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Clinical, laboratory and densitometric comparison of patients with coxarthrosis and femoral neck fractures.

Comparação clínica, laboratorial e densitométrica de pacientes com coxartrose e com fraturas do colo femoral.

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A B S T R A C T

Objective: to compare clinical, laboratory and densitometric data from patients with osteoarthrosis and femoral neck fractures. **Methods:** we conducted a cross-sectional study of patients with femoral neck fracture and hip osteoarthrosis submitted to hip arthroplasty. We collected clinical, laboratory and densitometric data. **Results:** we included 53 patients, 22 with femoral neck fractures and 31 with osteoarthrosis. Patients with femoral neck fractures were older than patients with osteoarthrosis, with lower BMI values, bone mineral density and palmar grip strength (sarcopenic patients), being more neurologically impaired and presenting a worse ASA score. Among the various biochemical parameters analyzed, we found statistically significant differences in total serum calcium, ionized calcium, vitamin D, free thyroxine, erythrocytes, hemoglobin, hematocrit, total white blood cells, neutrophils, lymphocytes and creatinine between the two groups. Other hormones analyzed and biochemical parameters did not differ significantly, although they showed trends between the two groups. **Conclusion:** patients with femoral neck fractures are older than patients with osteoarthrosis, have a lower weight and BMI, are more debilitated, many with anemia and reduced bone mass, and have a significant decrease in total calcium, ionized calcium, vitamin D and creatinine and a significant increase in free thyroxine.

Keywords: Arthroplasty, Replacement, Hip. Osteoarthritis. Femoral Neck Fractures. Hip Fractures. Densitometry.

INTRODUCTION

Osteoarthrosis (OA) is a chronic and degenerative disease that affects synovial joints, including the hip[1]. It is basically characterized by the wear of the cartilage that covers the surfaces of the joint formed by the femoral head and the acetabulum. It is considered as having a multifactorial etiology, therefore being influenced by several factors[2].

Fractures of the femoral neck occur more frequently in elderly patients, being uncommon in patients under 60 years of age. Most of these fractures occur in female patients, the incidence increasing exponentially with age. The risk of a hip fracture is high, ranging from 40% to 50% in women over 60 years and 13% to 22% in men[3].

Biochemical markers may reflect the status of bone metabolism and provide information on bone remodeling (turnover)[4], which is often altered in skeletal disorders. Few studies have investigated the potential differences in the characteristics of bone markers. Resmini *et al*. observed changes in serum calcium and PTH levels in the fracture group when compared with the control group (or with osteoarthrosis). All patients were vitamin D3-deficient, with no difference between groups[5].

The objective of this study is to compare clinical, laboratory and densitometric data of patients who underwent hip arthroplasty for neck fractures and for hip osteoarthrosis.

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METHODS

The research project was submitted to, and approved by, the Scientific Committee and the Ethics in Research Committee of our institution (CAAE 05745712.0.0000.5327). We clarified all subjects invited to participate about the research and its objectives prior to performing the surgical procedure and collecting material for blood analysis. The consenting subjects signed an Informed Consent Term. We collected the information between March 2014 and October 2016.

The research consists in a cross-sectional study of patients affected by femoral neck fractures and by osteoarthrosis of the hip that underwent hip arthroplasty. We included 53 patients, 22 with fracture and 31 with osteoarthrosis. We selected patients sequentially as they underwent total hip arthroplasty, at the same time as we checked the inclusion and exclusion criteria.

As inclusion criterion, we considered patients older than 60 years submitted to hip arthroplasty, having fracture of the femoral neck or hip osteoarthrosis as cause. As exclusion criteria, we considered those patients who did not wish to participate in the study and who did not sign the Informed Consent Term, those with femoral fractures other than of the femoral neck, with dysplasias and deformities of the femur or acetabulum, previously operated on the hip for other reasons, patients with osteoarthrosis associated with osteonecrosis, metabolic disorders (Morquio syndrome, etc.), patients with rheumatic diseases (Rheumatoid Arthritis, Ankylosing Spondylitis, Systemic Lupus Erythematosus), those using bisphosphonates, hormone replacement therapy, glucocorticoid use in the month prior to surgery, and supplementation of calcium, vitamin B12, folate or vitamin D.

We questioned and examined the patients the day before the surgical procedure. We collected information directly with the patient, such as demographic data and the cause of arthroplasty (fracture of the femoral neck or arthrosis), and measured the strength of the patients' palmar grip through a dynamometer regulated and measured by INMETRO. We collected blood samples for measuring serum total calcium, ionic calcium, sodium, potassium, phosphorus, complete blood count, thyrotropin (TSH), free thyroxine (T4L), 25-OH-vitamin D, aldosterone, androstenedione, estradiol, follicle-stimulating hormone (FSH), luteinizing hormone (LH), parathyroid hormone (PTH), progesterone, total testosterone, alkaline phosphatase, creatinine, urea, TP and TTPA. We performed densitometries in the immediate postoperative period.

We performed data analysis using the Statistical Package for The Social Sciences (SPSS 18.0) software. We determined the means and dispersion of the quantitative variables and the proportions of the qualitative ones. We assessed homogeneity with the Kolmogorov-Smirnov test. For analysis of possible differences, we used the Student's t, the chi-square or the ANOVA tests. We used the Mann-Whitney test to identify differences in non-parametric variables. We considered $p<0.05$ as statistically significant.

RESULTS

We evaluated 22 patients with fracture and 31 with hip osteoarthrosis. Tables 1 and 2 show the relations of the surgical intervention with gender, age and categorized age. In the fractures group, we observed that the majority of the patients were female (68.2%) and the mean age was higher than in the arthrosis group. There was no statistically

significant difference between genders (p>0.05), but there was for age between groups (p=0.005).

Table 3 shows patients' clinical data, with a higher age range in patients with fracture, as well as lower weight, lower body mass index (BMI) and lower palmar grip strength (PGS) in the right and left hands compared with patients with osteoarthrosis, all with statistical significance. The only parameter that did not differ significantly between groups was height.

Table 4 shows the comorbidities: neurological disease (Parkinson's, Alzheimer's and dementia) was significant, as well as previous surgeries. The use of tobacco (p=0.377) and alcohol (p=0.280) did not present significant differences. With respect to the ASA score, the number of ASA I, II, III and IV patients was 1, 8, 12 and 1, respectively, among patients with fractures, and 0, 25, 6 and 0 among patients with osteoarthritis, with statistical significance (p=0.002).

Among the various laboratory parameters evaluated, we found a statistically significant difference for total and ionic serum calcium, 25-OH-vitamin D, erythrocytes, hemoglobin, hematocrit, total leukocytes, lymphocytes, basophils, creatinine and free thyroxine. Other biochemical parameters showed tendencies between the two groups, such as alkaline phosphatase and testosterone, but were not statistically significant (Table 5).

Table 1. *Demographic data relating the reason for surgery with sex and age.*

	Fracture N=22	Osteoarthrosis N=31
Gender*		
Male	7 (31.8)	13 (41.9)
Female	15 (68.2)	18 (58.1)
Age**		
Male	78.3±11.8	69.8±8.0
Female	75.1±12.0	65.9±6.5

** number of patients (percentage); ** average ± standard deviation.*

Table 2. *Motive of surgery according to age groups.*

Age range (years)	Fracture** N*	N*=22	Osteoarthritis** N*	N*=31
60-69	8	63.5±3.1	21	63.2±3.0
70-79	4	73.5±1.7	7	74.0±2.7
≥80	10	87.2±5.8	3	82.7±2.3

** N= number of patients; ** average ± standard deviation.*

Table 3. *Clinical parameters evaluated.*

Parameter	Fracture**	Osteoarthritis**	p*
Age (years)	76.09±11.76	67.55±7.30	0.005
Weight (kg)	64.32±12.09	74.02±11.46	0.005
Height (m)	1.64±0.06	1.65±0.07	0.198
BMI (kg/m^2)	24.02±4.29	26.83±3.41	0.010
Right PGS (Kgf)*	21.67±9.26	29.96±8.40	0.016
Left PGS (Kgf) *	19.39±10.11	28.37±8.61	0.015

** PGS: palmar grip strength; ** average ± standard deviation.*

Table 4. *Comorbidities assessed.*

Comorbidity	*p*
Diabetes	0.720
Systemic arterial hypertension	0.218
Congestive heart failure	0.087
Arrhythmia	0.066
Acute myocardial infarction	0.133
Transient ischemic accident	0.087
Ischemic vascular stroke	0.087
Hemorrhagic vascular stroke	*
Asthma	*
Chronic obstructive pulmonary disease	0.395
Previous surgery	0.015
Neurological diseases	0.014
Kidney disease	0.395
Previous history of cancer	0.767
Other diseases	1.000
Number of comorbidities	0.985

* *Not enough data.*

Table 5. *Biochemical parameters evaluated.*

Parameter	Fracture*	Arthrosis*	References	*p***
Ionic calcium (mg/dl)	4.88±0.43	5.27±0.39	4.0-4.8	0.003**
Total calcium (mg/dl)	8.55±1.04	9.64±0.83	8.6-10.0	0.000**
Sodium (mEq/l)	140.09±3.19	140.35±2.64	136.0-145.0	0.744
Phosphorus (mg/dl)	3.97±0.83	3.63±0.60	2.5-4.5	0.093
Potassium (mEq/l)	4.52±0.50	4.37±0.55	3.5-5.1	0.108
Chlorides (mEq/l)	101.50±4.91	101.81±4.28	98.0-107.0	0.885
Alkaline phosphatase (U/l)	96.55±45.37	86.53±29.70	35.0-104.0	0,331
25-OH-vitamin D (ng/ml)	14.73±9.71	21.60±7.37	30-100	0.005**
Creatinine (mg/dl)	0.87±0.37	0.99±0.34	0.5-0.9	0.039**
Urea (mg/ml)	53.33±24.68	45.38±13.56	16.0-48.0	0.425
Erythrocytes (x10^6/µl)	3.99±0.76	4.49±0.58	4.0-5.4	0.015**
Hemoglobin (g/dl)	11.95±2.09	13.32±1.85	11.6-15.6	0.015**
Hematocrit (%)	36.30±6.14	39.95±4.99	36.0-48.0	0.021**
MCHC (g/dl)	32.91±0.78	33.41±1.20	30.5-37.2	0.096
MCV (fl)	91.28±4.70	89.06±4.70	80.0-98.0	0.098
MCH (pg)	30.01±1.69	29.67±1.80	27.0-32.0	0.483
RDW (%)	14.15±1.63	13.87±1.10	up to 15.0	0.569
Total leukocytes (x10^3/µl)	9.34±2.32	7.26±2.25	3.6-11.0	0.002**

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Parameter	Fracture*	Arthrosis*	References	*p***
Segmented (x10³/µl)	67.92±11.61	57.74±11.29	45.0-70.0	0.002**
Lymphocytes (x10³/µl)	19.14±9.78	29.41±7.36	20.0-50.0	0.000**
Basophils (x10³/µl)	0.25±0.17	0.53±0.31	0.0-3.0	0.000**
Eosinophils (x10³/µl)	4.02±3.75	2.95±1.67	0.0-7.0	0,607
Monocytes (x10³/µl)	8.84±2.13	8.09±2.40	2.0-10.0	0.127
Platelets (x10³/µl)	254.77±112.39	253.23±61.68	150.0-400.0	0.950
TP (seconds)	12.55±1.18	12.58±0.72	Control 13s	0.907
INR	1.04±0.10	1.03±0.05	up to 1.2	0.816
TTPA (seconds)	26.93±2.78	27.43±2.98	25.0-34.0	0.539
Thyrotropin (TSH) (uUI/ml)	3.30±3.07	3.07±3.04	0.27-4.20	0.705
Free thyroxine (ng/dl)	1.44±0.25	1.25±0.24	0.93-1.70	0.011**
Parathyroid hormone (PTH) (pg/ml)	85.30±47.52	82.84±47.47	15.0-68.3	0.824
Aldosterone (ng/dl)	9.03±12.39	10.35±8.65	2.5-39.2	0.262
Androstenedione (ng/ml)	1.49±1.27	0.92±0.67	0.6-3.1	0.123
Estradiol (pg/ml)	19.38±10.45*** 26.33±6.01# 16.13±10.62(e)	16.67±15.26*** 30.88±14.27# 7.19±5.29(e)	Men 7.63-42.6 Women (post menopause) <5.0-54.7	0,476
Progesterone (ng/ml)	0.30±0.27*** 0.30±0.17# 0.29±0.31(e)	0.28±0.31*** 0.33±0.42# 0.24±0.20(e)	Men 0.2-1.4 Women (post menopause) 0.1-0.8	0.827
Testosterone (ng/ml)	1.00±1.54*** 2.74±1.75# 0.19±0.19##	1.57±2.06*** 3.68±1.76# 0.16±0.14##	Men 1.93-7.40 Women (post menopause) 0.03-0.41	0.287
Follicle-stimulating hormone (FSH) (mIU/ml)	42.89±28.57*** 18.47±21.95# 54.29±24.08##	49.83±40.48*** 10.87±9.97# 73.21±34.21##	Men 1.5-12.4 Women (post menopause) 25.8-134.8	0,495
Luteinizing hormone (LH) (mIU/ml)	18.91±14.88*** 15.49±18.67# 20.50±13.20##	26.23±20.55*** 10.88±9.97# 36.47±19.45##	Men 1.7-8.6 Women (post menopause) 7.7-58.5	0.162

** mean ± standard deviation; ** values with p statistically significant; *** mean ± standard deviation among patients in the group (osteoarthritis or fracture); #mean values ± standard deviation between men in the same group; ##mean ± standard deviation among women in the same group. # mean values ± standard deviation between men in the same group; ## mean ± standard deviation among women in the same group.*

Table 6 shows the values obtained through densitometry. The group with femoral neck fractures presented inferior bone mineral density (BMD), both in the femoral neck and in the lumbar spine region, as well as for the Tscore and Zscore values, all with statistical significance.

Table 6. *Bone densitometry.*

Parameter	Fracture	Arthrosis	*P*
BMD* L1-L4 (g/cm^2)	0.945±0.150	1.098±0.149	0.010
BMD* femoral neck (g/cm^2)	0.677±0.162	0.974±0.151	0.000
Tscore	-2.700±1.09	-0.837±1.00	0.000
Zscore	-0.855±0.99	0.141±1.03	0.012

** BMD: Bone mineral density.*

DISCUSSION

Aging is a natural and physiological process that occurs in human beings. Due to it, each individual experiences emotional, psychological and environmental experiences that make it unique and individual[6]. Although old age is not synonymous with illness and inactivity, aging may be accompanied by chronic and multiple diseases, depending on the economic context, social and cultural development of the individual. In this sense, the physiological changes, when added to the other diseases, weaken the functional capacity of the elderly, compromising their quality of life. Osteoarthrosis is one of these chronic diseases that affects the elderly, presenting a multifactorial etiology[2]. The genetic component and obesity[7], age[8], cellularity at articulation[6], degree of apoptosis[9], gender and hormones[10] and morphology[11] have been mentioned.

Epidemiological studies have identified numerous risk factors for femoral neck fractures, such as BMI below 18.5, low exposure to sunlight, low recreational activity, smoking, previous history of osteoporotic fracture, maternal history of hip fracture, and corticosteroid treatment[12]. In addition, 70% of patients with femoral neck fractures have ASA III or IV at the time of fracture[3]. In the present study, we also found a lower BMI in patients with femoral neck fractures, with a higher mean age, being 68.2% of female patients, 59% with ASA III or IV. We did not observe differences for smoking and alcohol use in our sample. The acute use of corticoid was an exclusion factor.

The reduction of bone mass caused by osteoporosis has an unequivocal relationship with hip fracture and is present in more than 84% of patients with fracture of the femoral neck. Only one standard deviation doubles the risk of hip fractures[3]. In this study, we also observed lower mineral density in patients with fractures compared to those with hip osteoarthrosis.

Bone diseases alter the production pattern of biochemical markers. Diseases leading to osteopenia tend to increase the relationship between reabsorption markers and formation markers, as appears to be the case in osteoporosis[13]. Vitamin D deficiency states are characterized by a change in osteoblast differentiation, with a disproportionate increase in levels of alkaline phosphatase[14]. Resmini *et al*. observed changes in serum calcium and PTH levels in the fracture group when compared with the control group (or with osteoarthrosis). All patients were vitamin D3-deficient, with no difference between groups[5]. In the present study, PTH was not statistically significant, but we observed a significant reduction in vitamin D values, in addition to ionic and total calcium, in the group with femoral neck fracture. In both groups, the measured vitamin D values were below the standard used by the method. Although there was no statistically significant difference, we observed an increase in alkaline phosphatase in response to a decrease in vitamin D.

The group with femoral neck fractures presented a more debilitated clinical picture, with anemia in the majority of the times and a significant reduction in the values of palmar grip strength (evidencing sarcopenia), besides an increase in free thyroxine, in the attempt of the organism to stimulate the basal cell metabolism. Although significant, the difference found in creatinine is probably associated only with patient stabilization for surgery, since there is a large standard deviation.

Although not strong enough to diagnose patients with bone loss in isolation, large prospective studies correlated bone markers with risk of fractures and prediction of bone loss. Naturally, markers also present fluctuations due to several factors, such as diurnal and nocturnal variations, menstrual period, seasonal variations, age, metabolism and clearance, among other conditions, such as increase after fractures, prolonged stay in the bed, malnutrition, rheumatoid arthritis, connective tissue diseases, multiple myeloma, bone metastases, use of anticonvulsants, corticoids, and heparin. Studies are thus still necessary to indicate the best combination of markers[7]. To avoid these confounding factors, the exams were always collected at the same time of day, there were no women of childbearing age, all of them being menopausal, all patients were older than 60 years, none of them had rheumatoid arthritis, connective tissue disease, multiple myeloma or bone metastases, and no one had used corticosteroids or heparin acutely prior to surgery. In this study, we used clinical, laboratory and densitometric factors to evaluate the patients affected by neck fracture or hip osteoarthrosis. Several parameters evaluated were not statistically significant, despite tendencies, as can be observed in tables 3, 4 and 5.

Patients affected by fractures are generally debilitated, being more exposed to complications such as delirium, infection, iatrogenic complications, which in turn contribute to functional decline, increased nursing care needs and risk of death. Geriatricians should be trained to discover these comorbidities, to identify and manage patients who are at increased risk for adverse outcomes, particularly patients who will be operated on for hip fractures[15]; this type of fracture has been described as a "geriatric condition, rather than an orthopedic disease"[16]. The present research aims to contribute in this sense.

The authors recognize the difficulties in comparing patients submitted to osteoarthrosis or fracture of the femoral neck. However, the inclusion and exclusion criteria applied established a scientific rigor in this research. The number of individuals evaluated also reflects the difficulty of including patients in the study due to the rigor of the criteria. We corroborate several authors that show the multifactorial nature of the risk factors, and the trends found point to the need for a multidisciplinary medical approach.

We conclude that patients with femoral neck fractures present more advanced age, lower weight and lower BMI than patients with osteoarthrosis. The former also displayed a more debilitated clinical picture, with anemia most of the times and reduction of bone mass and of palmar grip strength, in addition to decreased levels of total and ionic calcium, vitamin D and creatinine, with an increase in free thyroxine.

R E S U M O

Objetivo: *comparar dados clínicos, laboratoriais e densitométricos de pacientes com osteoartrose e com fratura do colo femoral.* **Métodos:** *estudo transversal de pacientes com fratura do colo femoral e osteoartrose do quadril, submetidos à artroplastia de quadril. Dados clínicos, laboratoriais e densitométricos foram coletados.* **Resultados:** *cinquenta e três pacientes foram incluídos, 22 com fraturas do colo femoral e 31 com osteoartrose. Pacientes com fratura do colo do fêmur apresentaram maior idade do que os pacientes com osteoartrose, tendo valores de IMC, densidade mineral óssea e força de preensão palmar (pacientes sarcopênicos) inferiores, estando mais incapacitados neurologicamente e apresentando um pior escore ASA. Entre os vários parâmetros bioquímicos analisados, diferenças estatisticamente significantes foram encontrados no cálcio sérico total, cálcio ionizado, vitamina D, tiroxina livre, eritrócitos, hemoglobina, hematócrito, glóbulos brancos totais, neutrófilos, linfócitos e creatinina entre os dois grupos. Outros hormônios analisados e parâmetros bioquímicos não diferiram significativamente, apesar de mostrarem tendências entre os dois grupos.* **Conclusão:** *pacientes com fraturas do colo do fêmur são mais idosos do que pacientes com osteoartrose, apresentam um menor peso e IMC, são mais debilitados, muitos com anemia e massa óssea reduzida, além de terem uma diminuição significativa no cálcio total, cálcio ionizado, vitamina D e creatinina e um aumento significativo na tiroxina livre.*

Descritores: *Artroplastia de Quadril. Osteoartrite. Fraturas do Colo Femoral. Fraturas do Quadril. Densitometria.*

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