Hip prosthetic loosening: A very personal review

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Abstract
Hip prosthetic loosening is often difficult to detect at an early stage, and there has been uncertainty for a long time as to when the loosening occurs and thus to the basic causes. By comparing different diagnostic methods, we found that loosening is best defined as prosthetic migration and measured by radiostereometric analysis. Convincing evidence indicates that poor interlock, poor bone quality, and resorption of a necrotic bone bed may initiate loosening during or shortly after surgery; this forms the basis of the theory of early loosening. Biomechanical factors do affect the subsequent progression of loosening, which may increase subclinically during a long period of time. Eventually, the loosening may be detected on standard radiographs and may be interpreted as late loosening but should to be interpreted as late detection of loosening. The theory of early loosening explains the rapid early migration, the development of periprosthetic osteolysis and granulomas, the causality between wear and loosening, and largely the epidemiology of clinical failure of hip prostheses. Aspects discussed are definition of loosening, the pattern of early migration, the choice of migration threshold, the current understanding of loosening, a less exothermic bone cement, cemented taper-slip stems, a new exciting computed tomography-based technique for simpler implant migration studies, and research suggestions.

Key Words: Hip prosthesis; Prosthesis failure; Radiostereometric analysis; Bone resorption; Bone cements; Radionuclide imaging

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Core Tip: Much evidence indicates that prosthetic loosening is initiated during or shortly after surgery. The prosthetic micromovements may increase subclinically during a long period of time. Eventually, the loosening may be detected on standard radiographs and may be interpreted as late loosening but should to be interpreted as late detection of loosening. The discussion includes the definition of loosening, the pattern of early migration, the choice of migration threshold, the current understanding of loosening, a less exothermic bone cement, cemented taper-slip stems, a new exciting...
INTRODUCTION

Hip arthroplasty is one of the most successful of all orthopedic operations, but the results do deteriorate with time because of loosening. Radiographic changes indicating loosening are often difficult to detect at an early stage, and there has been uncertainty for a long time as to when the loosening occurs and thus to the basic causes. Confusion also arose because some hips with obviously loose prosthetic components are not painful[1-3]. To solve these issues, a few steps are required. First, the definition of loosening must be clarified. Second, the loosening must be carefully followed from its earliest detection. Third, the most important triggering factors must be identified, as well as other factors that affect the subsequent progression of loosening. Then the simplest scientific explanation that fits the evidence should be chosen.

DEFINITION OF LOOSENING

When I, as a newly graduated orthopedic surgeon in the early 1980s, started studying hip prosthetic loosening in Lund (in Southern Sweden), the diagnosis of loosening was based on insensitive radiographic criteria (periprosthetic radiolucent lines wider than 2 mm, prosthetic migration exceeding 4 mm, cement fracture, etc.). Several poorly defined terms were used, such as allergic loosening, aseptic loosening, mechanical loosening, progressive loosening, and reactive loosening – all without clear distinctions between each other.

Radiostereometric analysis (RSA) was introduced in Lund in 1974 by Göran Selvik (1938–1990). It is a technique for obtaining reliable three-dimensional measurements from radiographs and is based on implantation of tantalum bone markers, roentgen calibration equipment, and rigid-body kinematic analysis[4,5]. RSA was mainly used for studies of various bone growth disorders but was also found feasible for the study of hip prostheses[6,7].

My tutor, Lars Ingvar Hansson (1937–1987), advised me to use RSA to look for any pattern in loosening. We used analog films measured with a photogrammetric instrument and assessed (by double examinations) the limit for significant migration along the longitudinal axis to be 0.2 mm. However, later RSA studies have reached a detection limit of 0.08 mm when using fully digital technology[8,9]. By comparing contrast arthrography[10,11], radionuclide arthrography[12,13], bone scintigraphy (99m Tc-MDP)[14,15], and RSA (comprising both instability under load and migration with time) in 14 painful hip arthroplasties, we found that loosening is best defined as migration[16]: All prosthetic components unstable by RSA, or with abnormal arthrogram, or with increased bone scintigraphic activity, or loose at revision were migrating, but no non-migrating components demonstrated any of these signs of loosening. Interestingly, increased activity at the tip of the femoral component by bone scintigraphy (Figure 1) had high sensitivity and specificity in detecting loosening, which was also pointed out earlier[14,15].

PATTERN OF EARLY MIGRATION

To study early prosthetic migration, RSA was performed prospectively on cemented primary hip arthroplasties in two series followed for 2–3 years after surgery[17,18]. Taking these two studies together, we found that 19 of the 36 acetabular components migrated cranially and seven of the 34 femoral components migrated distally during computed tomography-based technique for simpler implant migration studies, and research suggestions.
the observation period (two femoral components in the latter series[18] were excluded due to insufficient tantalum bone markers); and that in all the cases, but three (two acetabular and one femoral), migration was detected within 4 mo after surgery (Figure 2). We also did not find any correlation between wear and early migration of either prosthetic component[19]. We concluded: (1) That RSA may distinguish between a migrating and a non-migrating prosthetic component within 4 mo after surgery; (2) That the initial migration may be caused by insufficient initial fixation or by resorption of a necrotic bone bed formed due to the heat from curing cement but not by wear products; and (3) That “late loosening” may be the result of late detection rather than of genuine late onset of loosening.

**HIGH OR LOW MIGRATION THRESHOLD?**

Many RSA studies of hip prostheses have now shown that early migration poses a risk of future failure[9,20-24]. This does not mean that all early migrating components will fail in the foreseeable future. Indeed, certain early migrating uncemented femoral components appear to achieve stability during the healing period[25-27], but it does mean that the failing prosthetic components are recruited from the group of early migrating components.

Some authors have determined a high migration threshold to predict an unacceptably high risk of future clinical failure, e.g., 1.2 mm and 2.6 mm distal migration after 2 years for cemented composite-beam femoral components to predict a revision rate exceeding of 50% and 95%, respectively, within 7 years[20]. As far as I know, no migration threshold values have yet been published for either cemented taper-slip or uncemented femoral components[23].

Others have determined a low migration threshold below which an early migration poses no or almost no risk of future failure, e.g., 0.2 mm cranial migration after 2 years for acetabular components[22] and 0.15 mm distal migration after 2 years for cemented composite-beam femoral components[23] to predict a revision rate of less than 5% within 10 years. Between these extremes (2.6 mm and 0.15 mm), of course, there is a large gray zone. The choice of migration threshold depends on the purpose. In my opinion, a high probability of permanent prosthetic fixation is a more advantageous prediction.

**CURRENT UNDERSTANDING OF LOOSENING**

Inadequate preparation and cementing technique were probably the main causes of loosening during the pioneering years and greatly reduced rates of loosening were demonstrated after improved technique[3,28-30]. Convincing evidence from both clinical and experimental research indicates that the initial fixation may be insufficient...
due to poor interlock (inadequate cement filling, interposition of tissue debris, etc.) [31-34] or because of poor bone quality (osteoporosis, rheumatoid arthritis, etc.) [35-38]. Adequate initial fixation does, however, not eliminate the risk of loosening; resorption of a layer of a necrotic bone bed may result in early loss of otherwise optimal fixation [39,40].

The theory of early loosening [41,42] postulates (the hypothetico-deductive method) that loosening is initiated during or shortly after surgery by these factors alone: Insufficient initial fixation (poor interlock or poor bone quality) or early loss of fixation (resorption of a layer of a necrotic bone). Interestingly, the resorption of necrotic bone can be inhibited with a bisphosphonate during the healing period, which reduces early migration [43] and consequently increases the mean prosthetic survival time [44].

If initiated, the progression of loosening is affected by the degree of early instability, the bone quality, and by the magnitude of the mechanical stresses to which the prosthetic components are exposed during normal daily activity. Thus, femoral components with a high offset [24] or in a varus position [3,34] can be expected to be over-represented among prosthetic failures due to faster increase in the micromovements of the components in which loosening has been initiated. Similarly, acetabular components that are eccentric (due to design [45] or wear [46]) or have high frictional torque (e.g., metal-on-polyacetal [46] or metal-on-metal articulations [47,48]) can for purely biomechanical reasons be expected to be overrepresented among prosthetic failures. However, such individual components (e.g., femoral components with a high offset or in a varus position) can, if loosening has not been initiated, be well-fixed [3].

The micromovements of a loosened prosthetic component may cause devitalizing spikes of high fluid pressure in the periprosthetic interstice, which can induce osteolysis [49-51] by a complex series of inflammatory responses to the damage-associated molecular patterns of the generated necrotic cells and cell fragments [52]. The periprosthetic fluid may be forced further into the bone (Figure 3), devitalizing the bone tissue that is resorbed, and form a focal osteolysis that is invaded by granulation tissue [54]. The prosthetic micromovements and the subsequent periprosthetic osteolysis may increase subclinically during a long period of time.

The theory of early loosening explains the rapid early migration (Figure 2), the development of periprosthetic osteolysis and granulomas (Figure 3), the bone loss commonly seen in the proximal femur of distally apparently well-fixed stems, the causality between wear and loosening, and largely the epidemiology of clinical failure of hip prostheses [41,42]. But as always, if new data emerge that contradicts the predictions of the theory, the theory must be supplemented or replaced with a more complete theory.
Figure 3 Graph shows how prosthetic micromovements cause a focal osteolysis. The prosthetic micromovements (orange arrows) pump joint fluid under high pressure (orange dashed arrows) from the gap between the stem and the cement through a defect in the cement mantle. The pressure waves may devitalize the adjacent bone tissue, which is resorbed, thus causing a focal osteolysis. From Mjöberg[53] with permission.

THE COOLFIX CEMENT

The specific heat production is directly proportional to the amount of monomer in the cement dough: 556 J/g monomer[55]. A low-monomer bone cement, Coolfix, was developed in the mid-1980s that produced less heat and less evaporating toxic monomer during the polymerization. The basic idea was to minimize the interspaces between the powder beads (which are filled with the liquid monomer) by a bimodal particle size distribution: 20 mL of liquid monomer was mixed with 70 g of Coolfix powder (instead of just about 40 g of a conventional bone cement powder). The temperature rise of Coolfix was (as expected) two-thirds of that of a conventional bone cement. The compressive strength was about 85% compared to Palacos R, probably due to the fact that the cement was made too dry (i.e. unsaturated) in the ambition to reduce the amount of liquid monomer. Therefore, this prototype Coolfix cement had a high viscosity and was more difficult to handle, especially in the acetabulum. The initial migration of the components in 24 hip prostheses was studied using RSA following randomized use of Coolfix and Palacos R[56]. After 1 year, five of the 12 acetabular components with Palacos R had migrated 0.4–0.7 mm, while all 11 acetabular components with Coolfix (one acetabular component with Coolfix was excluded due to insufficient tantalum bone markers) had migrated less than 0.3 mm (Figure 4). Only one femoral component (with Palacos R) had migrated significantly by then (0.4 mm distally).

An improved composition of Coolfix (the PMMA powders were purchased from Röhm GmbH, Darmstadt, Germany) was developed (Table 1), which had several attractive properties in addition to being less exothermic than a conventional bone cement: The improved cement was easily modeled and non-sticky, had a short mixing time, and smelled less. Unfortunately, the leadership of the Department of Orthopedics, Lund University Hospital, suddenly did not allow further clinical trials unless highly extended preclinical tests after vacuum mixing of the cement were performed; in practice, the project was stopped, and shortly afterwards I left Lund (but after my retirement and after a new department leadership had taken office in Lund, I became affiliated with the Department of Orthopedics, Lund University, once again). The improved Coolfix cement was never clinically tested.

Later, another low-monomer cement (Cemex Rx) was marketed, where, unlike Coolfix, the smallest particles in the powder had been removed. However, compared to Palacos R, no significant difference was achieved in either curing temperature[57] or prosthetic migration[57,58].

CEMENTED TAPER-SLIP STEMS

The continuous migration of taper-slip stems has been reported to be consistent with
Table 1 Coolfix powder composition 70 g

| Ingredient               | Amount   |
|--------------------------|----------|
| Plexidon M489 (300–500 µm) | 32.0 g   |
| Plexidon M527 (30–60 µm)   | 22.3 g   |
| Plexigum M914             | 6.3 g    |
| Benzoyl peroxide          | 0.6 g    |
| Zirconium dioxide         | 8.8 g    |

Figure 4 Cranial migration of the acetabular components after 1 year. By then, six of the 12 with Palacos R and four of the 11 with Coolfix had passed the limit (0.2 mm) for significant migration. However, five acetabular components with Palacos R had migrated 0.4–0.7 mm, while all 11 with Coolfix had migrated less than 0.3 mm ($P < 0.04$, Student’s $t$-test, one-tailed).

Good long-term clinical results[59-62] and has even been considered beneficial by contributing to secure fixation[59,61]. But does continuous migration really contribute to secure fixation? Or otherwise expressed: How much can a stem migrate distally without failing[63]?

The Exeter THA has, according to the Nordic Arthroplasty Register Association database (consisting of 100000 hip arthroplasties)[64], a survivorship fairly on par with the Lubinus THA of up to about 10 years, but afterwards, its failure rate increases faster (Figure 5).

A plausible explanation is as follows: In cases of considerable subsidence, the self-locking effect of a cemented tapered stem declines because the stem and cement mantle no longer fit well together. A play space arises around the stem, and the micromovements of the loosened stem induces periprosthetic osteolysis (due to inflammatory responses to the damage-associated molecular patterns of the necrotic cells and cell fragments generated by devitalizing spikes of high periprosthetic fluid pressure from the unstable stem). When the cement is no longer sufficiently supported by the surrounding bone, the cement mantle will crack and the stem instability will increase, resulting in a rapid subsidence[60] and ultimately a fracture of the stem[65] or a fracture of the proximal femur[66,67].

No significant prosthetic migration is safer in the long run than good 10-year clinical results!

EXCITING NEW TECHNIQUE AND RESEARCH SUGGESTIONS

The recently developed low-dose computed tomography-based implant motion analysis has been shown to have an accuracy and a precision on par with RSA; this measuring method (without the need for bone or implant markers and specialized RSA equipment) “opens up the possibility for simpler implant migration studies”[68-70]. Very exciting technique! Maybe this is a future golden standard for implant
motion analysis?

The less heat production and less evaporating toxic monomer during the polymerization, the more the risk of superficial bone necrosis adjacent to the Coolfix cement is reduced. A locally applied bisphosphonate inhibits the resorption of necrotic bone during the healing period\textsuperscript{[41]}. The synergistic effect of this combination (the Coolfix cement and a locally applied bisphosphonate) should increase the probability of permanent prosthetic fixation. Although the improved Coolfix cement, unlike a chemically modified bone cement, after curing is chemically equivalent to conventional bone cements and should have similar mechanical properties, a preclinical characterization is required prior to a clinical trial.

Bone scintigraphy ($^{99m}$Tc-MDP) is extremely sensitive but generally non-specific for diagnosing loosening\textsuperscript{[71]}. The scan is usually normalized within 6–9 mo after surgery\textsuperscript{[14]}, indicating that the healing period is over and that the prosthesis has become osseointegrated. Persistent uptake beyond 1 year represents increased bone turnover and bone perfusion – and probably continuous prosthetic migration. However, no prospective RSA study has been combined with scintigraphy, which would be interesting from both a pathophysiological and diagnostic point of view.

In contrast to the many RSA studies of hip prostheses that have shown that early migration poses a risk of future failure (the larger the early migration, the greater the risk of future failure)\textsuperscript{[9,20-24]}, some RSA studies indicate (as mentioned earlier) that certain uncemented femoral components appear to achieve stability during the healing period despite significant early migration\textsuperscript{[25-27]}. However, do these femoral components, as suggested in these studies, really become osseointegrated or do some of them continue to migrate very slowly? Bone scintigraphy could probably tell.

**CONCLUSION**

Hip prosthetic loosening is often difficult to detect at an early stage. When loosening is eventually detected on standard radiographs it may be interpreted as late loosening but should be interpreted as late detection of loosening, initiated during or shortly after surgery by insufficient initial fixation or by early loss of fixation.

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