

# Densitometric evaluation might prevent failure of knee arthroplasty for aseptic loosening. An 8-year observational controlled study

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## ABSTRACT

**Objectives:** To study the correlation between quantitative ultrasound (QUS) expressed as stiffness index (SI) and the risk of aseptic loosening of knee arthroplasty.

**Methods:** An observational retrospective controlled study was performed on 85 female patients (mean age: 73.3 years) divided into 2 groups from January 2007 to March 2015 and carried out at the Orthopedic Rehabilitation Unit, Casa di Cura Eremo, Arco, Trento, Italy. Group A included 42 patients who had undergone a revision of knee prosthesis for aseptic loosening, and group B included 43 age-matched patients who underwent primary replacement of the knee without following aseptic loosening. Patients in both groups were evaluated for SI with Achilles - QUS system at the same side of the surgery.

**Results:** In group A, 20/42 patients (47.6%) had an SI T-score below -2.5. In group B, 14/43 (32.5%) patients had a SI T-score below -2.5. The difference between the 2 groups was statistically significant ( $p=0.015$ ).

**Conclusion:** Stiffness index appears to be an important predictor of aseptic loosening of the knee prosthesis. Therefore, densitometric evaluation, including SI, may be recommended before surgical knee replacement.

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Periprosthetic bone loss is the most common complication of arthroplasty. Some degree of bone loss is present in every failed total knee arthroplasty.<sup>1</sup> There are several factors leading to bone loss including wear debris and stress shielding. The implantation of exogenous material into the organism causes foreign body reactions characterized by the activation of macrophages and consequent release of a myriad of bio reactive agents (reactive oxygen intermediates,

degradative enzymes and acids). The reaction ends in the formation of foreign body giant cells at the material interface and the consequences can be devastating. Biomaterial surface properties play an important role in the development of the reaction. One of the primary causes of damage is the production of particulate wear debris, which is the consequence of the articular motion. Wear debris is able to induce inflammation at the interface between implants and bone, and osteolysis is the final result.<sup>2</sup> Extremely high blood metal ion levels have been found in patients after arthroplasty, even in asymptomatic patients with a stable prosthesis, but the ion levels were significantly higher in patients with severe bone loss.<sup>3</sup> Another factor is represented by the stress shielding: in a healthy person the bone will remodel in response to the loads it is placed under, therefore, the absence of the load causes bone loss. In addition to prosthetic shapes and sizes, implant fixation methods (including surface treatments), clinical installation, interface micromotions, and periprosthetic high hydraulic pressure can play a role in the mobilization of the prosthesis.<sup>4</sup> Previous osteoporosis may be an important cause of failure of prosthetic implants: it has been demonstrated that low systemic bone mineral density (BMD) evaluated with dual x-ray absorptiometry (DXA) increases migration, and delays osseointegration of cementless femoral stems in women who had underwent cementless total hip arthroplasty.<sup>5,6</sup> Quantitative ultrasound (QUS) is a recent developed technique that can assess both bone mass and architecture densitometry.<sup>7</sup> Frediani et al<sup>8</sup> in 2006 compared QUS (Achilles Express) and DXA for the evaluation of vertebral fracture risk: 764 post-menopausal women with non-traumatic vertebral fractures versus 770 post-menopausal women with normal morphometry were evaluated. The authors concluded that both QUS and DXA were able to discriminate women with from women without fracture and were independent predictors of fracture. Moreover, BMD and stiffness were both able to indicate the risk of fracture.<sup>8</sup> The aim of this study is to investigate the correlation between bone mass evaluated with practicable QUS, and the risk of aseptic loosening of knee arthroplasty.

**Methods. Participants.** The present study was carried out at the Orthopedic Rehabilitation Unit,

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Casa di Cura Eremo in Arco, Trento, Italy from January 2007 to March 2015. The study was performed according to the principles of the Helsinki Declaration.

**Inclusion and exclusion criteria.** Females in post-menopausal age and previous first knee prosthesis implant were included in the study, while male gender, hyperparathyroidism, osteomalacia, hypocalcemia, bone metabolic diseases other than osteoporosis, and rheumatological diseases other than knee osteoarthritis were excluded. Patients in treatment with estrogens, glucocorticoids or other drugs interfering with bone metabolism, affected by active hepatic, renal, cardiovascular, neoplastic, psychiatric or neurologic diseases, and drug or alcohol users were also excluded.

Bone status was assessed at the calcaneus by QUS (Achilles Insight, GE Medical System, Belgium): QUS of the calcaneus was performed and expressed as stiffness index (SI). The SI combines the parameters of speed of sound and broadband ultrasound attenuation. The coefficient of variation of the SI is 1.7%. Results were expressed as T-scores. The reference data were those provided by the sonography manufacturer. All data were expressed as mean  $\pm$  standard deviation (SD). Unpaired 2-tailed T-test was applied to test the differences between the groups. Differences were considered statistically significant when  $p < 0.05$ . Data were analyzed using GraphPad Prism statistical software (GraphPad Software, Inc., CA, USA).

**Study design.** This study is an observational retrospective controlled study. Two hundred and eighty-nine female patients affected by knee osteoarthritis were admitted to the Orthopedic Rehabilitation Unit in Arco, Trento, Italy in the year 2007 due to first knee prosthesis. In 2007, before surgery, all patients were evaluated for SI with Achilles-QUS system at the same side of the surgery. Following the inclusion criteria, in the year 2015, we enrolled in group A 42 patients out of them, who had underwent revision of the knee prosthesis for aseptic loosening. The prosthesis mean duration was 3.3 years. Following the same inclusion criteria, by an electronically generated randomization list, we enrolled further 43 patients in group B (control group): they all had underwent first replacement of knee prosthesis in 2007, but not a revision. Both groups had been subjected to similar surgical procedures and were coming from the same Orthopedic Department. Baseline characteristics of the patients of both groups are shown in Table 1. The Consolidated Standards of Reporting Trials (CONSORT) recommendations were followed in reporting the results of this study.

**Results.** Weight ( $p=0.97$ ), age ( $p=0.61$ ), and age of menopause ( $p=0.98$ ) were not statistically different in the 2 groups. In group A (revision) mean T-score was  $2.27 \pm 1.54$  and 20/42 patients (47.6%) had a SI T-score below -2.5. In group B (control) mean T-score was  $-1.24 \pm 1.17$  SD and 14/43 (32.5%) had a SI T-score below -2.5. The difference in mean T-score between the 2 groups was statistically significant ( $p=0.015$ ). In our patients with low SI (37/85) a treatment with calcium, vitamin D, and bisphosphonates (BP) was prescribed in 2007, but only 12 out of them continued to take the therapy until 2015.

**Discussion.** We demonstrated a relation between preoperative SI and probability of aseptic loosening of the knee prosthesis. This fact could imply the need to evaluate bone mass with SI before surgery. The second step could be the treatment of patients with low SI. It is well known that adherence is the most important problem in the treatment of osteoporosis. As reported in the literature, adherence to the treatment was very low in our patients. Previous osteoporosis may be an important cause of failure of prosthetic implants. It has been demonstrated that low systemic BMD evaluated with DXA increases migration and delays osseointegration of cementless femoral stems in women with cementless total hip arthroplasty.<sup>5,6</sup>

It was recently shown that the duration of hip and knee prosthesis is correlated to the use of BPs. In particular, Prieto-Alhambra et al<sup>9</sup> published the data provided by the United Kingdom General Practice Research Database relative to the years 1986-2006. Of the 41,995 patients undergoing primary hip or knee arthroplasty, 1912 BPs users were identified. The conclusions were as follows: in patients undergoing a lower limb arthroplasty, BP's use was associated with an almost 2-fold increase in implant survival time.<sup>9</sup> More recently, they showed the data of the Danish Nationwide Registries, where out of 80,342 eligible patients with a primary total joint replacement, the BPs users had a 59% reduced risk of revision surgery. This association was strongest in patients with the longest duration of

**Table 1** - Baseline characteristics of both groups.

Variables	Group A (n=43)	Group B (n=42)	P-value
Gender	F	F	
Mean age	71.04 (53-85)	71.65 (51-86)	n.s.
Unicompartmental prosthesis	7	9	n.s.
Total prosthesis	36	33	n.s.
Prosthesis survival (years)	3.26	>7	
Mean T-score	$-2.27 \pm 1.54$	$-1.24 \pm 1.17$	0.0007
Mean SI	$70.26 \pm 20.09$	$79.26 \pm 17.34$	0.029

SI - stiffness index, n.s. - not significant

treatment and/or the best adherence, and only when BPs were started after the arthroplasty surgery.<sup>10</sup> However, it is not clear if these effects were due to the benefits of BPs treatment on concomitant osteoporosis condition, or in the prevention of periprosthetic osteolysis.

Lin et al<sup>11</sup> performed a meta-analysis in 2012 on the effects of BPs on periprosthetic BMD after joint arthroplasty. Their conclusion was as follows: BPs confirmed a significantly short-term and middle-term efficacy on periprosthetic bone loss after joint arthroplasty. Bisphosphonates offer significant opportunity for improving the long-term durability of total joint replacement preventing bone loss associated with osteolysis and aseptic loosening around prosthesis. Considering the wear debris generation and the consequent inflammation, it is not clear whether osteolysis will continue to be suppressed after BPs are discontinued. In particular clodronate, a first generation BP seems to be effective in decreasing periprosthetic bone loss.<sup>12</sup> Trevisan et al<sup>13</sup> showed that intramuscular clodronate is able to significantly reduce the periprosthetic bone loss after total hip arthroplasty. Moreover, the study of Hilding and Aspenberg<sup>14</sup> showed that oral clodronate can diminish the risk of loosening by reducing prosthetic migration in a 4-year follow-up of a randomized radiostereometric study of total knee patients. Muratore et al<sup>15</sup> showed that ibandronate administered in the post-operative stage is able to reduce bone loss of the proximal femur in cementless total hip arthroplasty.

The most important limitation of this study is the evaluation of bone mass only with QUS approach as it was the only available instrument in Casa di Cura Eremo in 2007. Other limitations were the small patient number and the observational nature of the study.

In conclusion, previous osteoporosis is probably an important cause of aseptic prosthetic loosening. In particular, SI index appears to be an important predictor of aseptic loosening of knee prosthesis. Therefore densitometric evaluation, including SI, should be recommended before surgical knee replacement. Moreover, the treatment of osteoporosis, also before knee replacement, might be recommended.

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