalciferol (Vit D) level was significantly higher in Group I than in Group II by +6.199±0.323 ng/ml [18.48±2.26 ng/ml vs 12.28±2.37 ng/ml, respectively, p-value=0.000]. The daily OsCal-D tablet consumption rates were significantly distributed across the two tested groups for which the rates of 3 tab/day and 4 tab/day were allocated in Group I in percentages of 50% and 50%, respectively. While the OsCal-D consumption rate of 1 tab/day and 2 tab/day were allocated in Group II in percentages of 21.9% and 78.1%, respectively.

Participants in Group I had a regular consumption pattern for fruits and vegetables while participants in Group II had an intermittent consumption pattern rate of 21.9% and a regular consumption pattern rate of 78.1%. the odd ratio for FVCP was 2.47 (95% CI; 2.07-2.94. Contrarily, all participants in Group II had a sedentary lifestyle of daily activities while participants in Group I had a sedentary ADLS rate of 50% and an

active ADLS rate of 50%. The odd ratio of ADLS for our tested attended rheumatology clinic participants was 0.36 (95% CI; 0.29-0.45).

The overall protein density intake in the study was 3.19±1.59 g/100 Cal which was significantly higher in Group I participants compared to Group II participants by +2.77±0.11g/100 Cal [4.48±1.06 g/100 Cal vs1.71±0.21 g/100 Cal, respectively, p-value=0.000]. The Group I participants had a consumption rate of 97.3% and 2.7% for diets PD≥ 2.5 g/100 Cal and diets PD<2.5 g/100 Cal, respectively. While all Group II participants had a consumption rate of diet PD below 2.5 g/100 Cal. The odd ratio of diet PD for our tested participants in this study was 33.0 (95% CI; 10.8-100.6).

The participants' comorbidities distributions across the two tested groups and all the aforementioned comparative variables for cohort people who attended the rheumatology clinic between Sep 2021 and Nov 2021 at Prince Rashid bin Al-Hasan Military Hospital, Royal Medical Services, Irbid, Jordan, among 10-year Hip Fracture Risk≥3% Group (Group II) compared to 10-year Hip Fracture Risk<3% Group (Group I) were summarized in Table I-III.

The degree of correlations (R) and the coefficient of determination (R^2) results for the 4 tested variables from the conducted Univariate Linear Regression Test were 0.894 and 0.799, 0.600 and 0.361, 0.732 and 0.536, and 0.930 and 0.865 for PD (g/100 Cal), FVCP (Intermittent/Regular), ADLS (Sedentary/Active), and OsCal-D (1-4 Tab/day), respectively. The abstracted individual coefficients (B± SEM) of each aforementioned tested variable for the 10-year $_f$OHF risk prediction were -0.563±0.020, -1.983±0.185, -1.653±0.108, and -0.954±0.026, respectively. The necessary coefficients to collectively predict the 10-year Hip Fracture Risk and to present the final form of our proposed multiple linear regression model for the tested osteoporosis patients can be formulated as follows.

10-Year Osteoporosis related Fracture Risk (%) =5.406-0.325×PD-0.885×FVCP-0.447*ADLS-0.169*OsCal-D, Samer Alboun et al proposed a multiple linear regression model for prognosticating the % 10-Year Osteoporosis related Fracture Risk based on 4 tested dietary patterns and lifestyle factors, including PD: Protein density in g per 100 Cal, FVCP: Fruits/Vegetables consumption pattern (Intermittent pattern=0, Regular pattern=1), ADLS: Activities of daily lifestyle (Sedentary life style=0, Active life style=1), and OsCal-D: Supplementary tablet which contains 600 mg CaC03 and 400 IU Vit D3.

After the multiple linear regression model was constructed, we incorporated receiver operating characteristic (ROC) and sensitivity analyses to investigate the area under ROC curve (AUROC) and to explore the optimal cut-off point and the related performances indices for the 10-Year Risk of f Hip OPF percentages based on our proposed multiple regression equation results". Statistical analysis was performed using Statistical Package for Social Science (SPSS) software version 23.0. Statistical significance was set at 5%.

The AUROC for the constructed ROC based on the run participant's composing data into our proposed multiple linear regression equation against the 10-year risk of fHOP_FRAX score ≥3% (1) or <3% (0), was 0.992±0.05 (95% CI; 0.983-1). Also, we explored the optimal operating dichotomized level of 3.45% for our proposed regression equation to discriminate between lower risk and higher risk cohorts regarding the 10-Year risk of fHOP fracture with the prognosticating performance of 97.27%.

Table I. Comparatively, variables for cohort people who attended the rheumatology clinic between Sep 2021 and Nov 2021 at Prince Rashid bin Al-Hasan Military Hospital, Royal Medical Services, Irbid, Jordan, among 10-year Hip Fracture Risk≥3% Group (Group II) compared to 10-year Hip Fracture Risk<3% Group (Group I).

Variables		**Overall 206 Mean±SD**	**Group I 110, 53.39% Mean±SD**	**Group II 96, 46.60% Mean±SD**	**Mean diff±SEM or OD**	**p-Value**
Age (Yrs)		59.88±1.673	59.96±1.98	59.78±1.23	0.182±0.234	0.436
Gender	**Female**	176 (85.4%)	93 (84.5%)	83 (86.5%)	0.86 (95%CI; 0.39-1.87)	0.426
	Male	30 (14.6%)	17 (15.5%)	13 (13.5%)		
	F: M	5.87: 1	5.47: 1	6.38: 1		

BW (Kg)		76.85±7.672	76.90±7.83	76.80±7.53	0.098±1.07	0.927
Height (cm)		160.42±7.97	160.7±8.62	160.06±7.19	0.674±1.12	0.546
BMI (Kg/m^2)		30.16±4.87	30.13±5.214	30.19±4.48	-0.055±0.68	0.936
IBW (Kg)		56.12±6.815	56.37±7.29	55.83±6.25	0.538±0.95	0.573
Adj_BW (Kg)		64.40±4.464	64.59±4.52	64.19±4.41	0.399±0.62	0.524
BSA (m^2)		1.848±0.087	1.918±0.049	1.768±0.04	0.150±0.01	0.000
Hx of parental fracture	**No**	181 (87.9%)	107 (97.3%)	74 (77.1%)	10.60 (95%CI; 3.06-36.72)	0.000
	Yes	25 (12.1%)	3 (2.7%)	22 (22.9%)		
Co-Morbidities	**<3**	156 (75.7%)	110 (100.0%)	46 (47.9%)	0.29 (95% CI; 0.23-0.38)	0.00
	≥3	50 (24.3%)	0 (0.0%)	50 (52.1%)		
RA	**No**	189 (91.7%)	106 (96.4%)	83 (86.5%)	4.15 (95% CI; 1.31-13.19)	0.009
	Yes	17 (8.3%)	4 (3.6%)	13 (13.5%)		
HTN	**No**	101 (49.0%)	101 (91.8%)	0 (0.0%)	11.67 (95% CI; 6.25-21.79)	0.00
	Yes	105 (51.0%)	9 (8.2%	96 (100.0%)		
DM	**No**	140 (68.0%)	105 (95.5%)	35 (36.5%)	36.6 (95% CI; 13.62-98.38)	0.00
	Yes	66 (32.0%)	5 (4.5%)	61 (63.5%)		
CKD	**No**	183 (88.8%)	107 (97.3%)	76 (79.2%)	9.39 (95% CI; 2.69-32.71)	0.00
	Yes	23 (11.2%)	3 (2.7%)	20 (20.8%)		
PUD	**No**	142 (68.9%)	98 (89.1%)	44 (45.8%)	9.65 (95% CI; 4.69-19.86)	0.00
	Yes	64 (31.1%)	12 (10.9%)	52 (54.2%)		
CVD	**No**	177 (85.9%)	104 (94.5%)	73 (76.0%)	5.46 (95% CI; 2.12-14.08	0.00
	Yes	29 (14.1%)	6 (5.5%)	23 (24.0%)		

The comparative non-dichotomous variables between Group I and Group II were statistically analyzed by Independent T-Test and the results were expressed as Mean±SD and as Mean difference±SEM. While the comparative variables for the total sample were analyzed by One-Sample T-Test and the results were also expressed as Mean±SD. For dichotomous data, a Chi-Square Test was used to express the analysis outcomes as Numbers (Percentages). The correlation strengths of binary categorical variables were expressed as the odds ratio (OD). (At p-value< 0.05*).

- **Group I:** Attended rheumatological clinic patients who had assessed 10-year Hip Fracture Risk < 3% based on FRAX Score.
- **Group II:** Attended rheumatological clinic patients who had assessed 10-year Hip Fracture Risk ≥3% based on FRAX Score.

OD: Odd ratio.
IBW: Ideal body weight.
ABW: Actual body weight.
Adj_BW: Adjusted body weight.
BMI: Body mass index.
BSA: Body surface area.
RA: Rheumatoid arthritis.
HTN: Hypertension.
DM: Diabetes mellitus.
CKD: Chronic kidney disease.
PUD: Peptic ulcer disease.
CVD: Cardiovascular disease.

Table II. Comparatively, variables for cohort people who attended the rheumatology clinic between Sep 2021 and Nov 2021 at Prince Rashid bin Al-Hasan Military Hospital, Royal Medical Services, Irbid, Jordan, among 10-year Hip Fracture Risk≥3% Group (Group II) compared to 10-year Hip Fracture Risk<3% Group (Group I).

Variables		**Overall 206 Mean±SD**	**Group I 110, 53.39% Mean±SD**	**Group II 96, 46.60% Mean±SD**	**Mean diff±SEM or OD**	**p-Value**
On Thyroxin	**No**	158 (76.7%)	103 (93.6%)	55 (57.3%)	10.97 (95% CI; 4.62-26.07)	0.000
	Yes	48 (23.3%)	7 (6.4%)	41 (42.7%)		
FVCP	**Intermittent**	21 (10.2%)	0 (0.0%)	21 (21.9%)	2.47 (95% CI; 2.07-2.94)	0.000
	Regular	185 (89.8%)	110 (100.0%)	75 (78.1%)		
ADLS	**Sedentary**	151 (73.3%)	55 (50.0%)	96 (100.0%)	0.36 (95% CI; 0.29-0.45)	0.000

	Active	55 (26.7%)	55 (50.0%)	0 (0.0%)		
Post-Menopausal age		48.41±4.41	48.45±4.60	48.36±4.21	+0.090±0.67	0.893
f HipT-Score		-1.50±0.34	-1.25±0.19	-1.79±0.21	+0.54±0.03	0.000
f Hip Z-Score		-1.38±0.31	-1.15±0.18	-1.64±0.19	+0.49±0.03	0.000
f Hip BMD (g/cm^2)		0.75±0.038	0.78±0.023	0.72±0.023	+0.06±0.003	0.000
Lumbar T-Score		-0.062±0.987	0.676±0.578	-0.91±0.61	+1.583±0.083	0.000
Lumbar Z-Score		-0.06±0.89	0.61±0.53	-0.83±0.55	+1.439±0.075	0.000
Lumbar BMD (g/cm^2)		0.94±0.15	1.05±0.09	0.81±0.09	+0.237±0.012	0.000

The comparative non-dichotomous variables between Group I and Group II were statistically analyzed by Independent T-Test and the results were expressed as Mean±SD and as Mean difference±SEM. While the comparative variables for the total sample were analyzed by One-Sample T-Test and the results were also expressed as Mean±SD. For dichotomous data, a Chi-Square Test was used to express the analysis outcomes as Numbers (Percentages). The correlation strengths of binary categorical variables were expressed as the odds ratio (OD). (At p-value< 0.05*).

- **Group I:** Attended rheumatological clinic patients who had assessed 10-year Hip Fracture Risk < 3% based on FRAX Score.
- **Group II:** Attended rheumatological clinic patients who had assessed 10-year Hip Fracture Risk ≥3% based on FRAX Score.

- Cs: Corticosteroidal agents of at least Prednisolone 7.5 mg/day or equivalent for 3 months in the past year.
- **FVCP:** Fruits/Vegetables consumption pattern (Intermittent pattern=0, Regular pattern=1).
- **ADLS:** Activities of daily life style (Sedentary life style=0, Active life style=1).

fHip T-Score: T-Score for a femoral neck of the hip.
BMD: Bone mineral density in g per cm^2.
NA: Not mathematically applicable and can't be statistically
OPF: Osteoporotic fracture risk.

Table III. Comparatively, variables for cohort people who attended the rheumatology clinic between Sep 2021 and Nov 2021 at Prince Rashid Bin Al-Hasan Military Hospital, Royal Medical Services, Irbid, Jordan, among 10-year Hip Fracture Risk≥3% Group (Group II) compared to 10-year Hip Fracture Risk<3% Group (Group I).

Variables		**Overall 206 Mean±SD**	**Group I 110, 53.39% Mean±SD**	**Group II 96, 46.60% Mean±SD**	**Mean diff±SEM or OD**	**p-Value**
Cs*	**No**	176 (85.4%)	103 (93.6%)	73 (76.0%)	4.64 (95% CI; 1.89 11.38)	0.000
	Yes	30 (14.6%)	7 (6.4%)	23 (24.0%)		
Vit D (ng/ml)		15.59±3.86	18.48±2.26	12.28±2.37	+6.199±0.323	0.00
smoke Status	**No**	162 (78.6%)	103 (93.6%)	59 (61.5%)	9.23 (95% CI; 3.87-22.0)	0.000
	Yes	44 (21.4%)	7 (6.4%)	37 (38.5%)		
$CaCO_3$ (mg/wk)		2619±1138	3297±1153	1842±356	+1455±122	0.000
OsCal-D	**1 Tab/day**	21 (10.2%)	0 (0.0%)	21 (21.9%)	NA	0.000
	2 Tabs/day	75 (36.4%)	0 (0.0%)	75 (78.1%)		
	3 Tab/day	55 (26.7%)	55 (50.0%)	0 (0.0%)		
	4 Tab/day	55 (26.7%)	55 (50.0%)	0 (0.0%)		
PD (g/100 Cal)		3.19±1.59	4.48±1.06	1.71±0.21	2.77±0.11	0.000
PD	**≥ 2.5 g/100 Cal**	107 (51.9%)	107 (97.3%)	0 (0.0%)	33.0 (95% CI; 10.8-100.6)	0.000
	<2.5 g/100 Cal	99 (48.1%)	3 (2.7%)	96 (100.0%)		
10-year Hip fracture risk		2.99%±1.0%	2.25%±0.59%	3.86%±0.62%	-1.61%±0.084%	0.000
10-year major OPF		15.02%±7.04%	9.77%±4.12%	21.04%±4.35%	-11.27%±0.59%	0.000

The comparative non-dichotomous variables between Group I and Group II were statistically analyzed by Independent T-Test and the results were expressed as Mean±SD and as Mean difference±SEM. While the comparative variables for the total sample were analyzed by One-

Sample T-Test and the results were also expressed as Mean±SD. For dichotomous data, a Chi-Square Test was used to express the analysis outcomes as Numbers (Percentages). The correlation strengths of binary categorical variables were expressed as the odds ratio (OD). (At p-value< 0.05*).

- **Group I:** Attended rheumatological clinic patients who had assessed 10-year Hip Fracture Risk < 3% based on FRAX Score.
- **Group II:** Attended rheumatological clinic patients who had assessed 10-year Hip Fracture Risk ≥3% based on FRAX Score.

- Cs: Corticosteroidal agents of at least Prednisolone 7.5 mg/day or equivalent for 3 months in the past year.
- **PD:** Protein density in g per 100 Cal.
- **OsCal-D:** supplementary tablet which contains 600 mg CaC03 and 400 IU Vit D3.

Cs: Corticosteroids. **$CaCO_3$:** Weekly average of calcium carbonate supplements.	**NA:** Not mathematically applicable and can't be statistically computed. **Vit D**: 25-OH-Cholecalciferol (Vit D3 level) in ng per ml.

Table IV. Univariate regression analysis results for the 4 tested variables regarding 10-year Hip Risk Fracture percentages among attended rheumatology clinic patients between Sep 2021 and Nov 2021 at Prince Rashid Bin Al-Hasan Military Hospital, Royal Medical Services, Irbid, Jordan.

Tested variables	Model summary		F-ANOVA	Coefficient's summary			p-Value
	R	R^2		Constant±SEM	B±SEM	Beta	
PD (g/100 Cal)	0.894	0.799	808.896	4.795±0.070	-0.563±0.020	-0.894	0.000
FVCP	0.600	0.361	115.048	4.780±0.175	-1.983±0.185	-0.600	0.000
ADLS	0.732	0.536	235.479	3.441±0.056	-1.653±0.108	-0.732	0.000
OsCal-D (Tab/day)	0.930	0.865	1304.124	5.575±0.076	-0.954±0.026	-0.930	0.000

The Univariate Linear Regression Test was conducted to explore the degree of correlation, how much of the total variation in the dependent variable can be explained by the independent variable, and the quality of the prediction of the dependent variable. Also, this test was conducted to abstract the necessary coefficients to individually predict the 10-year Hip Fracture Risk.

- **PD:** Protein density in g per 100 Cal.
- **FVCP:** Fruits/Vegetables consumption pattern (Intermittent pattern=0, Regular pattern=1).
- **ADLS:** Activities of daily life style (Sedentary life style=0, Active life style=1).
- **OsCal-D:** supplementary tablet which contains 600 mg CaC03 and 400 IU Vit D3.

Table V: Multivariable linear regression analysis results for the 4 tested variables regarding 10-year Hip Risk Fracture percentages among attended rheumatology clinic patients between Sep 2021 and Nov 2021 at Prince Rashid Bin Al-Hasan Military Hospital, Royal Medical Services, Irbid, Jordan.

Tested variables	Model summary		F-ANOVA	Coefficient's summary		p-Value
	R	R^2		B±SEM	Beta	
	0.959	0.920	579.539			
Constant				5.406±0.084		0.000
PD (g/100 Cal)				-0.325±0.029	-0.516	0.000
FVCP				-0.885±0.111	-0.268	0.000
ADLS				-0.447±0.099	-0.198	0.000
OsCal-D (Tab/day)				-0.169±0.081	-0.165	0.038

The Multivariable Linear Regression Test was conducted to explore the degree of correlations, how much of the total variations in the dependent variable can be explained by the independent variables, and the quality of the prediction of the dependent variable. Also, this test was conducted to abstract the necessary coefficients to collectively predict the 10-year Hip Fracture Risk and to present the final form of our proposed multivariate logistic regression model for the tested osteoporosis patients which can be formulated as follows.

10-Year Osteoporosis related Fracture Risk (%) =5.406-0.325×PD-0.885×FVCP-0.447*ADLS-0.169*OsCal-D

- **PD:** Protein density in g per 100 Cal.
- **FVCP:** Fruits/Vegetables consumption pattern (Intermittent pattern=0, Regular pattern=1).
- **ADLS:** Activities of daily life style (Sedentary life style=0, Active life style=1).
- **OsCal-D:** supplementary tablet which contains 600 mg CaC03 and 400 IU Vit D3.

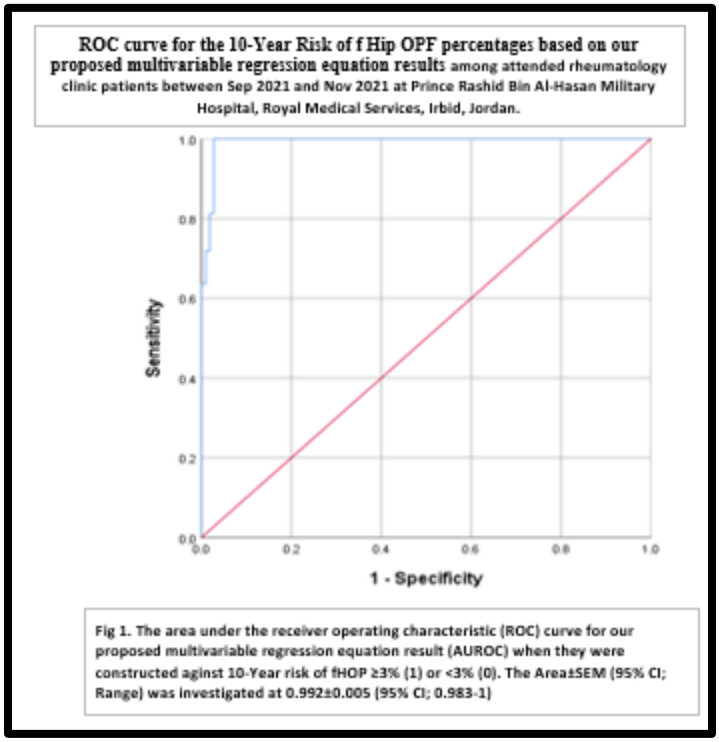

Fig 1. The area under the receiver operating characteristic (ROC) curve for our proposed multivariable regression equation result (AUROC) when they were constructed aginst 10-Year risk of fHOP ≥3% (1) or <3% (0). The Area±SEM (95% CI; Range) was investigated at 0.992±0.005 (95% CI; 0.983-1)

Table VI. The optimal cut-off points, sensitivities, specificities, positive and negative predictive values, Youden and accuracy indices, and the negative likelihood ratios for the 10-Year Risk of f Hip OPF percentages based on our proposed multivariable regression equation results among attended rheumatology clinic patients between Sep 2021 and Nov 2021 at Prince Rashid Bin Al-Hasan Military Hospital, Royal Medical Services, Irbid, Jordan.

Prognostic Indicator	Cut-off	TPR	FPR	YI	TNR	PPV	NPV	NLR	AI
10-Year risk of fHOP fracture	**3.45%**	100%	2.7%	97.27%	97.27%	96.97%	100.00%	0.00%	98.54%

- **The area under the receiver operating characteristic (ROC) analysis was constructed against the 10-Year risk of fHOP_FRAX score ≥3% (1) or <3% (0). Sensitivity analysis was processed on a total of 206 processed cases, 96-case were processed as positive actual state, and 110-case were processed as a negative actual state. 3 processed cases were dealt with as missing data. higher values of the test result variable(s) indicate stronger evidence for a positive actual state. The positive actual state is the 10-Year risk of fHOP fracture based on our proposed multivariate linear regression analysis.**
- **fHOP: Femoral hip osteoporosis.**

TPR: True positive rate (sensitivity).	**PPV: Positive predictive value.**
FPR: False positive rate.	**NPV: Negative predictive value.**
YI: Youden index.	**NLR: Negative likelihood ratio.**
TNR: True negative ratio (specificity).	**AI: Accuracy index.**

Figure 2. Calorie and protein chart of common foods.

DISCUSSION

The National Institutes of Health consensus conference defined osteoporosis as an aging-related increased skeletal fragility accompanied by low BMD diseases. Low BMD is numerically defined as a T score below −2.5 and the preferred diagnostic sites for calculating the T score are the hip, either at the total hip or the femoral neck [22-23]. Even though it would be beneficial to conduct routine osteoporosis screening tests, it is not feasible in most countries including our country due to the restricted availability of DEXA machines and their associated high-cost expenditure. So, it is therefore not feasible to screen all postmenopausal Jordanian women and aged males using DEXA screening.

The availability of a variety of osteoporosis-related effective pharmacotherapeutics emphasized the recommendation of T score assessment for patients considered at high risk. Various risk assessment tools have been developed to focus on subjects who are at increased risk, that way they can be referred for BMD measurement.[24-27] The OST, ORAI, SCORE, and OSIRIS indices were derived according to the algorithms suggested by their developers, and the following operating discriminative cut-offs were used: <2 for OST, >7 for SCORE, >8 for ORAI, and <1 for OSIRIS.[28-31]

Additionally, sensitivity was low when DEXA screening of the spine was used for analysis. This can be explained by the bone density within the spine would be increased in the presence of multiple vertebral fractures giving falsely overestimated T scores without affecting the overall osteoporotic statuses.[32-34]

A fracture risk assessment tool (FRAX) is developed based on the use of clinical risk factors that were previously mentioned, with DEXA screening to differentiate the screened patients with a debatable osteoporotic risk into a more meaningful way for proactively prescribing osteoporosis-related effective drugs when it is exceeded 3%.[35]

However, most of the tools have been developed for the Western population and the risk of osteoporotic fractures varies widely between ethnicities and populations. Thus, population-specific data are required to predict the risk of fracture in each population. However, few studies have developed an assessment model from the dietary and lifestyle risk factors of osteoporotic fractures which gives the uniqueness of our study.[36-40]

While the consumption of animal proteins-based sulfur amino acids and grains phytate-based phosphate increase physiological acidity, the consumption of fruits and green vegetables increases alkalinity owing to high alkaline potassium salts of weak organic acids contents. A higher protein: potassium (PRO: K) ratio is undesirable, as demonstrated by the finding that it is associated with higher renal net acid excretion. Oppositely to high PRO: K, a low PRO: K-based diet is associated with a lower potential for renal acid and calcium load which can be achieved by consuming a balanced diet.[41-43] Calcium intake may also be important. For example, in the Framingham study, the increased fracture risk associated with higher sulfur amino acids intake was only present in the participants with lower calcium intake (<800mg/d) while contrarily no association between higher sulfur amino acids and fracture risk when calcium intake was sufficient (≥800 mg/d) which suggests adequate calcium intake may offset any detrimental effects of high sulfur amino acids.[44-45]

Indeed, there is an argument for a whole diet approach for bone health, which includes a balanced intake of nutrients such as protein, potassium, calcium, and phosphate. As discussed earlier, one way of increasing potassium intake is to consume more fruit and vegetables. Adequate calcium intake may also help compensate for any sulfur amino acid-induced bone loss. Adequate protein intake ensures enough amino acids for the growth and repair of body tissues but should not be in excess.[46-50] In this study, we revealed in our dietary pattern and lifestyle derived proposed multivariate regression model that for each 1 g/100 Cal increment in PD, the 10-Year Osteoporosis related Fracture Risk (%) was decreased from baseline constant (5.406%) by 1.826%, 2.151%, 2.476%, and 2.801 %, respectively, as long as the tested participant maintained regular FVCP, active ADLS, and OsCal-D of at least 1 tab per day. Also, we mathematically extrapolated the optimal PD (g/100 Cal) and OsCal-D (tablet/day) to state the 10-Year Osteoporosis related Fracture Risk (%) below 3% in tested participants who maintained regular FVCP and active ADLS.

CONCLUSION

In this study, we revealed that the probability of 10-Year Osteoporosis related Fracture Risk was maximally set at 2.924% as long as the minimum PD didn't decrease below 2.5 g/100 Cal and the number of OsCal-D tablets was above 2 tablets per day in Jordanian participants who maintained regular Fruits/Vegetables consumption pattern and active daily lifestyle based on the following derived Multiple Linear regression Model. This explored model may be an initial step to conduct an osteoporosis risk tool that is valid and feasible for Jordanian people who are at risk of osteoporosis (to early assess their T-Score) and who already have T-Score on the osteopenia range but the decision to initiate a pharmacotherapeutic plan depends on the assessed osteoporotic risk.

10-Year Osteoporosis related Fracture Risk (%) =5.406-0.325×PD-0.885×FVCP-0.447*ADLS-0.169*OsCal-D

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