Total hip arthroplasty: recent advances and controversies

Introduction

Total hip arthroplasty (THA) has become one of the most successful and cost-effective procedures in modern medicine since its introduction and advancement in the 1960s by the British orthopaedic surgeon Sir John Charnley.\textsuperscript{1,2} He developed the fundamental principles of hip replacement and his design of prosthesis is still used today. For patients with hip pain caused by a variety of conditions, THA can relieve pain, restore function and improve quality of life.\textsuperscript{3-7} The World Health Organization (WHO) considers THA to be one of the most cost-effective interventions in medicine.\textsuperscript{8} Today, over 80,000 THAs are performed in England and Wales every year,\textsuperscript{9} and this is likely to rise by an estimated 170\% by 2030.\textsuperscript{10} These trends are driven by an ageing population wishing to remain active and an increasing number of obese individuals.\textsuperscript{11}

A THA procedure replaces diseased hip articular surfaces with synthetic materials. This alleviates pain and improves function. THA is usually considered as an option once all non-operative approaches to pain control have been exhausted. In people with severe hip disease, THA can be life-changing with major improvements in pain, function and quality of life.\textsuperscript{3-7} Evidence shows THA surgery has excellent long-term survivorship (defined as time from primary surgery to revision surgery) in both younger and older patients. Typical survival rates for conventional cemented, metal-on-polyethylene bearing joint replacement are greater than 90\%, 85\% and 80\% at 10, 15 and 20 years respectively.\textsuperscript{12-16}
Despite these excellent outcomes, there are some current areas of concern with regard to THA surgery. Recent studies and the National Joint Registry for England and Wales (NJR) report higher revision rates with some newer designs of THA, which have been reported extensively in the media. This has provoked debate into how medical devices are regulated in the UK, Europe and North America.

In addition, some analyses of data have suggested an increase in mortality associated with cement use in hip replacement surgery as compared to cementless fixation.

In this review we will discuss these topics in relation to the current evidence base.

**Metal-on-metal bearing surfaces**

Younger patients and active older patients typically suffer from increased wear and higher dislocation rates compared with less active older patients following conventional THA with small bearing surfaces (22.25–28mm). Metal-on-metal (MoM) devices were developed to address these problems, given the increasing demand for arthroplasty in this younger and more active population. Conventional hip replacements use a metal head articulating with a polyethylene-lined cup. Over time the plastic cup wears against the harder metal head. The resultant polyethylene-wear debris can result in an inflammatory reaction and subsequent osteolysis around the joint replacement components. MoM devices are made from cobalt-chrome, a very hard material. It can be manufactured to form very thin components (with large bearing surfaces) and has been demonstrated to have very low wear in hip simulator studies. There are theoretical benefits to using MoM bearings compared to metal-on-polyethylene bearings. These include the use of large-diameter heads that can reduce the rate of dislocation. Thinner components also enable bone conservation and more physiological femoral loading (normal forces through the hip joint). This aspect of MoM technology facilitated the development of hip resurfacing as a popular technique in younger patients.

MoM hip devices became widely used following the publication of initial results of 5-year follow-up from designer series (these report data from patients whose surgery was performed by surgeons involved in the design process of the prosthesis). By 2010 over 1,000,000 devices had been implanted worldwide. However, despite the theoretical advantages and initial good results, high failure rates have recently been reported with the use of MoM devices.

In 2006 the first major MoM-related problem was reported in a resurfaced hip. Subsequent case series demonstrated that failure of MoM devices was often associated with large masses and/or cysts visible on magnetic resonance imaging (MRI) or ultrasound. At revision surgery these masses were found to be associated with local soft tissue and bone destruction (Figure 2). Due to their locally destructive nature these masses were initially labelled ‘inflammatory pseudotumours’. They have subsequently been variously described as metallosis, aseptic lymphocytic vasculitis-associated lesions (ALVAL) and adverse reactions to metal debris (ARMD). Histological examination of these masses reveals a macrophage-dominated inflammatory response, associated with massive areas of necrosis. Subsequent in vitro studies have demonstrated that the process is initiated by metal-wear debris and that cobalt, in particular, is highly toxic.

The pathogenesis of MoM-induced pseudotumours has been extensively studied. Investigation of retrieved MoM implants demonstrates that 80% of pseudotumours are associated with high bearing-surface wear thought to be due to edge-loading of the socket (unequal load across the acetabular cup resulting in load on the rim of the cup). Many
factors affect this, including implant design, implant positioning and patient factors. However, studies also show that 20% of patients who develop pseudotumours have no evidence of high wear. It has been postulated that these individuals may be more sensitive to metal-wear debris than the general population. At present there is no good way of identifying these individuals, as cutaneous sensitivity correlates poorly with deep hypersensitivity.30

The incidence of MoM-related pseudotumours varies according to series, implant and geographical location. In particular, one resurfacing device, the DePuy Articular Surface Replacement (ASR), has a significantly higher failure rate than other designs.31 This is due to a number of disadvantageous design features, including a shallower acetabular component that results in greater edge-loading and thus wear compared to other designs.

Although designer series reported a cumulative revision rate of <0.5%,22 independent studies suggest a higher rate of revision, ranging between 1 and 9.8%.28 The factors associated with a higher risk of revision for adverse reaction to metal debris are female sex (eight-fold increase) and age <40 years (three-fold increase).25

The NJR has shown that the 9-year cumulative percentage probability of first revision for any fixation of primary THA regardless of the type of bearing used is 5.06%.32 However, cemented, cementless and hybrid metal-on-metal devices have revision risks of 21.43%, 17.66% and 14.86% respectively.32 The different types of resurfacing devices varied in performance, with the Birmingham Hip Resurfacing System having a probability of first revision of 6.61% at 8 years compared to the ASR with 29.69%. In addition, the NJR has suggested that particular problems occur with larger-head stemmed MoM implants.32 Studies have shown evidence of high wear in these devices at the trunnion-head interface (the junction where the femoral head component meets the femoral stem component).33 The Australian Joint Registry mirrors these findings, showing increased revision rates in MoM devices.44

It is thought that 4% of pseudotumours resulting from MoM hip replacements are initially asymptomatic.30 In addition, a study using MRI has described ‘silent’ pathology in 25% of patients with the best possible Oxford Hip Score.35 Therefore, the true prevalence of MoM-associated abnormalities is not yet known.

The future of MoM devices is unclear. However, their use is on the decline.9 The British Orthopaedic Association (BOA) and the Medicines and Healthcare Products Regulatory Agency (MHRA) have issued guidance on how to follow up patients with MoM hip replacement.36 All patients are to be followed up annually for the life of the implant. Patients with a stemmed component with femoral head diameter >36mm, or any DePuy ASR hip replacement require imaging, either with ultrasound or with MRI using Metal Artefact Reduction Sequence (MARS), and metal ion blood tests. Those patients with hip resurfacing devices or with a stemmed component with femoral head diameter <36mm require imaging only if symptomatic. If blood tests are positive (>7ppb) then a second blood test at 3 months is required. Revision surgery is considered if imaging is abnormal and/or blood metal ion levels are rising.

**Device regulation and evidence base**

The issues associated with MoM hip replacement surgery have reignited debate concerning medical device regulation.23,37-39 There have been calls by both the British Medical Journal (BMJ) and the BOA for significant change in the regulation of medical devices in Europe40,41 and a number of proposals put
forward by the European Commission are currently
the subject of negotiations with governments in the
EU member states.

Regulation in Europe differs from that in the USA,
where medical devices are regulated by a single
agency, the Food and Drug Agency (FDA). This pro-
cess is similar to the regulation of drugs in Europe
by the European Medicines Agency. However, the
American system has also come under recent scrutiny,
for example in relation to inadequate post-approval
monitoring of devices. Currently in Europe, medical
devices only need to achieve a Conformité Europé-
enne (CE) mark to be available for use by surgeons.
A CE mark can be achieved through any one of
76 Notified Bodies. These are appointed by Com-
petent Authorities in each of the EU member states,
such as the MHRA in the UK. Thus there is potential
for variation across Europe and for manufacturers to
shop around to achieve a CE mark for their device.
A second issue of concern is the potential for a device
to be awarded a CE mark based not on evidence but
on its claim to be equivalent to an already approved
device. Once a CE mark is achieved the device can be
used throughout the EU. Although joint replacements
were reclassified in 2007 from Level 2 to Level 3 de-
vices, requiring a higher level of scrutiny, at the time
of writing there is still limited post-market surveil-
lance of the performance of implants.

Proposals put forward by the European Commission
in September 2012 included changes such as: stronger
supervision of Notified Bodies by the Competent
Authorities, greater power for Notified Bodies to en-
sure thorough testing and regular checks, an extended
database on medical devices, improved traceability
to assist in effective recalls of failing devices, reinforced
rules on the required pre-market clinical data and
post-market assessment of devices, and the establish-
ment of a Medical Device Coordination Group com-
prising representatives of the national Competent
Authorities to improve coordination between member
states. If adopted, it is anticipated that new regulations
would come into force between 2015 and 2019.

However, calls for a change in regulation have met
with criticism – some authors arguing that excessive
regulation may limit innovation. In the UK a House
of Commons committee began to examine the ques-
tion in March 2012, and in response the Govern-
ment issued a report, in December 2012, outlining
its negotiating position. Meanwhile, the MHRA had
also initiated a consultation on ‘Revision of European
Legislation on Medical Devices’. In a joint submission
to the MHRA consultation, the BOA and Arthritis
Research UK expressed support for the principle of
improving pre- and post-market clinical evaluation
but urged caution that regulatory requirements for
clinical investigations do not become overly complex
and so a deterrent to those seeking to conduct
them. Following on from this consultation, the
BOA and MHRA together initiated a project named
‘Beyond Compliance’ with the overall aim of improv-
ing the regulation of new devices. Beyond Com-
pliance seeks to complement existing mechanisms
by providing guidance and support to manufacturers
for the safe introduction of innovations and by pro-
viding high-quality surveillance and monitoring to
identify promptly devices with high failure rates. How-
ever, Beyond Compliance is a voluntary scheme and
cannot replace current regulatory bodies because EU
law prohibits trade barriers between member states.

Fortunately, there are existing agencies and processes
that allow surgeons to compare the performances of
devices. The first of these is the NJR, which was set
up to monitor the performance of hip and knee de-
vices used in replacement surgery in England and
Wales (though its scope has since been extended).
However, the NJR’s design assesses long-term out-
come of implants and may fail to detect early failures
in new implants, in part because new devices are
implanted in small numbers, making outliers hard to
detect. MoM implants exemplify this problem, as
single-centre cohort studies identified problems with
MoM hip replacements several years before the NJR
identified these implants as outliers. Reporting to
the NJR was not mandatory for NHS hospitals until
April 2011. Perhaps better compliance and more data
might have resulted in earlier recognition of problems.

The second agency is the Orthopaedic Data Evalu-
ation Panel (ODEP). This is a branch of the NHS supply
chain to which manufacturers are requested to submit
data on their product. However, this is not mandatory.
Devices are classified firstly by the number of years
post-implantation for which evidence is available and
subsequently by level of evidence. The level of evi-
dence is determined by failure rates. Level A represents
the strongest level of evidence (failure rate of <5%);
Levels B and C are weaker in turn. Thus, 10A is the
highest-rated device, with 10 years of evidence of low
failure rates (Figure 3).

The National Institute for Health and Clinical Exce-
llence (NICE) has set a benchmark of a 10-year ODEP
rating with a revision rate of less than 10% for any
device. Those falling short of the 10-year NICE
benchmark should only be used as part of an ongoing
clinical trial. Any device evidence that spans less than
3 years may be classified as ‘pre-entry’ on the condition
that the manufacturers update ODEP with data on
post-market surveillance. However, inclusion as ‘pre-
entry’ does not require any evidence from peer-
reviewed publications of use at either the pre-clinical
or clinical stages of development. All other devices
are termed ‘unclassified’, meaning that no evidence
has been submitted by the manufacturers. Despite the potential benefit to surgeons from the ODEP system for comparison of devices, it may not contain sufficient data on clinical outcomes. For example, the DePuy ASR resurfacing device had an ODEP rating of 3A but was subsequently withdrawn following higher-than-acceptable failure rates.\(^{31}\)

Although the methodology for comparing hip-joint prostheses may be better than for some areas of device regulation, there still remains uncertainty behind the evidence supporting many devices available to the clinician. Reviewing data available from the NJR Annual Report of 2012, it becomes apparent that a significant proportion of the devices included in the NJR are ‘unclassified’. Despite being widely available for implantation by any orthopaedic surgeon, it is not known how many ‘unclassified’ or ‘pre-entry’ devices have evidence to support their use.

In 1995 Murray et al found only 30% of devices available had evidence to support their use.\(^{52}\) Since then, numerous calls for change have been made. However, a recent systematic review investigating the evidence base for all prostheses used in primary THA revealed that 24% had no evidence to support their effectiveness.\(^{53}\) A report conducted for the BOA highlights the need for ‘implants that demonstrate survival rates of at least 90% at ten years’ as the ‘gold standard’ and argues that ‘offering patients more expensive implants with little or no added benefit denies other patients orthopaedic care’.\(^{54}\) This correlates with NICE’s benchmark of implants that demonstrate survival rates of at least 90% at ten years as the ‘gold standard’ and long-term follow-up – published as the ‘IDEAL Recommendations’.\(^{55}\) The report encourages the ‘widespread use of prospective registries’ and suggests that, due to the difficulties in performing randomised clinical trials, measures should be sought to evaluate learning curves and alleviate ethical issues of randomising patients when the performance of a device is unknown. Furthermore, calls for the use of surrogate measures such as radiostereometric analysis (RSA) were highlighted. RSA is a 3-dimensional radiographic technique that can accurately measure the position of an implant in relation to fixed points (metal beads inserted at time of operation) within a grid matrix. It is a validated surrogate measure of outcome of THA within 2 years of implantation in a small cohort of patients.\(^{36-59}\) NICE has also recommended the use of RSA in the analysis of new implants.\(^{51}\) In 2011 Nelissen et al compared new implants tested using RSA versus those that were not and demonstrated that those new implants tested by RSA had a reduced revision rate of 22–35% without radiographic assessment.\(^{50}\) This study agreed with the Balliol Collaboration that a ‘phased clinical introduction of new prostheses with two-year RSA results as a qualitative tool could lead to better patient care’.

The NJR is linked to both the Hospital Episodes Statistics (HES) and Patient Reported Outcome Measures (PROMs) databases. There is the potential to use this combined database to create surrogate tools that can predict long-term outcome of THA devices. In the future there are plans for the Australian and Norwegian registries to be linked together with the NJR creating an international database.\(^{48}\) This will perhaps increase the chances of earlier identification of failing implants. DePuy have been piloting a method of Unique Device Identification (UDI) which could potentially help in establishing an international registry and improve traceability of implants.

Despite the calls for change in the systems for device regulation, progress has been slow. The reasons for this are unclear but may relate to the rapid expansion in the number of devices introduced into the UK market over the last two decades.\(^{49}\) In a 1996 study 62 primary hip replacement devices were available in the UK;\(^{52}\) this number had risen to 261 by 2011.\(^{9}\) Any impact from the proposed changes to EU regulation, if implemented, and from the voluntary Beyond Compliance service will only become apparent in the future. In the meantime, an expert working group set up by Arthritis Research UK has identified a number of research priorities across three broad thematic areas: gathering of data to support clinical decision-making, examination of biological response to wear debris and evaluation of implant design and durability.
**Effects of cement on mortality following THA**

Cemented THA was introduced by Charnley in the 1960s and cement is now used in nearly half of all primary THAs performed in the UK. The cement used in orthopaedic surgery is a substance called polymethylmethacrylate (PMMA) and strictly acts as a grout rather than cement (a grout is used to fill voids whereas cement binds materials). As cemented fixation has been used for over 50 years with excellent long-term results it very much remains the standard technique in the UK. The main advantage of using cemented femoral components in THA is that the implants are cheaper than those used in cement-free procedures.

Despite excellent long-term survivorship the use of cemented THA varies around the world. Countries in which cement is used regularly in hip replacement surgery include the UK (47% of THA procedures), Norway (52%) and Sweden (70%). However, Denmark and Canada have significantly lower rates of cement use at 16% and 4% respectively.

Recent data from the NJR on mortality rates following THA suggested that mortality rates in patients implanted with cemented femoral components may be as much as 16% higher than those with other types of fixation (cementless and resurfacing). The NJR reported a higher hazard ratio in cemented fixation compared to cementless at 1 year post-operation and up to 7 years post-operation. Similar findings have been reported from other joint registries such as the Catalan Joint Registry, which reported a three-fold increase in early mortality with cemented fixation compared to cementless procedures.

However, the NJR is not fully linked to medical records and does not include data on pre-operative risk factors. Thus it is not possible to explain the cause of increased mortality in patients having a cemented hip replacement. If cement is used more frequently in older, frailer patients including those with osteoporotic fractures, mortality is likely to be higher regardless of the procedure used. Efforts are being made to link the NJR to the Clinical Practice Research Datalink (CPRD – this replaced the General Practice Research Database (GPRD)). Until then analysis of other registries with data linked to medical records is required. More evidence is urgently needed to answer this important question, as a higher mortality rate may be regarded as a more important outcome than implant failure/revision in THA.

**Conclusion**

THA is one of the most successful procedures in modern medicine but has come under scrutiny in recent years. The failures of some MoM devices have highlighted the limitations of current regulations in Europe and in the UK. There is a case for a radical change in regulation policy. Further investigation into the use of surrogate outcome measures and linked databases are also required.

The NJR has demonstrated an increased risk of mortality following cemented primary hip replacements, and other joint registries have reported similar findings. Further studies are required to validate these findings and to assess the magnitude of any increase in mortality, and if confirmed, to investigate the reasons for this increase, particularly whether this reflects a true biological effect of the use of cement or other factors such as selection of higher-risk cases for cemented prostheses.
References


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