Metal-on-metal hip arthroplasty : local tissue reactions and clinical outcome

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Chapter 11

General discussion

Introduction

Survival of hip arthroplasty in young patients is not as excellent as in elderly hip arthroplasty patients. This can be explained by the higher demands younger patients have. Larger and different biomechanical stresses are put to the prosthesis and a longer life of the prosthesis is needed due to patient's longer life expectancy. These higher biomechanical stresses result in increased implant wear, and challenges the long term durability of artificial hip joints. Surgeons, biomedical engineers and scientists constantly strive to develop and improve designs and used materials that are better able to withstand these stresses and show reduced bearing surface wear characteristics. These materials are tested first in the laboratory using wear simulators and computerized models. When these materials are introduced in clinical practice, post market surveillance of their performance is limited and often left to individual surgeons. Increasingly however, national joint replacement registers report on the long term implant survival.

The constant drive to improve the clinical performance of hip prostheses has resulted in the re-introduction of Metal-on-Metal (MoM) implants during the late 1990s. Surgeons used this type of surface bearing previously between 1950 and 1970, but almost completely discontinued its use due to high failure rates. In the same period the successful concept of "low friction" arthroplasty was developed by sir John Charnley, using Ultra High Molecular Weight Polyethylene (UHMWPE) as a bearing surface. This became the most widely used bearing material. But wear rates for standard UHMWPE proved to be high in younger, more active patients, resulting in osteolysis, implant loosening and ultimately revision surgery. This high wear resulted in less favorable implant survival rates in these younger patients. This gave MoM bearings a second chance. With advanced production techniques allowing tighter material tolerances, these implants now were

believed to have reduced wear rates, as demonstrated in wear simulators. Wear rates were so much lower that the second generation of MoM bearings were introduced as “a life-time implant”, and were to be considered for the younger and more active patient. The issue of hip implant failure in younger patients is a concern of each surgeon. When a younger patient presents himself with severe clinical and radiological hip osteoarthritis and failed conservative treatment, hip surgery can be considered. In this case, the surgeon has to choose a bearing surface which will last as long as possible and leaves room for future revision surgery. When the research in this thesis was initiated, hip resurfacing became a popular option around the world. However, the clinical results achieved by this second generation MoM hip resurfacing were still under debate. We therefore started with prospectively collecting clinical outcomes and radiological data on our complete cohort of MoM hip resurfacing patients. Most chapters in this thesis present clinical results of implants using a MoM bearing surface, but we also report on implants using UHMWPE in age-matched patients with the MoM group, to have a baseline comparator. These results confirmed our assumption that survival in young patients is not as optimal as we expected. We found a high proportion (53.4%) of implants being above the accelerated wear threshold rate of >0.2 mm per year, after a mean follow-up of 8.3 years. Somewhat in contrast, implant survival at a maximum of 12 years was acceptable (Kaplan-Meier survival probability 90.1%), and just compliant to international guidelines such as the NICE criteria. To benchmark the results of our MoM hip resurfacing cohort, we systematically reviewed the peer-reviewed literature on the survival of these resurfacing implants. We found that aseptic loosening was the most frequent failure mode and that none of the contemporaty hip resurfacing designs met the full 10 year NICE benchmark for survival. With the increasing attention in the international literature on the adverse reactions to metal debris (ARMD) in soft

tissue surrounding the MoM implant, we intensified our research on MoM resurfacing and focussed the research more to the role of cross-sectional imaging in diagnosing these reactions. The results of several investigations on the role of cross-sectional imaging in detecting and grading of these adverse reactions are presented in of the second part of this thesis and will be discussed in detail in this general discussion.

Hip implant survival in younger patients using different bearing materials

As described in chapter 2, long term hip joint replacement survival is often disappointing in younger patients and usually fails to meet the criteria of the National Institute for Clinical Excellence (NICE) for implant survival.[1] Wear of the implant bearing surfaces is seen as one of the main failure reasons. This is the case for implant types that use standard UHMWPE as a bearing surface but, in retrospect, also for so called hard-on-hard bearings such as MoM and Ceramic-on-Ceramic (CoC).[2] With the reintroduction of MoM bearings (both as THA and as hip resurfacing designs) during the 1990s, the main failure mode of the first generation MoM bearings was believed to be solved. The unacceptable high failure rate of the first generation MoM hip arthroplasty was mainly caused by short term aseptic implant loosening, due to high numbers of wear particles being released directly after implantation.[3] The second generation MoM held the promise of low wear rates compared to standard UHMWPE and tighter production tolerances allowed the use of a thin acetabular shell with a large diameter femoral component, reducing the risk for dislocation. In case of MoM hip resurfacing, the preserved amount of bone stock compared to THA promised the benefit of easier future revision. These three promises of a longer lasting bearing surface combined with a reduced dislocation risk and easier future

revision surgery were tailored to the needs of younger and more active patient indicated for hip joint replacement surgery.

During the introduction of MoM on the marked, the proposed benefits outweighed the concerns on metal ion debris released after implantation. Although these proposed advantages were tempting, the available evidence on MoM hip arthroplasty at that time was less than encouraging. In retrospect there is much debate about why large diameter MoM hip arthroplasty was (re)introduced around the millennium. With hindsight, marketing by orthopaedic device companies, media attention, internet and claiming patients can all be blamed for the introduction of MoM without the proper solid scientific evidence or a phased, controlled introduction in the market. Another big problem was the unavailability of MRI or CT that could deal with implanted metal implants. Scientific evidence was and still is conflicting regarding the benefits and complications associated with MoM arthroplasty. In 2000, Doorn, in his thesis on wear and biological aspects of MoM hip arthroplasty, concluded that wear volume was significantly less with MoM bearings compared to metal on polyethylene bearings, that less histocytic reactions occur with MoM bearings and that sensitivity and toxicity were not observed with MoM bearings.[4] In 2011, Murray et al discussed possible risk factors for pseudotumor formation. Based on the argument that most of these risk factors could be avoided, they supported the continued use of resurfacing in appropriately selected patients by appropriately trained surgeons.[5] However, several other authors were unable to confirm all these risk factors using data from their own case series.[6,7] This conflicting evidence prompted us to study our MoM patients. In our prospective case series of 298 MoM hip resurfacings we found a six year survival rate of 92.7%. In comparison, we retrospectively found a 90.7% survival rate for implants using UHMWPE after 12 years. Held against the benchmark of a 90% survival rate after

10 years follow up as set by the NICE guideline, the first conclusion is that UHMWPE is compliant with this guideline, although only by a small margin, and the MoM implant is not meeting the 95% at five year landmark. This latter showed an insufficient follow up period of this particular MoM resurfacing device. In our systematic review of implant survival of MoM hip resurfacing devices, this finding was confirmed: none of the included MoM hip resurfacing designs met the NICE criteria. Moreover, at the time of review, there were no studies available on the particular hip resurfacing device used in our clinic. Later, a case series on this particular MoM hip resurfacing design was published by Gross.[8] Although their survival rate, 96.4%, was better at 7 years, it was still not convincing. Another limiting factor of this study was that it was limited to clinical outcome scores and plain radiography only. This was comparable to our study first study on clinical follow-up of MoM resurfacing.[9] In retrospect, clinical outcome scores and standard radiographs were insufficiently capable of detecting pseudotumors, as demonstrated in our pilot screening study using cross sectional imaging and confirmed after we screened our complete MoM hip resurfacing cohort using Metal-Artefact Reduction Settings (MARS) MRI. Applying MARS-MRI resulted in a 36.3% pseudotumor prevalence patients. These results were comparable with other cross-sectional imaging studies using different MoM designs, for example 28% for the Birmingham Hip Resurfacing (BHR)[10], 33% for the Articular Surface Replacement (ASR)[11] and 29% for the Durom design.[12] The most severe cases were revised, adding a relatively new failure mechanism that negatively impacts implant survival of MoM hip implants.

Although survival rates with our implants which used UHMWPE were better than with our MoM hip resurfacing implants, the observed mean wear rate with standard UHMWPE was far from satisfactory. Further follow up of this particular case series should provide new data on whether this high wear rate will result in

an increased revision rate for osteolysis and implant loosening after the first decade. The few studies available on wear rates of UHMWPE with 10 to 20 years of follow up show that after so called “bedding in phase” during the first year, wear rates remain fairly stable up to around 8 to 10 years, but then increase again. The clinical relevance of this second decade of increased wear is not fully known, but a number of long term studies on the survival of the acetabular component report revision rates of 20% at 11 years[13] up to 65% at 16 years.[14] Future research should be directed towards constructing guidelines for implant survival in which the patients’ age at implantation is a consideration. Ideally, the implant survival in younger patients should not only be held against a 10 year benchmark but also against a 15 or 20 year benchmark, since the majority of younger patients will live more than 10 years after implantation. The Swedish hip register makes separation between different age categories, but NICE just uses 10 years as a benchmark.

During the last decade, more advanced UHMWPE materials have been developed to withstand wear and material fatigue. Clinical studies using cross-linked UHMWPE and second generation highly cross-linked UHMWPE are now published and compared to other bearings for wear performance and implant survival.[15,16] Five to ten year clinical results of highly cross-linked UHMWPE reveal excellent clinical and wear results. Short term reports of vitamin infused highly cross-linked UHMWPE (developed to reduce material aging in highly cross-linked polyethylene in addition to wear resistance) are also encouraging. For now, we conclude that both standard UHMWPE and MoM bearings still not have succeeded in significantly improving implant survival in hip arthroplasty for younger patients. For MoM the unexpected occurrence of ARMD is the most important downside, for UHMWPE the high amount of wear with subsequent osteolysis and implant loosening.

Surveillance for soft-tissue lesions after MoM hip arthroplasty

The limited regulations for market introduction of hip implants have resulted in unforeseen problems. Currently there is attention to these deficits, but it needs to be seen if this is continued and applied to prevent future repetitions of this process, or if the orthopedic community, including surgeons, national boards and the medical device industry, turns its attention to a new design and forgets about the problems discussed in this thesis.

Fortunately, recent scientific publications have discussed how a more controlled introduction of joint replacement designs could be done, while balancing the protection of patients with the benefits of introducing new designs which might outperform current designs. With this reconsideration of how new joint replacement designs are introduced into the market, there is the possibility to define the role and responsibilities of all stakeholders involved.

The focus on improved implant introduction to the market should leave room for following up on the clinical results of currently used designs and on previousy used but discontinued designs. Ongoing research on (discontinued) implant designs will benefit patients by making the optimal selection of revision implant designs and will learn us at what time point after the index surgery, revision surgery is best done if indicated in these cases. For example, if clinical results from early revisions for pseudotumor formation after MoM THA are worse than expected, surgeons should be more resistant to perform revision surgery.

To objectively study these issues, there are several needs. First there is a need for further development of pseudotumor classification systems and these systems should be more rigorously validated researching the consequent clinical actions based on the classification systems and other findings. These developments need to be incorporated into national guidelines to help clinicians treating their MoM patients. Secondly, more knowledge is needed on the development of

pseudotumors over time, their occurrence in non-MoM THA and which details of pseudotumors are predictive for the clinical outcome of conservative therapy and revision surgery. More research is also needed on the validation of imaging techniques like MRI. Can the circumstances under which conditions cross-sectional imaging was done, such as positioning of the patient, time of the day, etc., influence the results? In addition, not only in MoM hip arthroplasty, but also in non-MoM hip arthroplasty we need more insight in adverse soft tissue reactions incidences and consequences. Already, numerous case reports have been published on the occurrence of soft tissue masses near non-MoM total hip implants.[17] So far, only very small observational studies have researched the occurrence of these adverse reactions in non-MoM hip arthroplasty, leaving the need for a larger study using cross-sectional imaging.

It is also relevant for surgeons faced with a patient diagnosed with severe pseudotumor after MoM arthroplasty needing revision surgery, to have evidence on what bearing option to choose for the revision implant. Currently there is only a limited number of studies available presenting the clinical and radiological outcomes of MoM revision surgery for pseudotumor, all of them with only short follow up on a very limited number of cases.[18,19] Different bearing options for MoM revision surgery are used such as large diameter ceramic-on-ceramic, dual mobility heads, or more standard THA using ceramic-on-polyethylene or metal-on-polyethylene.[20]

Introduction of hip implant designs into clinical practice

The current questions around MoM implants, combined with issues like PIP (Poly Implant Prostheses) breast implants and failure of ICD implantable-cardioverter defibrillator (ICD) leads, have led to a global discussion on bringing medical devices to the market. Both the CE marking (Europe) and the IDE (US) process are

criticized.[21,22] Currently a process in the European parliament is going on to change the CE marking legislation, however this is a quite complex process and it is questionable whether this will solve the current problems.

Orthopaedic surgeons and biomedical engineers primarily question the use of specific implants from a performance perspective. Increasingly, national associations, medical insurance companies and hospital administrators also question the use of specific implants, often both from a performance and a costs perspective. All these stakeholders communicate with the medical device manufacturers that engineer and produce these implants, often in close collaboration with designer orthopaedic surgeons. In orthopaedic surgery, medical device companies have the infrastructure and knowledge for developing new orthopaedic devices, including laboratory testing. With the required testing standards (ASTM and ISO) and vigilance plan, the request for the CE mark is made. However, in contrast to pharmacy, the companies only need to present a vigilance plan since blinded, dose finding or placebo controlled studies are not possible. Dependency of post market surveillance is completely on orthopaedic surgeons who are the only ones that can apply these new techniques in the clinic. Many innovations or changes to the devices are made together and per request of the market (i.e. the surgeons).

Still, in comparison to pharmaceuticals which require multiple controlled clinical trials prior to approval, which take a mean of nine years and cost an average of 800 million U.S. dollars, medical devices such as a new hip implant design can be released onto the market after in vitro testing and limited supportive clinical data.[23] To improve on this situation, several authors have advocated a stepwise clinical introduction of new implants. This involves pre-clinical testing, small prospective trials using high-precision methods such as Radiographic RadioStereometric Analysis (RSA) to assess initial fixation to predict long term

survival, larger multicentre trials and finally population-based register studies to keep devices on track.[24,25] RSA studies limit the number of patients at risk while at the same time, with a short follow up period, provide sound predictions of long term implant performance.[25] Uniform reporting of RSA and clear descriptions of the predicted migration pattern beforehand are essential to get high quality RSA results.

Surveillance of implant performance after introduction onto the market is done in a number of countries, but not all, by national joint replacement registries. For example in the United States, which is one of the largest markets, less than 200 of the 5724 registered hospitals participate in the American Joint Replacement Register (AJRR). Other countries such as Sweden however have a long history of nationally registering joint replacement procedures, with data entry compliance near 100%, enabling them to identify outliers in implant performance after market introduction. Still, a significant number of patients are put at risk before national joint registries can identify underperforming implant designs.

The re-introduction of second generations MoM bearings into clinical practice, which compromised the confidence of patients and professionals after reports on failing implants and even the recall of particular products, is now used to identify the shortcomings of the process governing the introduction of new THA implant designs in practice.[25,26] There are however many considerations. For example RSA, a key element in the stepwise introduction of new implants, is a predictor for survival. The current issues raised with the MoM bearings could not have been prevented with RSA. For example, the RSA results of the Recap MoM resurfacing (the prosthesis described in this thesis) were excellent.[27] It is therefore necessary that a balanced introduction will not only rely on clinical data of implant fixation, but that also both local tissue reactions and systemic reactions to released wear particles are monitored.

This phased introduction should strike a balance between optimizing patient safety while at the same time allowing maximum technology development. New testing protocols have been developed, in which THA surface bearings are tested in adverse conditions such as non-optimal mechanical placement, oxidative stress and more extreme temperatures. This should increase the validity of these test results for performance in clinical practice. In Europe, medical devices are allowed onto the marked after CE (Conformité Européenne) approval but since the number of medical devices regulated by CE marking is approximately 500.000, ranging from scoot mobiles and drapes to artificial joints or heart valves, it is extremely difficult to design specific guidelines for each medical device in Europe. Further from notified bodies cannot be expected to be experts on all devices and materials. They rely on the quality of the presented documents.

Benchmark criteria on THA implant survival are nowadays used to evaluate implant performance. The National Institute for Health and Care Excellence (NICE) criteria set a rate of revision for failure of 10% or less for a given prosthesis at 10 years.[1] These guidelines however do not take into account factors such as indication or age. With the increasing number of patients who have received a THA, national benchmark guidelines should consider extending their criteria beyond the first decade.

A recent study by Anand demonstrated that the level of implant performance in modern hip arthroplasty is hard to beat: none of the new implant designs outperformed current hip implant designs, most even did worse.[28] But one has to be careful to interpret these findings in such a way that development of new materials and designs is not halted. Moreover, there are examples of implant designs of which the use was discontinued after initial reports predicted poor long term performance. For example, based on RSA studies, the SHP stem was predicted to have poor long term performance but recent clinical studies showed

equal implant survival compared to well-established implants.[29,30] An even more complicated discussion is raised on the issue of implant design changes. During the lifecycle of a certain implant, there might be one or more modifications to the original design. All these changes are made to further improve products to meet market demands. Although these minimal changes can have major consequences, it is difficult to say what research is needed to back up these changes. It might be useful to copy the automotive industry in this matter, where small changes to a certain model results in the addition of 'Mark 2' or 'Mark 3' suffix to the model name. This would allow surgeons to better judge the available evidence for certain implant designs and their alterations.

Future research on hip joint replacement performance

Finally, the most difficult consideration in the management of problematic MoM patients are the patients' experiences and preferences. There are patients who want a revision but with no or mild symptoms, normal or slightly elevated metal ion levels and no pseudotumor visible with imaging techniques. Other patients are very hesitant to revision surgery but have large, pseudotumors visible on CT or MRI but are without symptoms or elevated metal ion levels. The phased introduction of new orthopedic implant designs should prevent future recurrenc of these dilemma's. Not only RSA studies on implant fixation should be a part of such a balanced introduction, but also local tissue reactions should also be monitored with either ultrasound, CT or MARS-MRI, while possible systemic reactions to released wear particles should be studied with blood analyses. Ultimately, these preliminary findings should be validated with strong clinical research results, thereby ensuring long term patient safety and guiding the orthopaedic community in which implant types to use for best results in the younger, more active patients.

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