Bisphosphonates Reduce the Number of Patients with Excessive Migration of Knee Prostheses

Per Aspenberg*1, Philippe Wagner, Maria Hilding, Jonas Ranstam
Orthopaedics, Linköping, Sweden
Per.Aspenberg@inr.liu.se

Background: Migration of hip and knee prostheses, measured by Radio Stereometric Analysis (RSA), is said to predict late loosening. This is based on studies on mixed patient groups from the 1980-ies, with a very high loosening risk and early migration. With modern operating techniques, the early migration is much less. It is not known if a small increase in early RSA migration infers an increased risk of loosening with modern operating techniques. RSA cannot discern whether a single prosthesis is fixed or migrating below the detection level. Samples of patients usually show neither. The values that appear to be continuously distributed. Is there such continuity, or is there a dichotomy between stable and migrating prostheses? In the latter case, also small migration could make a difference.

In a previous randomized study on cemented knee replacements using Radio Stereometric Analysis (RSA), we showed that oral bisphosphonates reduced the mean migration distance during the first 6 months. The difference persisted up to 4 years (1). In a similar randomized study, bisphosphonates applied locally at the operation had a similar effect (2). However, these studies compared mean values between groups. Although statistically significant, the magnitude of the difference was only 0.1 mm. Does this small difference matter? It would matter, if it reflects a reduction of the number of patients belonging to a separate subgroup with excessive migration. The present study addresses this question by use of a mixture distribution algorithm, which is not generally available in commercial statistical packages.

Methods: The patients from the 2 previous studies were combined for analysis, and designated as bisphosphonate (n=44) or placebo (n=49) per protocol. We analysed the migration vector (for the center of the rigid body) by use of a new set of algorithms for frequency distribution analysis called Rmix (3). The migration vector lengths were assumed to be a compound of log-normal distributions. The frequency analysis determined if the observed frequency distributions were best described as a single, or a sum of 2 or more lognormally distributed subgroups.

Results: After 6 months, the control patients had formed 2 subgroups, one comprising 85% of the patients, with a mean migration distance of 0.14 mm, and the other with a mean of 0.34 mm. The dichotomy in 2 groups was statistically significant (p=0.016). After 2 years, the dichotomy persisted (p=0.027). One subgroup comprised 73% of the patients, with a mean migration distance of 0.15 mm, and the other had a mean of 0.34 mm (Figure 1).

In the bisphosphate-treated patients, no dichotomies could be found. The distribution of the migration vector length in these patients appeared similar to the larger and less migrating subgroup among the controls, with a mean of 0.13 mm at 6 months and 0.17 mm at 2 years. There was no difference between the oral (clodronate) or the local (ibandronate) treatments.

Discussion: The risk of aseptic loosening for cemented knees is extremely small in this material, which had the normal age for idiopathic osteoarthritis. In young and physically active patients the risk may be considerable. However, the initial fixation and its biology should be similar. The smaller and more migrating subgroup among our control patients may be at risk of loosening, and would have run a high risk if they were young and active. This subgroup did not appear with bisphosphonate treatment.

In a larger material of cemented acetabular cups we found a similar dichotomy, and were able to show that the larger group was completely stable, whereas the smaller group apparently comprised the “true” migrators (article in press). We have not demonstrated this for the knees, but because there were two distinct postoperative courses, and the patients fell into one or the other, it is likely that the course which involves more migration is ominous, if combined with high physical activity.

Summary: The possibility to detect subgroups within a seemingly continuous sample might become useful in many medical fields.

In previous comparisons we found a slight decrease in mean value with bisphosphonates. The present analysis shows that this reflects the disappearance of a small subgroup with large migration. This result suggests that bisphosphonate treatment might be even more beneficial than indicated by the significant difference in mean values in the randomised studies (1, 2).

Figure 1. Frequency distribution of the length of the migration vector (mm) from postop to 2 years. Histogram indicates observations. Curves indicate the estimated distributions under the assumption that the material consists of one or more groups with lognormal distribution. Triangles indicate the mean of the 2 subgroups. Dichotomy significant, p=0.027

References:
3. www.math.mcmaster.ca/peter/mix/mix.html