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Reliability and Relation to BMD
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Published in:
Jacobs Journal of Orthopedics and Rheumatology

Publication date:
2016

Document version
Final published version

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Citation for published version (APA):
Cortical Marrow Ratio in Plain X-rays of Femoral Neck Fractures - Reliability and Relation to BMD

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Received: 04-26-2016
Accepted: 11-09-2016
Published: 01-26-2016

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Abstract

Objectives: The purpose of this study is to evaluate Cortical Marrow Ratio (CMR) for reliability and relation to low Bone Mineral Density (BMD) in patients with femoral neck fractures.

Methods: A total of 132 consecutive femoral neck fracture patients (median age 81.2 years, IQR 70.6-86.1) were assessed with DXA scans and digital hip x-rays. CMR was measured twice by two independent raters and analysed for reliability. CMR was then compared to BMD by means of a sensitivity/specificity analysis.

Results: Using total hip BMD, 47 patients had a T-score ≤ -2.5 with a median CMR of 1.61(IQR 1.44-1.74), and 85 patients had a T-score > -2.5 with a median CMR of 1.89 (IQR 1.77-2.11). The ICC was 0.87-0.98 for intra-rater and 0.86-0.90 for inter-rater reliability. CMR showed a correlation coefficient of 0.58-0.59, a sensitivity of 72.3-76.6 % and a specificity of 75.3-76.5 % in relation to low BMD.

Conclusions: CMR was found to be a highly reliable measure with acceptable sensitivity and specificity in relation to low BMD.

Keywords: Femoral Neck Fracture; BMD, X-Ray; Reliability; Sensitivity; Specificity

Abbreviations

BMD: Bone Mineral Density;
CI: Confidence Interval;
DXA: Dual-energy X-ray Absorptiometry;
IQR: Inter Quartile Range;
ICC: Intraclass Correlation Coefficient
Background

The failure proportion for surgical treated femoral neck fractures is approximately 35% in dislocated fractures [1] and 11% in undisplaced fractures [2]. Predictors for failure should therefore be investigated and made feasible to implement in clinical practice. One possible predictor for failure of osteosynthesis is osteoporosis. Several experimental studies have shown that low BMD affects the strength of osteosynthesis [3,4] and have proposed a limit for high failure risk at 0.4 g/cm² [4,5]. However, clinical studies have yet proven an association between low BMD and failure [6] but a clinical study showed a tendency towards an association between failure in undisplaced femoral neck fractures and low BMD [7]. DXA scan has been recognized as the gold standard for diagnosing osteoporosis [8]. However, in a clinical setting it can be logistically very difficult to obtain a DXA scan before surgery and it may cause a surgical delay which could increase the in-hospital mortality [9].

A preoperatively investigation of low BMD should be fast and feasible and could be done by using the existing x-ray image used for diagnosing the fracture. The Singh Index [10] is the oldest and best known geometric measure for osteoporosis, but the Singh Index’ reliability is either poor [11,12] or acceptable [13-15]. The major drawback of most studies using the Singh index is, however, that they only show poor to moderate correlation with BMD [11,12,14,16-20]. Several other geometrical measures have been suggested [14,17,21-25]. Of these, the canal bone ratio, the cortical thickness index, and the Dorr classification have shown good reliability by having an ICC above 0.8, but only canal bone ratio had a correlation with BMD above 0.7.

The canal bone ratio study [23] is on cadavers and uses a fixed measurement point which does not account for the morphological differences of small and large femora. In order to take account for the variability of femoral geometry CMR was developed. The purpose of this study is to evaluate CMR for reliability and relation to low BMD in patients with femoral neck fractures.

Methods

Subjects

Patients and BMD measurements were retrieved from a prospective consecutive cohort of patients with hip fractures [26], which included all hip fracture patients who were older than 45 years and treated at the Department of Orthopaedic Surgery and Traumatology, Odense University Hospital. 158 femoral neck fracture patients with DXA-scans had their x-rays retrospectively assessed. One patient was excluded due to an old fracture, three patients due to transferrals and 22 patients were excluded due to the femoral portion for measurement was not included. This left a total of 132 patients with femoral neck fracture and DXA-scans, who comprised the final study cohort. All patients were treated with closed reduction and IF using two Uppsala screws. All patients were postoperatively treated with Calcium and Vitamin D. The median time from operation to the DXA-scan was 80 days (IQR 42-142). All x-ray images from the cohort were evaluated to ensure correct fracture diagnosis. Any discrepancies in diagnosis were discussed and resolved.

Measurements

Preoperative x-rays of the patients in the final cohort were used. Based on a pilot study of 20 patients, the CMR was assessed by the following method:

1. A circle was drawn just below the lesser trochanter containing the femoral diameter. A second circle was drawn approximately two femoral diameters below the first circle. A line was drawn based on the centers of the two circles depicting the midline (Figure 1a).

2. The circles were removed and a new line perpendicular to the midline was drawn placed at the crossing point between the dense trabecular structure of the lesser trochanter and the cortex below (Fig. 1b). The length of the line was then set to the width of the femur.

3. Two new lines were placed perpendicular to the midline at one and two x’ distal (x = length of first line) to the first perpendicular line, and at these lines the femoral cortical and marrow diameter were measured (a-d in Fig. 1c).

CMR = femoral diameter / marrow diameter = a / b or c / d

Two independent observers analysed all x-rays twice (approximately 12 weeks apart) to obtain inter- and intra-rater reliability and agreement. Rater 1 was an orthopaedic resident and rater 2 was a radiology resident. For the purpose of inter-rater...
reliability and agreement, the first measurement of both raters was used. The BMD from the DXA-scans were compared to the first measurements of rater 1. The DXA-scanner was a Hologic Discovery and NHANES III was used as reference material [27]. The contralateral hip was scanned and low BMD level using total hip BMD was defined as a T-score ≤ -2.5 [28]. All x-rays were digital and measurements were carried out on a 21-inch screen or larger using Sectra AB’s RIS/PACS x-ray viewing system. Edge detection and reinforcement was not used. The raters were blinded to each other’s measurements and BMD results, which were merged with the CMR results after completion of the second CMR measurements.

Statistical analyses

The statistical software programme STATA 11 was used for the analyses. Data for group analyses was tested graphically and statistically (Shapiro Wilk) for distribution and was not normally distributed. Therefore the Wilcoxon rank-sum test (Mann-Whitney two-sample) was used for group analyses. Reliability is in this context defined by de Vet et al. [29] and based on the ICC_expression reliability parameter which was calculated with a multilevel mixed-effects linear regression technique [30,31]. For a graphical estimate of systematically bias and agreement, a software extension (SJ7-3: st0015_4) for STATA was downloaded to give the Bland-Altman plot. A sensitivity/ specificity analysis (extension SJ-4-4: sbe36_2) was applied to evaluate CMR in relation to low BMD. ROC analysis was used to find optimal cut-off thresholds of sensitivity and specificity. The correlation coefficient (Spearman’s rank) was calculated.

A retrospective power analysis for the reproducibility study using STATA’s sampicc extension was done with a hypothesized ICC value of 0.9 and a null value of 0.8, which gives a power of 100 %. A post-hoc analysis on the sample size of the sensitivity/specificity analysis using precision 0.05, prevalence 0.36, and specificity = 0.76 gave a sample size of 438 [32]. The reporting of this article is done according to both GRASS and STARD guidelines [33,34].

Results

X-ray images were included for 132 patients (32 men and 100 women), median (IQR) 81.2 (70.6-86.1) years, and no age difference between the sexes (Wilcoxon rank-sum test: p<0.72) (Table I). A total of 47 patients (35.6 %) were found to have low BMD levels using total hip BMD with a median (IQR) BMD of 0.57 g/cm² (0.50-0.61).

<table>
<thead>
<tr>
<th>Total hip BMD</th>
<th>T-score ≤ -2.5</th>
<th>T-score &gt; -2.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>47</td>
<td>85</td>
</tr>
<tr>
<td>BMD, g/cm² (IQR)</td>
<td>0.57 (0.50-0.61)</td>
<td>0.74 (0.70-0.81)</td>
</tr>
<tr>
<td>CMR1 (IQR)</td>
<td>1.51 (1.35-1.63)</td>
<td>1.73 (1.62-1.42)</td>
</tr>
<tr>
<td>CMR2 (IQR)</td>
<td>1.61 (1.44-1.74)</td>
<td>1.89 (1.77-2.11)</td>
</tr>
<tr>
<td>Age (IQR)</td>
<td>82.8 (75.9-87.2)</td>
<td>80.0 (69.6-84.9)</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>4/43</td>
<td>28/57</td>
</tr>
</tbody>
</table>

Table 1. Study population by total hip BMD (g/cm²) status.

Reliability analysis

For CMR1 the median measurements were 1.81-1.84 and for CMR2 they were 1.65-1.69 (Table II). The calculated reliability parameter ICC gave an ICC_expression of 0.87-0.98 for intra- and interrater of CMR1 and CMR2 (Table III).

<table>
<thead>
<tr>
<th>CMR1 (IQR)</th>
<th>CMR2 (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rater 1, measurement 1</td>
<td>1.65 (1.51-1.80)</td>
</tr>
<tr>
<td>Rater 1, measurement 2</td>
<td>1.66 (1.51-1.80)</td>
</tr>
<tr>
<td>Rater 2, measurement 1</td>
<td>1.65 (1.53-1.78)</td>
</tr>
<tr>
<td>Rater 2, measurement 2</td>
<td>1.69 (1.55-1.80)</td>
</tr>
</tbody>
</table>

Table 2. Median CMR measurements.

<table>
<thead>
<tr>
<th>ICC CMR1 (CI)</th>
<th>ICC CMR2 (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intrarater for rater 1</td>
<td>0.98 (0.97;0.99)</td>
</tr>
<tr>
<td>Intrarater for rater 2</td>
<td>0.90 (0.86;0.93)</td>
</tr>
<tr>
<td>Interrater</td>
<td>0.90 (0.86;0.93)</td>
</tr>
</tbody>
</table>

Table 3. Intra- and interrater ICC Agreement

No systematic difference (bias) between the raters were found, but there was an intra-rater difference for rater 2 in the CMR2 measurements of 0.05 (p<0.001, multilevel mixed-effects linear regression). A Bland-Altman plot was applied to the data, and there was a uniform distribution of the differences for the whole range of CMR1 and CMR2 values.

Sensitivity and specificity analysis

The ROC-analysis resulted in an optimal cut-off threshold value at 1.75 for CMR1 and 1.62 for CMR2. Table 4 shows the result yielding a sensitivity of 72.3-76.6 % and a specificity of 75.3-76.5 % for CMR1 and CMR2. The overall correlation coef-
Sufficient was r=0.59 (p<0.0001) for CMR1 and r=0.58 (p<0.0001) for CMR2. Figure 2 shows a scatter plot of the CMR2 values in comparison to the T-score.

Table 4. CMR in relation to total hip BMD.

<table>
<thead>
<tr>
<th></th>
<th>T-score≤-2.5</th>
<th>T-score &gt; -2.5</th>
<th>SN</th>
<th>SP</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMR1</td>
<td></td>
<td></td>
<td>72.3</td>
<td>75.3</td>
<td>61.8</td>
<td>83.1</td>
</tr>
<tr>
<td>Low BMD (CMR &lt; 1.62)</td>
<td>34</td>
<td>13</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal BMD (CMR &gt; 1.62)</td>
<td>21</td>
<td>64</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CMR2</td>
<td></td>
<td></td>
<td>76.6</td>
<td>76.5</td>
<td>64.3</td>
<td>85.5</td>
</tr>
<tr>
<td>Low BMD (CMR &lt; 1.75)</td>
<td>36</td>
<td>11</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal BMD (CMR &gt; 1.75)</td>
<td>20</td>
<td>65</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SN sensitivity, SP specificity, PPV positive predictive value, NPV negative predictive value.

Three studies [11,13,18] have analysed sensitivity and specificity of low BMD in relation to the Singh Index which gave results from 11 to 97 % but only sensitivity or specificity was high. Neither of them was on hip fracture patients. Only Bes et al. [13] got high sensitivity (71%) and specificity (93 %) but the analysis only included 5 patients. Sah et al. [14] showed acceptable results with sensitivity ranging from 62-85 % and specificity 58-84 % for the cortical thickness index and the Dorr classification. Even though the study has interesting results the study has a low number of participants (n=32) and the risk for a type 2 error is quite large. The present study have present study has similar results with sensitivity and specificity of 76 %.

The following limitations are noted: a major underpowering shown in the post-hoc analysis, and 14 % of the routine x-rays excluded due to insufficient femoral shaft length used for CMR measurement on the x-rays. There is a small systematic bias in the repeated measurement by rater 2, possibly due to the application of a different zooming level on the second measurement. In further studies specification of zooming should be specified for reading the digital x-rays.

In perspective low BMD should be investigated as a predictor for failure especially in the undisplaced femoral neck fracture. The DXA scan is the gold standard for diagnosing osteoporosis [8] but is not fast or feasible as a preoperative measure.

Therefore x-ray images could be an option for quick ascertainment of osteoporotic status in the immediate clinical setting before surgery. CMR has in contrast to other measurement a high reliability and acceptable sensitivity/specificity and should therefore with other BMD measurements be investigated in further studies.

Conclusions

CMR was found to be a reliable measure with intra- and inter-rater ICC between 0.86 and 0.98. CMR also have acceptable sensitivity of 72.3-76.6 % and specificity of 75.3-76.5 % in relation to low BMD.

Acknowledgement

The study was carried out on the department of Orthopaedic Surgery and Traumatology, Odense University Hospital.
References


Cite this article: Bjarke Viberg. Cortical Marrow Ratio in Plain X-rays of Femoral Neck Fractures - Reliability and Relation to BMD. J J Ortho Rheum. 2016, 2(1): 019.


