Received:
18 June 2013

Revised:
31 January 2014

Accepted:
13 February 2014

doi: 10.1259/bjr.20130358

Cite this article as:

Ripamonti C, Lisi L, Avella M. Femoral neck shaft angle width is associated with hip-fracture risk in males but not independently of femoral neck bone density. *Br J Radiol* 2014;87:20130358.

FULL PAPER

Femoral neck shaft angle width is associated with hip-fracture risk in males but not independently of femoral neck bone density

C RIPAMONTI, MD, L LISI, MD and M AVELLA, MD

Struttura Semplice Dipartimentale di Medicina Generale, Istituto Ortopedico Rizzoli, Bologna, Italy

Address correspondence to: Mr Claudio Ripamonti
E-mail: claudio.ripamonti@ior.it

Objective: To investigate the specificity of the neck shaft angle (NSA) to predict hip fracture in males.

Methods: We consecutively studied 228 males without fracture and 38 with hip fracture. A further 49 males with spine fracture were studied to evaluate the specificity of NSA for hip-fracture prediction. Femoral neck (FN) bone mineral density (FN-BMD), NSA, hip axis length and FN diameter (FND) were measured in each subject by dual X-ray absorptiometry. Between-mean differences in the studied variables were tested by the unpaired *t*-test. The ability of NSA to predict hip fracture was tested by logistic regression.

Results: Compared with controls, FN-BMD ($p < 0.01$) was significantly lower in both groups of males with fractures, whereas FND ($p < 0.01$) and NSA ($p = 0.05$) were higher only in the hip-fracture group. A significant inverse correlation ($p < 0.01$) was found between NSA and

FN-BMD. By age-, height- and weight-corrected logistic regression, none of the tested geometric parameters, separately considered from FN-BMD, entered the best model to predict spine fracture, whereas NSA ($p < 0.03$) predicted hip fracture together with age ($p < 0.001$). When forced into the regression, FN-BMD ($p < 0.001$) became the only fracture predictor to enter the best model to predict both fracture types.

Conclusion: NSA is associated with hip-fracture risk in males but is not independent of FN-BMD.

Advances in knowledge: The lack of ability of NSA to predict hip fracture in males independent of FN-BMD should depend on its inverse correlation with FN-BMD by capturing, as the strongest fracture predictor, some of the effects of NSA on the hip fracture. Conversely, NSA in females does not correlate with FN-BMD but independently predicts hip fractures.

Hip fracture is the worst osteoporotic fracture with regard to cost^{1,2} and adverse consequences,^{3,4} so its prevention by checking for the related fracture risk factors is an important goal. Although low bone mineral density (BMD) is generally recognized as the main risk factor for hip fracture,^{5,6} there is growing evidence that other bone characteristics, such as proximal femur geometry (PFG) parameters, are implicated in determining the risk profile for hip fracture.^{7,8} This evidence, however, mainly derives from studies carried out in females,^{9–13} whereas contradictory results characterize studies carried out in males.^{14–20} Authors' opinions seem to vary widely about the ability of the neck shaft angle (NSA), one of the PFG factors, to predict osteoporotic hip fractures in males,^{14–16,21} whereas its association with the risk of hip fracture in females^{10,11,14,22} is generally accepted. Gender differences in the hip anatomy²³ have been put forward as a possible explanation for the different relationship of NSA with the hip-fracture risk between genders, whereas geographic and racial differences²⁴

among the examined male populations have been advocated as a possible cause of authors' discrepancies on the relationship between NSA and the hip-fracture risk in males.

This topic is therefore still under debate, and further studies are required to clarify the association of the NSA with hip-fracture risk in males. The authors of the current study contribute to this topic by studying the relationship between NSA and the hip fragility fracture in a sample of white Italian males.

METHODS AND MATERIALS

The clinical data of consecutively examined males, both in- and out-patients, who had undergone femoral neck BMD (FN-BMD) measurement at the authors' centre by dual X-ray absorptiometry (DXA) were used in this retrospective study. The males were representative of a subsample of those who were community dwelling. They were selected from among those who have undergone a DXA examination of

the FN within 3 months of the diagnosis of a fragility fracture (*i.e.* fracture that occurred without manifest trauma or following a low-energy trauma) or who have had their FN-BMD measured to check bone mass in the absence of a reported fracture. Only hip fractures and vertebral fractures of subjects who were symptomatic at the time of radiological diagnosis were included. Fractures were determined on the basis of expert radiologist diagnosis when the fracture occurred. On the basis of the case sheet, subjects with previous fractures, malignancies, major rheumatic diseases, endocrine diseases of the thyroid or parathyroid, soreness, paralysis or treated with drugs known to affect bone, or with chronic liver, kidney and lung diseases were excluded from the study. The subjects matching the study criteria were grouped for subsequent statistical analysis into subjects without a history of fracture; subjects with hip fracture; and subjects with clinical spine fracture. Age, weight and height of each subject were available. DXA measurements were performed using a Norland XR-36 pencil-beam densitometer (Norland Corporation, Fort Atkinson, WI). For scan acquisition, the males were positioned, according to the manufacturer's instructions, with both legs placed in slight internal rotation by using a dedicated leg fixture device. DXA measurements were performed on the left femur except for subjects with left femur fractures. BMD was measured at the FN region by manually adjusting the FN box when necessary for its correct positioning. FN diameter (FND), hip axis length (HAL) and NSA were the geometric parameters measured. FND was measured perpendicular to the FN axis (automatically generated by the Norland densitometer dedicated software) at the narrowest region of the FN. HAL was measured from the lateral side of the greater trochanter to the clearly detectable inner pelvic brim along the hip axis. Both the FND and HAL were measured by using the dedicated calliper of the densitometer software. The NSA, automatically measured by the machine software, was the angle formed by the intersection of the FN axis and the femoral mid-shaft axis. The measurement coefficient of variation for both the FN-BMD and PFG parameters studied was not tested in this study for ethical reasons, having been already tested by the authors in previous studies^{10,25} and consistently documented with expected values. Daily quality assurance was performed by scanning the dedicated phantom according to the manufacturer's instructions. All DXA acquisitions were performed by expert

technologists, and the geometric measurements were carried out by one of the authors who was blinded to the fracture status and the DXA scan operator. Local ethical committee consent was obtained for the study.

Statistical analysis

Mean $\pm$ standard deviation was used to present the continuous variables since they were all normally distributed according to the Kolmogorov–Smirnov test. Between-mean differences in the studied variables were tested by the unpaired *t*-test after checking for the homogeneity of variances using the Levene test. The correlation between continuous variables was tested by Pearson's correlation analysis. The ability of the independent variables FN-BMD, NSA, HAL and FND to distinguish males with hip or spine fracture from those without fracture was tested by logistic regression after adjusting for age, height and weight. Fracture predictors were first separately tested as covariates in the multivariate logistic regression by using the standardized values of the studied parameters. Then logistic regression with Wald's forward method was used to select and present the best hip fracture predictive models. For each logistic regression, the calculated odds ratio (OR) and confidence interval (CI) were presented.

RESULTS

The study sample included 315 males with an average age of 68.4 ± 9.5 years. Of these males, 38 had hip fracture, 49 had clinical spine fracture and 228 had no fracture. The biological characteristics of each group are reported in Table 1 together with the statistical significance (unpaired *t*-test) of the parameter differences between the control group and each individual group with hip and clinical spine fractures, respectively. Males with hip fracture were significantly older, shorter and lighter than the controls. They also had larger FNDs and lower BMDs. The NSA was wider in males with hip fracture than in the controls, although the difference reached only borderline statistical significance ($p = 0.05$) (Table 1).

Concerning clinical spine fractures, FN-BMD, being lower in males with clinical spine fracture, was the only parameter among those considered to significantly differentiate males with fracture from those without fracture (Table 1).

Table 1. Baseline characteristics of study patients: comparison between the biological parameters of males without fracture, with hip fracture and with clinical spine fracture

Characteristics	Without fracture ($n = 228$)	Hip fracture ($n = 38$)	Clinical spine fracture ($n = 49$)
Age (years)	67.8 ± 8.7	73.1 ± 12.5^a	67.7 ± 9.6
Height (cm)	171.5 ± 6.4	169.4 ± 6.1^b	170.5 ± 6.0
Weight (kg)	75.1 ± 10.8	71.5 ± 9.9^b	75.3 ± 12.6
FN-BMD (mg cm^{-2})	0.736 ± 0.118	0.618 ± 0.106^a	0.667 ± 0.107^a
NSA (degrees)	125.3 ± 4.9	127.2 ± 6.2^b	126.4 ± 5.3
HAL (cm)	12.2 ± 0.8	12.2 ± 0.6	12.2 ± 0.8
FND (cm)	3.7 ± 0.3	3.8 ± 0.3^b	3.8 ± 0.3

FN-BMD, femoral neck bone mineral density; FND, femoral neck diameter; HAL, hip axis length; NSA, neck shaft angle.

^aUnpaired Student's *t*-test: $p \leq 0.01$ compared with controls.

^bUnpaired Student's *t*-test: $p \leq 0.05$ compared with controls.

Table 2. Pearson's correlation between the studied parameters of the selected population

Parameters	Height	Weight	FN-BMD	NSA	HAL	FND
Age	−0.203 ^a	−0.132 ^b	−0.276 ^a	−0.053	−0.009	0.182 ^a
Height		0.485 ^a	0.182 ^a	0.000	0.391 ^a	0.312 ^a
Weight			0.335 ^a	−0.021	0.242 ^a	0.304 ^a
FN-BMD				−0.154 ^a	−0.043	−0.112 ^b
NSA					0.296 ^a	−0.014
HAL						0.410 ^a

FN-BMD, femoral neck bone mineral density; FND, femoral neck diameter; HAL, hip axis length; NSA, neck shaft angle.

^a $p < 0.01$

^b $p < 0.05$.

Correlation coefficients among NSA and the other parameters are reported for the whole population in Table 2. A statistically significant inverse correlation of the NSA was found with the FN-BMD, whereas a statistically significant direct correlation was found with HAL. Age was significantly correlated with FN-BMD but not correlated with NSA.

NSA, FND and FN-BMD, separately tested as covariates in the multivariate logistic regression after adjusting for age, height and weight, were significant predictors of hip-fracture risk. FN-BMD (also separately tested as a covariate in the multivariate logistic regression after adjusting for the same confounders considered above) was also a significant predictor of clinical spine fracture, whereas none of the PFG parameters was associated with clinical spine fracture (Table 3).

In Wald's forward multivariate logistic regression with the PFG parameters, age, height and weight as covariates, NSA (OR, 1.074; 95% CI, 1.008–1.162; $p = 0.030$) and age (OR, 1.074; 95% CI, 1.028–1.122; $p = 0.001$) were the best models to separate males with hip fracture from those without fracture.

By using the same predictors in Wald's forward logistic regression, none of them entered the best model to separate clinical spine fracture from controls. When FN-BMD was also used in Wald's forward logistic model together with age, height, weight and the PFG parameters, only FN-BMD entered the best model to predict

both hip (OR, 0.989; 95% CI, 0.985–0.993; $p = 0.001$) and spine fractures (OR, 0.994; 95% CI, 0.991–0.997; $p = 0.001$). Similar results were obtained by using the backward instead of the forward stepwise method in Wald's multivariate logistic regressions (data not presented).

DISCUSSION

In this study, the authors assessed the ability of NSA to predict hip fragility fractures in males. A group of males with clinically relevant vertebral fractures was also studied to verify the specificity of the geometric parameters for a hip-fracture risk prediction.

First, the ability of PFG parameters to predict hip fracture was explored, separately considered from FN-BMD. NSA was found to be the only parameter to predict the hip-fracture risk in males, together with age. Then, the authors looked at the ability of the PFG parameters to distinguish males with clinical spine fracture from those without fracture. Neither NSA nor the other PFG parameters were entered into the logistic model to predict spine fracture. These results suggest that males with wider NSAs have an increased risk of hip fracture in agreement with Alonso et al.¹⁴ The present results also indicate that the correlation between the fracture and NSA is specific for the hip fracture, as it does not play a role in assessing the clinical spine fracture risk in males, as already reported by Tuck et al.¹⁶ and in line with what has already been shown by other authors in females.²⁶ In

Table 3. Standardized odds ratio (OR) by multivariate logistic regressions (each one including age, height, weight and one of the four test variables) showing the association of the neck shaft angle (NSA), hip axis length (HAL), femoral neck diameter (FND) and femoral neck bone mineral density (FN-BMD) (each one separately tested from the others) with the risk of hip and spine fragility fracture in males

Test variable	Standardized OR (95% CI)	Standardized OR (95% CI)
	Hip fracture	Clinical spine fracture
NSA	1.512 (1.040–2.198) ^a	1.248 (0.899–1.713)
HAL	1.092 (0.721–1.653)	0.910 (0.649–1.274)
FND	1.669 (1.097–2.540) ^a	1.377 (0.965–1.964)
FN-BMD	0.280 (0.161–0.504) ^b	0.408 (0.262–0.636) ^b

CI, confidence interval.

^a $p < 0.05$.

^b $p < 0.01$.

addition, the present data therefore indicate that in males NSA width is associated with the FN resistance to stress when falling on the greater trochanter. This follows the biomechanical concept that the wider the femoral NSA the higher the bending moment at the FN and the higher the impact force imposed on the FN, which results in a greater probability of fracture.^{19,21,27,28}

Therefore, the ability of NSA to predict hip fracture in males independent of BMD was examined. It was found not only that FN-BMD was the best hip fracture predictor in males but also that NSA does not predict hip fracture independent of FN-BMD. This agrees with reports by some authors^{16,18} but is in contrast to the findings of Alonso et al¹⁴ and the majority of reports in the literature about NSA hip fracture prediction in females.^{10,11,14,22,26}

Concerning the independence of the ability of NSA to predict hip fracture, the contrasting results between previous studies in females^{10,29} and the present one in males might be a result of a statistical weakness of the present study because of the low number of fractures in males. Nevertheless, it should be pointed out that in males, a statistically significant inverse relationship between the NSA and FN-BMD was found, as already reported by others,^{14,18} which was not observed in females.^{26,29} The latter finding was also reported by other authors,^{9,30} who found NSA to be an independent predictor of hip fracture in females. Therefore, it may be that the negative correlation of FN-BMD with NSA leads BMD to capture some of the effects of NSA on hip fracture; thus explaining, at least partially, the disagreement between males and females regarding the independence of the ability of NSA to predict hip fracture. Zhang et al,¹⁸ who found that NSA does not independently predict hip fracture in females thus showing a significant relationship between NSA and BMD, also seem to support this hypothesis.

The contribution of NSA to hip fracture might therefore be inversely proportional to its (inverse) correlation with BMD, and the independent ability of NSA to predict hip fracture might be more common in females than in males because of the intergender difference in the NSA/FN-BMD correlation. This difference is supported by generally higher weight-bearing activity and manual labour in males, in agreement with the finding that weight-bearing activity is inversely related to femoral NSA³¹ and directly related to the BMD.³² Lifestyle differences together with geographic and racial differences in hip geometry¹⁵ might also generate differences in the

NSA/BMD relationship among different male populations and might explain the differences between authors on the role of NSA as a hip fracture predictor among different male populations. Differences in the methods to measure NSA, by fan or pencil-beam densitometers, or by radiographs because of the fan beam magnification error or inconsistencies in the femur internal rotation at the DXA scan acquisition time among different studies, might also affect the NSA measurement, thus leading to different evaluations of the relationship of the NSA with hip-fracture risk. Exhaustive conclusions on the role of the NSA as a risk factor for hip fracture in males cannot be drawn from the present study because of the uncertainty due to its numerous limitations. The study was not prospective or population based (particularly, the not-fractured males might not be fully representative of the general population being DXA-referred patients) and the vertebral morphology was not tested in all the studied subjects; there is lack of information about lifestyle habits and only part of the geometric and structural parameters of the hip was investigated. In particular, the study lacks a volumetric measure of the cortical and trabecular bone components considered separately, which might help in defining the nature of the different reported relationships of the NSA with the BMD and their role in hip-fracture risk. Finally, the population examined is not strong enough for robust statistical results as a larger number of hip-fractured patients than those enrolled are needed for a good estimate of proximal femur geometric parameter values (by a power analysis based on the authors' data, at least 150 or 593 hip-fractured males should be needed to estimate their NSA value with an error range, respectively, within 1° or 0.5° with a 95% CI).

Nevertheless, the present data seem to support the existence of a positive relationship between NSA and hip fracture in males, although they are not strong enough for clinical purposes, because the data are statistically weak and lack independence from FN-BMD. Because of the numerous environmental and genetic factors that interact in determining hip fragility fracture, the role of NSA as a risk factor for male osteoporotic hip fracture needs, in the authors' opinion, to be further tested in different populations to determine the effect of environmental and genetic confounders on NSA's role in hip-fracture prediction in males.

ACKNOWLEDGMENTS

The authors wish to thank Dr Saverio Gnudi for commenting on an earlier draft of the manuscript.

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