Chapter 2

RSA and Registries:

The Quest for Phased Introduction of New Implants

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Abstract

Although the overall survival of knee and hip prostheses at ten years averages 90%, recent problems with several hip and knee prostheses have illustrated that the orthopaedic community, industry, and regulators can still further improve patient safety. Given the early predictive properties of roentgen stereophotogrammetric analysis (RSA) and the meticulous follow-up of national joint registries, these two methods are ideal tools for such a phased clinical introduction. In this paper, we elaborate on the predictive power of RSA within a two-year follow-up after arthroplasty and its relationship to national joint registries. The association between RSA prosthesis-migration data and registry data is evaluated.

The five-year rate of revision of RSA-tested total knee replacements was compared with that of non-RSA-tested total knee replacements. Data were extracted from the published results of the national joint registries of Sweden, Australia, and New Zealand.

There was a 22% to 35% reduction in the number of revisions of RSA-tested total knee replacements as compared with non-RSA-tested total knee replacements in the national joint registries. Assuming that the total cost of total knee arthroplasty is $37,000 in the United States, a 22% to 35% reduction in the number of revisions (currently close to 55,000 annually) could lead to an estimated annual savings of over $400 million to the health-care system.

The phased clinical introduction of new prostheses with two-year RSA results as a qualitative tool could lead to better patient care and could reduce the costs associated with revision total knee arthroplasty. Follow-up in registries is necessary to substantiate these results and to improve post-market surveillance.

Introduction

The clinical introduction of new prosthetic designs by the orthopaedic industry has been compared with the introduction of new clothing designs by the fashion industry[1,2]. New prostheses with fashionable design features, such as a matte instead of a polished surface on the Exeter hip stem (Exeter, Exeter, United Kingdom), have been launched to the market without extensive clinical testing. Under the promise of theoretically superior clinical performance, such prostheses were chosen over very satisfactory standard prostheses with outstanding long-term implant survival records[3,4].

In 1991, the Capital hip (3M Health Care Ltd, Londonborough, United Kingdom) was introduced in the United Kingdom as a low-cost total hip replacement. Within six years, almost 5000 patients in ninety-five different centers were managed with a Capital hip. With a failure rate of 20% at five years, the use of this implant turned out to be disastrous[2,5].

However, such disasters do not stop at implant design features. Another disaster was the introduction of Boneloc cement (Polymers Reconstructive, Farum, Denmark) in the early 1990s. The cement was designed to have a lower curing temperature and a decreased release of toxic monomers. Theoretically, this would lead to a decrease in the incidence of aseptic loosening of prostheses. However, quite the opposite happened: the incidence of loosening of hip prostheses that were fixed with Boneloc cement was up to fourteen times higher in comparison with conventional cement[6]. After the first signs of clinical failure emerged, a small-scale randomized clinical roentgen stereophotogrammetric analysis (RSA) study involving fourteen patients who were managed with Boneloc cement and fifteen patients who were managed with Palacos cement was initiated[7]. Within one-half year, the migration of both the femoral and acetabular components was substantially increased in the patients managed with Boneloc cement. Furthermore, no tendency toward stabilization was seen and progressive continuous implant migration was present.

One would expect that these disasters could not happen today. However, in general, the introduction of new prostheses is still done in almost the same way as it was twenty years ago. Although Malchau proposed a much more controlled introduction of new prostheses in 1995[8], recent problems with the ProxiLock hip (Stratec Medical, Oberdorf, Switzerland)[9], ASR hip (DePuy, Warsaw, Indiana)[10,11], Accord knee (DePuy International Ltd., Leeds, United Kingdom)[12], and St. Leger knee (Covision, Carlton in Lindrick, United Kingdom)[13] are examples of situations in which the orthopaedic community, industry, and regulators can further improve patient safety.

There has been an upgrade in regulatory classification of hip, knee, and shoulder joint replacement prostheses by the European Union (EU) (2007) and by the United States Food and

Drug Administration (US FDA). This was important but, as hip and knee prostheses generally have a long survival, a difference between a ten-year survival of 95% and one of 80% will be detected only after years of follow-up involving a considerable number of patients[14]. Early detection might expose far fewer patients within a period of one or two years.

Most orthopaedic surgeons and decision-makers with a clinical background know and understand the concept of preclinical tests, randomized clinical studies, and registries. But what is the concept of RSA, and why can it play an important role in the phased introduction of new prostheses or related developments?

RSA is a highly accurate stereoradiographic technique for assessing the three-dimensional migration of prostheses. The accuracy of RSA for the measurement of prosthetic translations is between 0.2 and 0.3 mm, and the accuracy for the measurement of rotations is between 0.2° and 1.2°. The accuracy of RSA is ten to twenty times better than that of conventional radiographs. RSA provides highly detailed insight into the migration behavior of prostheses in the short term (i.e., one to two years) and with relatively small patient cohorts (i.e., thirty to forty patients)[15].

As the turnover of new prostheses is high, such a fast measurement technique would be beneficial. But the question is: are the early migration measurements indicative of future loosening?

Association of RSA Migration Results and Registry Data

It is no coincidence that several research groups that have initiated or are highly active in national registries of joint replacement prostheses are also involved in clinical RSA studies as both methods prove invaluable in different stages of the quality control of prostheses. For instance, clinical RSA originated in Sweden, which was also one of the first countries with a national joint registry. Sweden has the lowest national revision rates in the world for both total knee arthroplasty and total hip arthroplasty. The performance of RSA studies with follow-up in a national joint registry has proved to be highly successful.

Evidence supporting the assumption that early migration is indicative of late failure due to aseptic loosening is increasing. The relationship between short-term RSA results and future loosening of prostheses was described in detail by Ryd et al.[16] and Kärrholm et al.[17]. Ryd et al. studied 158 tibial components that were used for total knee arthroplasty and were followed for a maximum of ten years[16]. Fifteen implants were revised because of mechanical loosening. After six months of follow-up, these implants had a significantly larger migration rate than the nonrevised implants but were asymptomatic at that time. Kärrholm et al. found the same correlation in a study of eighty-four hip stems[17]. After a period of five to eight years, eight stems had been revised. The revised components exhibited significantly higher migration after six months as demonstrated with RSA.

In 1998, Nelissen et al. demonstrated in a randomized controlled trial that the uncoated, uncemented Interax Total Knee (Stryker-Howmedica, Rutherford, New Jersey) migrated excessively[18]. Therefore, this total knee replacement was considered to be at risk for a high rate of failure due to aseptic loosening. Recently, this prediction was confirmed in a systematic review, which demonstrates that the revision rate for the uncoated Interax total knee replacement was more than three times higher than that for the cemented Interax total knee replacement, underlining the early predictive value of RSA[19].

In a clinical RSA study of the ProxiLock hip stem (Zimmer, Warsaw, Indiana), six of forty-one stems showed nonstabilizing migration of up to 4.7 mm of translation and 12.2° of retroversion[9]. Early migration is associated with an increased risk of possible future loosening and revision, and therefore the use of this prosthesis was stopped and the manufacturer discontinued its production.

These observations on the clinical effect of RSA echo through several of the national joint registries. When an RSA study has been performed for a particular total knee replacement, there has been a 22% to 35% reduction in the number of revisions compared with that after total knee arthroplasty without RSA testing, as shown by data from the registries of Sweden, Australia, and New Zealand (Fig. 1)[20-22]. This phenomenon can be at least partially explained by the fact that RSA allows early identification of implants with poor performance. Once identified, such high-risk implants may be taken off the market in an early stage, preventing widespread introduction and large numbers of subsequent revisions.

Thus, the RSA-tested total knee replacements that are recorded in the registries represent a selection of the total knee replacements. They have low expected revision rates for aseptic loosening due to good early RSA results. Concomitantly, the use of RSA-tested total knee replacements with excessive early migration is discontinued early on and, as such, these prostheses will not be recorded in the registries. At the same time, this selection process is amplified by the transparent nature of the registries: poor hospital performance and subsequent low hospital ranking due to usage of inferiorly performing prostheses can be avoided by usage of prostheses with either excellent long-term results in registries or by usage of prostheses introduced after good RSA results.

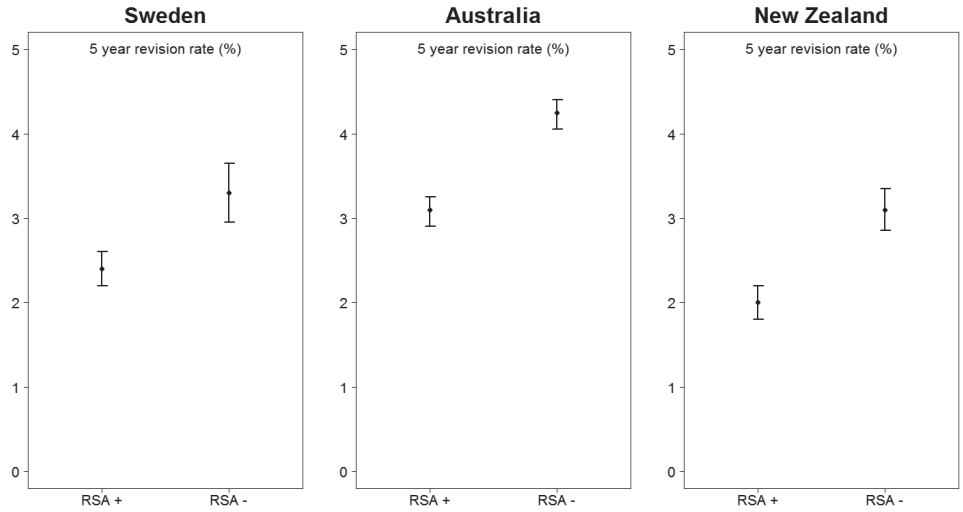

Figure 2.1 Revision rates for the national joint registries of Sweden, Australia, and New Zealand for RSA-tested total knee replacement (RSA +) compared with non-RSA-tested total knee replacement (RSA –), expressed in mean five-year revision rates with 95% confidence intervals. The revision rate for RSA-tested total knee replacement is significantly lower in all registries.

Cost-Effectiveness of RSA

The 22% to 35% reduction in the number of revision total knee arthroplasties associated with the use of with RSA can translate into considerable annual savings. While we did not perform any formal cost-effectiveness analyses, even modest reductions in revision arthroplasties can lead to substantial cost savings. For example, assuming that the total cost of revision total knee arthroplasty in the US is $37,000[23], a 22% to 35% reduction in the number of revisions (currently approximately 55,000 for total knee arthroplasty[24]) could lead to an estimated savings of over $400 million for the US health-care system. These savings could be even more substantial if RSA is used for each new total knee replacement prior to marketing. Future work will clarify the percent reduction in revision that can be attributed to RSA alone, but there is good evidence that the reduction is substantial. With these crude estimates of reduction in revision, such impressive savings will outweigh any concerns that RSA studies may be too expensive to conduct, even without taking into account the ethical issue of exposing patients to new, and as such potentially inferior, designs without optimal testing[25,26].

Standardization of RSA

Mandatory RSA studies require that the results of different RSA studies can be compared. Therefore, an international RSA group published RSA standardization guidelines in *Acta Orthopaedica* in 2005[27] and a larger consortium with RSA experts from all over the world is now establishing an actual ISO (International Organization for Standardization) standard for RSA. This draft of the standard is labeled Committee Draft and is currently being reviewed by all member countries. The standard is expected to be finalized in 2012. In addition, an international RSA network is being established currently. This network is intended to be a platform for improving the quality of clinical RSA research by sharing knowledge between research groups with different levels of RSA expertise and RSA-related developments.

The Era of Phased Introduction of New Prostheses

As outlined above, the potential of using RSA as a method of early (premarketing) assessment of implant performance is substantial. This potential is currently being recognized by various regulatory organs on different levels. The NICE (National Institute for Health and Clinical Excellence) guidelines of 2000 (United Kingdom) require adequate long-term clinical data for hip prostheses and indicate that RSA is a promising technique that may be an alternative for long-term follow-up studies[28]. However, additional proof of its predictive value for future loosening is demanded. The Dutch Orthopaedic Association has adopted in its new guidelines for hip prostheses—published in the beginning of 2011[29]—that any new hip prosthesis that is being considered for (commercial) introduction to the Dutch market has to pass a phased introduction. This phased introduction includes mandatory RSA studies even before larger clinical trials can be initiated.

A phased introduction of new implants or related developments has been proposed by several authors[8,30-32]. The stepwise introduction described by Malchau may be the most widely known proposal[8]. This phased introduction consists of the following three steps: (1) preclinical tests, (2) large clinical trials (ideally multicenter and randomized), and (3) postmarket surveillance in national registries. In this proposal, Malchau acknowledged the potential of RSA and recommended the application of RSA follow-up in both Step 1 and Step 2[8].

In this position statement, we propose to modify this stepwise introduction of new implants or related developments by introducing an additional, intermediary step that explicitly requires RSA studies after the initial first step of preclinical testing: (1) preclinical tests, (2) two-year clinical RSA trials, (3) larger multicenter clinical studies, and (4) postmarket surveillance in national registries. In this way, advantage is taken of the great potential of RSA regarding patient protection in the introduction of new implants.

Implementation of this phased introduction of new prostheses, with RSA as an early qualitative tool, will establish safer and more effective patient care.

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