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EDITORIAL

Scientific Evaluation of Spinal Implants

An Ethical Necessity

Wouter A. Moojen, MD, PhD, MSc,*† Annelien L. Bredenoord, MA, PhD,‡ Roderik F. Viergever, MD, PhD, MSc,§¶ and Wilco C. Peul, MD, PhD, MBA*†

The clinical introduction of novel medical devices often occurs without evidence of good methodological quality and with relatively little oversight and regulation. As a consequence, the safety, efficacy, and long-term effects of devices are frequently insufficiently known upon device approval. Recent controversies surrounding the *Poly Implant Prothèse* (PIP) breast implants, metal-on-metal hip implants, and interspinous implants underscore the need to reconsider how innovation in medical devices can adhere to sound ethical standards without inhibiting surgical research and development. In this article, the introduction of spinal implants is taken as an example to firstly discuss the scientific and ethical challenges of developing, testing, and introducing novel medical devices and to secondly identify avenues for improving the existing regulatory frameworks for such innovation. Two measures for improvement are most feasible in the short term: demanding prospective studies before device introduction and developing registries to monitor and evaluate new medical devices.

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The clinical introduction of novel medical implants, particularly high-risk spine implants, often occurs with relatively little oversight and regulation.[1] This is in contrast with the strong regulatory requirements that are in place for the introduction of novel pharmaceuticals. As a consequence, the safety, efficacy and long-term effects of medical implant devices are often insufficiently known before they are used in patients.[1,2] Adoption of the novel device is frequently driven by other factors than evidence, such as the enthusiasm of the surgeon or marketing.[3] Recent controversies surrounding the PIP breast implants, metal-on-metal hip implants, and spinal implants underscore the need to reconsider how patients can be protected from ineffective, or potentially harmful, medical devices without inhibiting surgical research and development.[4–12] In this article, the introduction of spinal implants is taken as an example to firstly discuss the scientific and ethical challenges of developing, testing, and introducing novel medical devices, and to secondly identify avenues for improving the existing regulatory frameworks for such innovation. We argue that prospective comparative effectiveness studies should be mandatory before approval of a device, and that postmarketing surveillance for all medical devices, as proposed by the European Union, should be introduced as soon as possible.[13,14]

HISTORY OF SPINAL IMPLANTS: THE INTERSPINOUS PROCESS DEVICES

Spinal implants are widely used for different indications, ranging from indisputable indications such as reconstruction of the destabilized spine by trauma and reconstruction after surgical resection of vertebral tumors to less clear reasons such as stabilization for degenerative spinal conditions. Most implants are used for the latter group of degenerative spinal diseases, one of which is lumbar spinal stenosis (LSS). LSS is caused by arthrosis (degeneration) of the facet joints and development stenosis, which can result in lumbar nerve root compression. Removal of the bone and arthrosis around the nerve (bony decompression, *e.g.*, laminectomy) is the "gold standard" to treat LSS in the elderly population. The reported successful clinical outcome after bony decompression is only 64%, and many patients remain to have associated low back pain.[15–18] In an effort to improve clinical outcome, a French group introduced a new nonrigid fixation (interspinous process devices [IPDs]) for patients with LSS and associated back pain in 1984: the Wallis system.[19–21]

The Wallis system implants were tested for durability in cadaveric studies and were first implanted in humans in 1986.[20] The results of these first procedures were retrospectively studied.[20] Only after this period were patients included in a (noncomparative) prospective study, during which the

From the *Department of Neurosurgery, Leiden University Medical Center, Leiden, the Netherlands; †Department of Neurosurgery, Medical Center Haaglanden, The Hague, the Netherlands; ‡Department of Medical Humanities, University Medical Center Utrecht, Utrecht, the Netherlands; §Department for Health Evidence, Radboud University Medical Centre, Nijmegen, the Netherlands; and ¶ Department of Health Services Research and Policy, London School of Hygiene & Tropical Medicine, London, United Kingdom.

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Address correspondence and reprint requests to Wouter A. Moojen, MD, PhD, MSc, Department of Neurosurgery, Leiden University Medical Center, Albinusdreef 2, Postbus 9700, J11R30, 2300RC, Leiden, the Netherlands (wouter@moojen.eu).

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device was implanted in more than 300 patients. The study showed good recovery in 60% of patients.[21] After this study, commercial development of the system was started. Although the research group was planning to perform a randomized controlled trial, such a prospective comparative study of this implant is not available in PubMed.[20,21] After the introduction of this implant by Senegas, the development of other IPDs followed, such as Minns, X-stop, and Coflex.[22–25] Cadaveric studies did not show any biomechanical difference between the various IPDs and they were, therefore, considered as interchangeable, although differences in clinical effectiveness were not investigated.[24]

After introduction of these devices, various studies were conducted to test the effectiveness and safety of IPD treatment of LSS. However, most of these studies did not compare the results with other interventions and most did not have prospective study designs.[21,25,26] It took 30 years (from 1984 until 2013) until 2 prospective studies were published that compared IPD treatment with conventional (surgical) care.[16,27–30] These studies showed that treatment with IPD was *not* superior to bony decompression without implants and that IPD treatment resulted in a higher reoperation rate.[16,30] A third study was terminated because of the high number of reoperations (complications) in the experimental (IPD) group.[28]

The problem of lacking evidence for IPD use extends beyond LSS. Nowadays, there are multiple questionable indications for implantation of IPDs: some are used as standalone for LSS, others as adjuvant to surgical bony decompression for LSS in the hope to decrease back pain, and yet others to prevent disease at adjacent lumbar segments.[16,28,31] For these indications, IPDs remain in use without any evidence of treatment benefit. Furthermore, the lack of evidence for treatment of LSS extends beyond IPDs. Before the introduction of IPDs, lumbar spines that were "destabilized" after LSS were frequently rigidly stabilized by pedicle screws, and since the mid-1900s of the last century, vertebral interbody cages were added to this process.[32–34] However, pedicle screws and discal interbody cages, whose use is widespread for LSS, were introduced without any evidence of added value compared with conventional surgical decompression without implants, or even any evidence of incidence of spinal instability.[35–37]

Thirty years after the first introduction of IPDs for LSS, it is now clear that there is no justification for treating patients with LSS with IPDs.[16] Although precise numbers about the number of implanted IPDs are not available, at least 300,000 patients have undergone implantation with these devices since their introduction.[38] How was it possible that patients were not protected from these harmful devices and society was not protected from the use of these costly implants by regulations or any other measurements?

PRESENT REGULATORY PRACTICE IN THE EUROPEAN UNION AND THE UNITED STATES

In Europe, what is needed since 1993 for market introduction of a device (such as spinal implants) is the "Conformité Européenne". The Conformité Européenne approval guarantees that implants do not fall apart or have harmful material in them. However, a Conformité Européenne approval will not guarantee that the medical device will work in patients, or that it does not cause harm in other ways, such as higher reoperation rates as compared with other interventions. Recently, the European Committee has begun to realize the inadequacy of these regulations and in 2013 released a recommendation for a common framework for a unique device identification system (a monitoring system or registry) of medical devices in the European Union.[14] From 1990 till 2013, the European Committee launched several directives, recommendations, and proposals to realize such an identification system for safe, effective, and innovative medical devices. The first amending directive that urges for a registry dates from 1993.[13] However, none of these directives were ever implemented.[13] The suggestions made in the Commission Recommendation of 2013 to ensure traceability are sound, yet to this day, they remain just a proposal.[14]

The US Food and Drug Administration (FDA) has a stricter system for device approval, in which inventors are required to perform randomized studies before introduction of high-risk devices (such as spinal implants). However, the LSS case shows that this system also shows some shortcomings, because the FDA does not demand that the experimental treatment is compared with the "gold standard."[6] Interspinous process device treatment with bony decompression is nowadays approved in the United States, after the publication of an FDA study on IPD treatment.[27] However, this study did not compare the experimental treatment (IPD) with the "gold standard" (bony decompression) but with another experimental treatment (bony decompression with fixation techniques). This has happened before in the spine research field: the FDA study of the CHARITÉ artificial disc for low back pain compared artificial disc (experimental treatment) with another fusion technique (and not with the standard care).[39]

ETHICAL LESSONS

In contrast to pharmaceuticals, where rigorous safety and comparative effectiveness research are required for approval, novel medical devices can be introduced in patients without sound evidence and with relatively little oversight and regulation in patients. The reluctance to set up surgical research and generate systematically collected evidence on the safety and effectiveness of devices is sometimes defended by "*surgical exceptionalism*," the view that the somewhat exceptional ethical or regulatory status of surgery is justified by the unique dynamic nature of surgery.[40] There are several reasons why surgeons have taken this view. First, surgical techniques, unlike drugs, do not have chemical compositions, physical properties, routes and rates of excretion, or other qualities that can be measured precisely. Second, surgical procedures are rarely introduced as fully defined, easily reproducible techniques. Rather, they come as principles for solving particular problems, sometimes of an urgent nature.[41] Finally, in situations in which known interventions are of questionable value or where effective interventions do not exist, some state that a rigid regulatory paradigm cannot be applied to the innovative activities at the frontiers of surgical practice without adversely impacting the prospects for advancing the state of the art.[40]

We partially adhere to surgical exceptionalism, accepting that surgery is sufficiently unique in that it should not be governed by the same rules/requirements that apply in pharmaceuticals but resisting that the entire domain of surgery (*e.g.*, nonacute diseases such as LSS) would not be suitable for rigorous scientific evaluation of interventions.[40] The need for more rigorous evaluation of novel surgical procedures and medical devices is increasingly acknowledged in this era of evidence-based medicine.[42–45] Furthermore, unnecessary and/or unproven treatments can harm patients and can be unnecessarily expensive for societies with growing health care expenditures. The dynamic nature of surgical practice does not preclude rigorous evaluation of new interventions in the surgical domain and vice versa. It is a wide misunderstanding that if interventions do no good, they will at least do no harm and, therefore, nothing would be lost—this "no lose philosophy" has already been criticized in the 1970s.[46]

Fifty percent of all new drugs have important side effects discovered only after approval and marketing.[6] Taking into account the statement of FDA officials that "New devices are less likely than drugs to have theirs safety established clinically before they are marketed," the amount of side effects caused by surgical innovation and devices is potentially even higher.[47] Medical devices are complex assemblies of multiple components, making it impossible to design an implantable device without risks or harms.[48] Because "implanted body parts cannot be recalled as easily as defective auto parts," inadequately tested devices should be prevented from coming on the market, and systems for monitoring safety after a medical device is marketed should be implemented.[2,4] This is true, in particular, given the lack of informed decision making for patients, who are commonly operated on without sufficient awareness of the potential harm of experimental implants, and given the substantial commercial interests and aggressive marketing tactics of large international producers of devices.

WAY FORWARD FOR THE INTRODUCTION OF MEDICAL IMPLANT DEVICES

The case study set out above gives strong arguments for introducing a stepwise approach to introducing new implant devices.[6,49] We limit our discussion of this approach to implant devices because of the large differences between various (types of) medical devices and their consequences for regulation in this field.[6,50] Several authors have made suggestions for what needs to be done to avoid harmful and costly mistakes as have occurred in the introduction of IPDs for LSS. In our view, two measures are most feasible in realizing a regulatory system that ensures that medical implant devices are safe and effective. First, prospective controlled trials that compare the experimental device width the present "gold standard" for that disease should be required for device approval. To be approved, the effectiveness of the new device should be at least equal compared with the "gold standard," and it should be safe. Second, a monitoring system (postimplementation registries) for all medical devices, as suggested by the EC, could help trace these implants and ensure rigorous clinical follow-up. The establishment of registries would allow the collection of reliable data on adverse events and monitoring of long-term safety and efficacy.[2] By early detection of negative results, the use of an implant could be stopped or modified to avoid further damage. Moreover, it will give a clear overview of the innovations present in the field, so other innovators are not likely to repeat failed surgical procedures with certain implants.

CONCLUSION

Medical implant devices are frequently introduced without adequate evidence of safety and efficacy. This results in harmful medical practices for patients. Steps should be taken to strengthen regulation for device development and introduction, without unnecessarily inhibiting research and development. Two measures are most feasible in the short term: (1) requiring prospective studies before device approval, and (2) developing registries to monitor and evaluate new medical devices and all surgical implants.

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