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RISK EVALUATION IN FRAGILE FRACTURE FORMATION*

PROCENA RIZIKA ZA NASTANAK FRAGILNIH PRELOMA

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Key words
osteoporosis; risk; FRAX; fractures.

Ključne reči
osteoporoza; rizik; FRAX; prelomi.

Abstract

INTRODUCTION: Osteoporosis represents bone mineral density deficiency which can lead to fracture. Our aim is to detect patients with high risk of fracture in order to apply the adequate therapy. **AIM**: To identify patients with high risk of osteoporosis fracture. **MATERIAL AND METHODS**: Prospective studies included 65 patients of both genders aged ≥50. Bone mineral density was measured in all of the patients of hip and lumbar area of the spine.The results are given in absolute numbers and in the form of T score and are interpreted by the current definition of osteoporosis. All patients were asked identical questions from the FRAX questionnaire – model for Italy and all patients signed an agreement to be included in the study. Exclusion factors: pre-menopausal patients, the presence of some other metabolic disease, and patients who use drugs for osteoporosis. Statistic processing and analysis were done on the computer program SPSS ver.20.t **RESULTS**: Average age is M=63,4±7,4 years. Most were women 84%, and the Body Mass Index value in 1/3 participants was in normal values. There are no statistically significant risk factors for bigger fractures when there is a T score ($p>0.05$), and without the T score they are: the number of fractures, glucocorticoids, age, secondary osteoporosis, rheumatoid arthritis, prior fractures and hip fractures that occur in the family (mother or father) ($p<0.01$) Significant risk factors in care of hip fractures with the T score are: secondary osteoporosis, the number of factors, glucocorticoids, rheumatoid arthritis ($p<0.01$), while in hip fractures without the T score we find age and prior fractures significant alongside previously listed factors($p<0.01$). **CONCLUSION**: Frax index is a useful tool for evaluating patients which have a ten year risk for fragile osteoporotic fracture occurrence, even when we do not know bone mineral density value.

INTRODUCTION

Osteoporotic bone is a bone of reduced bone density and as such has greater risk of fracture occurrence.(1) As a gold standard in diagnostic procedures Dual Energy X-ray Absorptiometry (DXA) is highly recommended. This method emits negligible amount of radiation by which bone density of the lumbar spine and hips are measured.(2) Large-scale osteoporotic fractures have harmful effects on health and life quality of all patients, especially those older than 65. Patient screening and identification of those with higher risk for these kinds of fractures would have great influence on prevention improvement.(3)

Generally, risk factors are attributes, characteristics or exposures that increase the likelihood of a person developing a disease or health disorder in a certain population. Smoking and old age are the most frequently cited risk factors for developing osteoporosis.(4) Identification of factors that can affect fragile fractures in postmenopausal women, as well as examining which factors have the largest influence on osteoporotic fracture development, is of great importance.(5)

Fracture Risk Assessment (FRAX®) is an algorhytm for evaluating the risk for fracture occurrence developed by World Health Organisation with the help of other medical organisations.(6) This tool is a mathematical model for cal-

culation of suspected ten-year risk of bone fracture.(7) The instrument consolidates the following risk factors: age, gender, earlier fractures, fractures in family, use of glucocorticoids, rheumatoid arthritis, secondary osteoporosis, alcohol consummation and smoking. FRAX tool can be used both with T score and without it which gives it wider use in everday praxis. Treating patients whose ten year risk for hip fracture by FRAX tool is ≥3% or ≥20% regarding large-scale fractures is highly recommended.(8) FRAX questionnaire flaws are: not including the dosis and time period of glucocorticoid usage, daily alcohol intake, number of cigarettes smoked, number and type of fracture, and it cannot be used by patients who take treatment of osteoporosis or by patients younger than 40.(9)

Our country does not have its validated Frax questionnaire yet, we use replacement from other countries. There is only one more scientific research work regarding the same subject in Serbia, in which they used Frax questionnaire for Turkey (3) whereby in our work the questionnaire is for Italy.

Frax tool can be used as an aid in institutions of primary health care for risk detection in patients with reduced bone density. It also serves as prevention of fracture occurrence in patients with the highest risk.(7) Ten year risk represents a guideline for treatment decision making.Every decision must be adapted individually.(10)

Aim:identify the patients in risk of osteoporotic fracture occurrence.

Material and methods: Prospective studies included 65 examinees of both genders. Their number is determined by Sample size method. Calculated sample size has the trust interval of 90% and maximal error of ±10% along critical incidence value of 50%. Study includes examinees of both genders, aged ≥50, directed to osteodensiometric scan in Special Hospital for Rheumatic Diseases Novi Sad. All were measured in hip and lumbar spine bone density by Dual Energy X-ray Absorptiometry on a LUNAR device. Results are shown in absolute numbers (g/cm^2) and by T score and interpreted according to the current definition of osteoporosis.

All patients were asked identical question from the FRAX questionnaire – model for Italy and all patients signed an agreement about inclusion in the study.

Exclusion factors: pre-menopausal patients, the presenceof some other metabolic disease, and patients who use drugs for osteoporosis. Planned time for obtaining information: 3 months since acquiring the consent from the Ethic committee of Special Hospital for Rheumatic Diseases Novi Sad.

Statistical importance is defined on the level of null hypothesis expectancy from $p \leq 0,05$ to $p < 0,001$. Statistic processing and analysis were done on the computer program SPSS ver.20.tors.

Results:

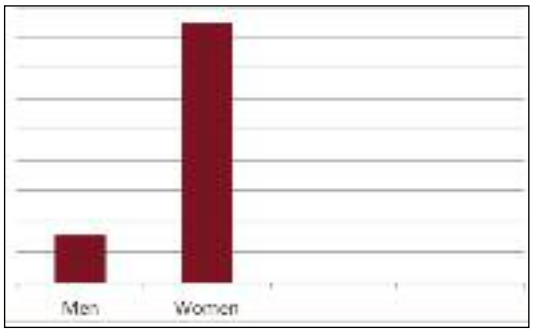
Average age is M=63,4±7,4 years, average height is M=164,2±8,4 cm and average weight is M=76,6±14,5 kg, which is presented in Table 1.

Table 1. *Sample structure*

	N	Min	Max	M	SD
Age	65	51	79	63,46	7,446
Weight	65	47,50	126,00	76,6692	14,51085
BMI	65	19,39	47,42	28,4502	5,31163
Height	65	147,00	186,00	164,2692	8,46042

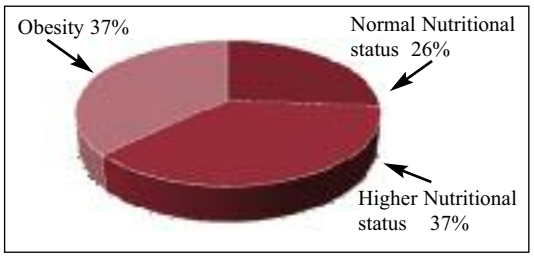
N-number of examinees; Min.-Minimal value of sample variable; Max.-Maximumvalue of sample variable; M-Arithmetic mean; SD-Standard deviation

Most examinees comprised of women 84,6%, while men were15,4%. (Graph 1.)



Graph 1*.Gender structure*

Most of the examinees had Body Mass Index - BMI beyond normal values (74%), and only 26% had normal nutritional status while there were no underfed examinees. (Graph 2.)



Graph 2*. BMI of examinees*

Table 2. *Ten year risk for large scale fracture occurrence and hip fracture with and without T score by FRAX index*

	N	Min	Max	M	SD
Large scale fractures with T score (%)	65	2,70	402,00	18,2908	49,00278
Hip fractures with T score (%)	65	0,00	26,00	2,9369	4,21499
Large scale fractures) without T score (%	65	1,40	58,00	13,5262	10,51599
Hip fracture without T score (%)	65	0,20	30,00	4,0892	5,16291

N-number of examinees; Min.-Minimal value of sample variable; Max.-Maximumvalue of sample variable; M-Arithmetic mean; SD-Standard deviation

With knowledge of T score, ten year risk for large scale fracture occurrence is18,29 ± 49%, while it is 2,9±4,2% for hip fractures. When T score is not used in FRAX index, ten year risk is 13,53 ± 10,51%, and for hip fractures it is 4,08 ± 5,16%.

Table 3. *T score and risk factors with ten year risk for large scale fracture occurrence relation*

		M	SD	F	p
Did you have fractures	Yes	15,16	8,35	,198	,658
	No	20,66	64,83		
Did your mother/father have fractures	Yes	21,57	10,06	,035	,853
	No	17,89	51,81		
Are you an active smoker	Yes	11,17	7,53	,651	,423
	No	21,69	59,25		
Do you use glucocorticoids	Yes	21,64	10,75	,082	,775
	No	17,37	55,13		
Are you diagnosed with rheumatoid arthritis	Yes	18,78	9,97	,002	,964
	No	18,13	56,31		
Do you have secondary osteoporosis	Yes	18,82	10,88	,003	,958
	No	18,09	57,42		
Do you consume alcohol	Yes	6,40	.	,059	,809
	No	18,48	49,37		
BMI	Normal (18,5 - 25)	14,35	9,81	,718	,492
	Excessive (25 - 30)	11,62	7,59		
	Obesity (>30)	27,75	80,04		
Gender	Male	10,58	8,97	,289	,593
	Female	19,69	53,10		
Age	51 - 59	9,36	5,41	,953	,391
	60 - 69	28,36	78,30		
	70 - 79	16,40	9,48		

M-Arithmetic mean; SD-Standard deviation; f frequency

Table 4. *Risk factors and ten year risk in hip fractures with T score relation*

		M	SD	F	p
Did you have fractures	Yes	2,89	3,26	0,01	0,94
	No	2,97	4,86		
Did your mother/father have fractures	Yes	3,09	3,28	0,01	0,92
	No	2,92	4,34		
Are you an active smoker	Yes	3,97	6,19	1,88	0,18
	No	2,45	2,80		
Do you use glucocorticoids	Yes	6,13	6,78	11,99	0,00
	No	2,06	2,68		
Are you diagnosed with rheumatoid arthritis	Yes	5,63	6,48	9,88	0,00
	No	2,06	2,71		
Do you have secondary osteoporosis	Yes	6,02	6,63	16,51	0,00
	No	1,76	1,83		
Do you consume alcohol	Yes	1,80		0,07	0,79
	No	2,95	4,25		
BMI	Normal (18,5 - 25)	3,92	6,15	0,62	0,54
	Excessive (25 - 30)	2,58	3,17		
	Obesity(>30)	2,60	3,49		
Gender	Male	4,47	7,73	1,58	0,21
	Female	2,66	3,25		
Age	51 - 59	1,40	1,62	2,93	0,06
	60 - 69	3,74	6,08		
	70 - 79	4,17	2,51		

M-Arithmetic mean; SD-Standard deviation; f frequency

As all independent variables are categoric, for examination of relation with depentant variable (ten year risk for large scale fracture occurrence with T score) analysis of variance (ANOVA) is used. None of the risk factors turned out to be statistically important. All statistical significance was higher than the borderline value of 0,05.

Ten year risk for large scale fracture occurrence and hip fracture occurrence with T score.

Examinees who use and those who do not use glucocorticoids significantly differ statistically in risk values for hip fracture occurrence (with T score) (F=11,99, p=0,000). This index is greater in those who use glucocorticoids (M=6,13 vs M=2,06). There is a difference between those who have and those who do not have diagnosed rheumatoid arthritis (F=9,88, p=0,000). It is greater in those who are diagnosed with rheumatoid arthritis (M=5,63vs M=2,06). Likewise, statistically significant difference exists among those who have and who do not have secondary osteoporosis (F=16,51, p=0,000). This index is also greater among those who are diagnosed with secondary osteoporosis (M=6,02vs M=1,76).

Ten year risk for large scale fracture occurrence and hip fracture occurrence without T score.

Examinees who had previous fractures have significantly increased statistical index than those who did not have fractures (M=19,01vs M=9,38). Those whose parents had hip fractures have higher index than those whose parents did not have noted hip fracture (M=22,6vs M=12,4). Examinees who use and those who do not use glucocorticoids have statistically significant differences in risk values for large scale risk occurrence (with T score) (F=33,41, p=0,000). This index is higher among those who use glucocorticoids (M=25,2vs M=10,3). However, there is a distinction between those who have and those who do not have diagnosed rheumatoid arthritis (F=6,57, p=0,001). The index is greater in those with diagnosed arthritis (M=19,14vs M=11,69). Also, statistically significant difference exists among those who have and who do not have secondary osteoporosis (F=18,08, p=0,000). This index is higher in those who have secondary osteoporosis (M=21,49vs M=10,48). The oldest examinees have the highest index (M=20,85).

Table 5. *Risk factors and ten year risk in large scale fractures without T score relation*

		M	SD	F	p
Did you have fractures	Yes	19,01	11,70	16,65	0,00
	No	9,38	7,27		
Did your mother/father have fractures	Yes	22,69	17,83	6,46	0,01
	No	12,42	8,90		
Are you an active smoker	Yes	11,31	8,81	1,39	0,24
	No	14,58	11,18		
Do you use glucocorticoids	Yes	25,25	13,64	33,41	0,00
	No	10,31	6,64		
Are you diagnosed with rheumatoid arthritis	Yes	19,14	11,70	6,57	0,01
	No	11,69	9,52		
Do you have secondary osteoporosis	Yes	21,49	14,18	18,08	0,00
	No	10,48	6,73		
Do you consume alcohol	Yes	6,70		0,42	0,52
	No	13,63	10,56		
BMI	Normal (18,5 - 25)	16,04	12,49	0,65	0,52
	Excessive (25 - 30)	12,56	9,87		
	Obesity(>30)	12,71	9,77		
Gender	Male	7,92	3,51	3,49	0,07
	Female	14,55	11,05		
Age	51 - 59	8,89	5,93	7,25	0,00
	60 - 69	13,77	9,33		
	70 - 79	20,85	14,14		

M-Arithmetic mean; SD-Standard deviation; f frequency

Table 6. *Risk factors and ten year risk in hip fractures without T score relation*

		M	SD	F	p
Did you have fractures	Yes	5,92	6,23	6,72	0,01
	No	2,71	3,70		
Did your mother/father have fractures	Yes	6,86	10,40	2,30	0,13
	No	3,76	4,18		
Are you an active smoker	Yes	3,37	3,73	0,60	0,44
	No	4,43	5,73		
Do you use glucocorticoids	Yes	9,62	7,75	29,66	0,00
	No	2,57	2,75		
Are you diagnosed with rheumatoid arthritis	Yes	6,87	5,29	6,70	0,01
	No	3,18	4,84		
Do you have secondary osteoporosis	Yes	8,21	7,40	20,69	0,00
	No	2,51	2,77		
Do you consume alcohol	Yes	2,10		0,15	0,70
	No	4,12	5,20		
BMI	Normal (18,5 - 25)	5,22	6,96	0,54	0,58
	Excessive (25 - 30)	3,71	4,61		
	Obesity(>30)	3,67	4,24		
Gender	Male	2,00	1,28	1,96	0,17
	Female	4,47	5,51		
Age	51 - 59	1,73	1,87	12,04	0,00
	60 - 69	3,62	3,94		
	70 - 79	8,80	7,43		

M-Arithmetic mean; SD-Standard deviation; f frequency

Examinees who had fractures have statistically significantly higher index in relation to those who did not have fractures (M=5,92vs M=2,71). Examinees who use and those who do not use glucocorticoids have significant difference by risk value for large scale fracture occurrence (with T score) (F=29,66, p=0,000). It is greater in those who use glucocorticoids (M=9,62vs M=2,57). Also, this index differs in those who have and those who do not have rheumatoid arthritis diagnosed (F=6,70, p=0,001), and it is higher in those who are diagnosed (M=6,87vs M=3,18). There is a difference aswell among those who have and do not have secondary osteoporosis (F=20,69, p=0,000). This index is higher in those who have secondary osteoporosis (M=8,21vs M=2,51). The oldest examinees have the highest index (M=8,80).

There is statistically significant difference in between examinees with different risk factor numbers regarding variables: Hip fractures with T score (F=5,57, p=0,000), large scale fractures without T score (F=11,47, p=0,000), hip fractures without T score (F=9,54, p=0,000). The highest scores in which there is statistically significant difference is in examinees with the highest number of risk factors (M=6,38, M=24,56, M=9,36).

Table 7. *Relation between number of risk factors and ten year risk*

		Large scale fractures with t score (%)	Hip fractures with t score (%)	Large scale fractures without t score (%)	Hip fractures without t score(%)
Without risk factors	M	35,14	1,31	6,76	1,57
	SD	105,64	1,67	4,16	2,51
1	M	8,74	1,47	10,22	2,23
	SD	3,67	1,22	5,69	1,87
2	M	11,99	3,08	13,70	3,91
	SD	4,47	3,71	7,96	4,03
> 2	M	22,50	6,38	24,56	9,36
	SD	10,18	6,76	14,25	7,55
	F	0,92	5,57	11,47	9,54
	p	0,44	0,00	0,00	0,00

M-Arithmetic mean; SD-Standard deviation; f frequency

	Dependent variable			
	Large scale fractures with t score (%)	Hip fractures with t score (%)	Large scale fractures without t score (%)	Hip fractures without t score(%)
Adjusted R2	/	0,194	0,414	0,235
Anova F	/	4,857**	46,14**	20,69**
Did you have fractures	/	/	,457**	,311*
Did your mother/father have fractures	/	/	,305*	/
Are you an active smoker	/	/	/	/
Do you use glucocorticoids	/	,400**	,589**	,566**
Are you diagnosed with rheumatoid arthritis	/	,368**	,307*	,310*
Do you have secondary osteoporosis	/	,456**	,472**	,497**
Do you consume alcohol	/	/	/	/
BMI	/	/	/	/
Gender	/	/	/	/
Age	/	/	,530**	,596**
Number of risk factors	/	,425**	,650**	,589**

Table 8. *Influence of risk factors on ten year risk factor value*
***p < 0.01; *p < 0.05;standardized Beta coeficients are displayed*

Those predictors that were statistically significant in previous analysis have entered regressed analysis. Factors that hold great significance for ten year risk for large scale fracture occurrence without T score are: previous fractures, age and the number of risk factors (p<0.01), whereby family fracture risk factors are of lesser significance (p<0.05). There is no statistically significant risk factors for large scale fracture occurrence when T score is known. Significant risk factors when we do not have T score for ten year risk in hip fractures are: glucocorticoids, secondary osteoporosis, age and number of risk factors, while fractures and rheumatoid arthritis are of lesser significance. Risk factors of higher significance when we do not have T score for ten year risk in hip fracture occurrence are: glucocorticoids, secondary osteoporosis, age and number of risk factors, while fractures and rheumatoid arthritis are of lesser significance. Concerning ten year risk when there is a T score, risk factors that hold high value are: glucocorticoids, rheumatoid arthritis, secondary osteoporosis and risk factor numbers.

Discussion

We used Fracture Risk Assessment (FRAX)-model for Italy for analysis of risk factors in our work. As Serbia does not have its Frax model, we used our neighbouring country model considering the similarities which our two countries have. *Average age of our examinees is M=63,4±7,4, while most of our examinees were women.* Regarding Zvekić-Svorcan and associates (2013), sample comprised of 1323 patients, by which 96% (1258/1323) were women. (11) When dealing with risk factor problems for osteoporosis occurrence in men, we targeted analyzing men in our work.(12)

Most of our examinees were beyond normal BMI values, which is characteristic for the region we live in. Grujić and associates (2005) discuss this problem where they correlate obesity with sedentary lifestyle and excessive energy intake. They point out that obesity is greater in women than men.(13)

Glucocorticoid usage and rheumatoid arthritis diagnosis are linked with significantly higher risk for hip fracture occurrence. In their work, Janković and associates (2013) point out these two risk factors stating that chronic glucocorticoid therapy additionally contributes to osteoporosis development since it affects bone density in patients with rheumatoid arthritis.(14) The most common complication in glucocorticoid usage are asymptomatic vertebral low-energy fractures.(15)

Examinees who had secondary osteoporosis run greater risk of fractures. Kovačev-Zavišić and associates' (2015) work deals with problems regarding secondary osteoporosis. Osteoporosis in gluten enteropathy is a consequence of secondary hyperparathyreoidism. The diseased have higher resorption of bone tissue which requires usage of biphosphate therapy. (16)

In our research we compared the relation of risk factors with ten year risk in large scale fracture occurrence without T score where positive anamnesis in fracture stood out relating to those who did not have fractures. Johnell O. and associates (2004) made similar conclusion in their research, where they cited that patients who had previous fractures due to osteoporosis run the risk as great as 5 times of fracture repetition.(17) Also, Zvekić-Svorcan and associates (2011) did research that highlighted the significance of previous fractures.(1) Vujasić-Stupar and associates (2009) cite that people who had suffered a fracture have 50-100% higher chance for reccuring fractures, stating that older people and people who already suffered fractures are the likely candidates for preventive measures.(18)

In our work we proved that age is a very significant risk factor for hip fracture occurrence and that the risk of these fractures increases with age. Schneider (2008) in his work also describes that osteoporotic frequency is far greater in geriatric population, and especially cites hip fractures as a serious complication and stresses the importance of prevention.(19) Liberman and associates (2015) also state that every person older than 65 regardless the gender, has to be tested for risk factors so that risk for osteoporotic fracture occurrence can be evaluated. They state that bone densiometry is a primary method for early detection of osteoporosis, aswell.(20)

FRAX tool is used in the work of Epanov and associates (2015) in evaluating the ten year risk factor of large scale fracture occurrence. In 50-59 age group osteoporosis is diagnosed in 30% of women. Risk for fracture occurrence

increases with age. It is considered that women aged ≥70 have osteoporosis in 70% of the cases.[21]

Using the FRAX tool most patients had high ten year risk for fracture occurrence, and hereby the prevention of osteoporosis will increase in Hungary.[22] Countries from Balkan region like Croatia and Hungary have a validated FRAX questionnaire which they use as a screening method for identifying individuals exposed to risk of osteoporotic fracture occurrence.[22]

CONCLUSIONS:

1. Ten year risk for large scale fracture occurrence when we use T score is 18,3%, while without T score is 13.5%

2. Ten year risk for hip fracture occurrence when we use T score is 2.9%, whereas without T score is 4% which means the risk is high.

3. Statistically significant risk factors for hip fracture occurrence when we use T score are: secondary osteoporosis, risk factor number, glucocorticoids and rheumatoid arthritis. By these variables 19% of the hip fracture index is justified.

4. Important risk factors for large scale fracture occurrence without using T score are: risk factor number, glucocorticoids, age, secondary osteoporosis, existing fractures, rheumatoid arthritis and occurrence of hip fractures in family. These variables explain 41% large scale fractures without T score.

5. Statistically significant risk factors for hip fracture occurrence when T score is not used are: age, risk factor number, glucocorticoids, secondary osteoporosis, existing fractures and rheumatoid arthritis. Herewith, 23% of hip fractures without T score are explained by these variables.

Sažetak

UVOD: Osteoporoza predstavlja smanjenje mineralne koštane gustine koje može dovesti do preloma na malu traumu. U cilju prevencije preloma potrebno je što pre detektovati pacijente sa povećanim frakturnim rizikom kako bi se pravovremeno sprovela adekvatna terapija. **CILJ:** identifikovati pacijente koji su u riziku za nastanak osteoporotičnog preloma. **MATERIJAL I METODE:** Prospektivnom studijom preseka, obuvaćeno je 65 pacijenata oba pola starosti ≥50 godina. Svima je merena mineralna koštana gustina na kuku i lumbalnom delu kičmenog stuba. Dobijeni rezultati su izraženi u apsolutnim brojevima (g/cm^2) i u vidu T skora i interpretirani prema važećoj definiciji osteoporoze. Takođe, svim pacijentima su postavljana identična pitanja iz upitnika Fracture Risk Assessment (FRAX) – model za Italiju i na osnovu toga je analiziran njihov frakturni rizik. Svi ispitanici su potpisivli informisani pristanak o uključenju u studiju. Faktori isključenja: ispitanice koje su u premenopauzi, postojanje neke druge metaboličke bolesti kostiju i pacijenti koji uzimaju lekove za osteoporozu. Statistička obrada i analiza je urađena u kompjuterskom programu SPSS ver.20. **REZULTATI:** Prosečna starost je M=63,4±7,4 godina.Većinu su činile žene 84%, a vrednosti indeksa telesne mase u 1/3 ispitanika spadao je u grupu normalnih vrednosti. Nema statistički značajnih faktora rizika na nastanak velikih preloma kada imamo T skor ($p>0.05$). Statistički značajni faktori rizika za nastana kvelikih preloma bez T skora su: broj faktora, glikokortikoidi, starost, sekundarna osteoporoza, reumatski artritis, predhodni prelomi i postojanje preloma kuka kod majke/oca ($p<0.01$). Kod preloma kuka sa T skorom faktori od značaja su: sekundarna osteoporoza, broj faktora, glikokortikoidi i reumatski artritis ($p<0.01$), dok se pored ovih faktora kod preloma kuka bez T skora ističu još starost i predhodni prelomi ($p<0.01$). **ZAKLJUČAK:** FRAX indeks je korisna alatka za procenu pacijenata koji su u desetogodišnjem riziku za nastanak fragilnih osteoporotičnih preloma, čak i kada ne znamo vrednost mineralne koštane gustine.

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