Short stem total hip arthroplasty : potential explanations for persistent post-surgical thigh pain

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SUMMARY

Short stem uncemented femoral implants were developed with the aim of preserving proximal bone stock for future revisions, improving biomechanical reconstruction, aiding insertion through smaller incisions and potentially decreasing or limiting the incidence of thigh pain. Despite all the advantages of short stem designs, it remains unclear whether they are able to limit post-surgical thigh pain. In patients with short stem hip arthroplasty and persistent thigh pain, it is of the utmost importance to understand the potential etiologies of this chronic pain for selecting the appropriate treatment strategy. Therefore, this manuscript explores the hypothetical etiologies of persistent thigh pain in short stem total hip arthroplasty, including both peripheral factors (structural or biomechanical causes) and central factors (involvement of the central nervous system).

First, intrinsic causes (e.g. aseptic femoral loosening and prosthetic joint infection) and extrinsic sources (e.g. muscle pathology or spinal pathology) of persistent thigh pain related to hip arthroplasty are explained. In addition, other specific peripheral causes for thigh pain related to the short stem prosthetic reconstruction (e.g. stem malalignment and micro-motion) are unraveled. Second, the etiology of persistent thigh pain after short stem hip arthroplasty is interpreted in a broader concept than the biomechanical approach where peripheral structural injury is believed to be the sole driver of persistent thigh pain. Over the past decades evidence has emerged of the involvement of sensitization of central nervous system nociceptive pathways (i.e. central sensitization) in several chronic pain disorders. In this manuscript it is explained that there might be a relevant role for altered central nociceptive processing in patients with persistent pain after joint arthroplasty or revision surgery. Recognition of a potential role for centrally-mediated changes in pain processing in total hip replacement surgery has important implications for treatment. Comprehensive treatment addressing peripheral factors as well as neurophysiological changes occurring in the nervous system may

help to improve outcomes in patients with short stem hip arthroplasty and chronic thigh pain. Working within a biopsychosocial approach in orthopaedic surgery, specifically in relation to total hip arthroplasty, could be very important and may lead to more satisfaction. Further research is warranted.

INTRODUCTION

Over the past decades, total hip arthroplasty (THA) has been reported as clinically effective in treating pain and disability in patients with end-stage hip osteoarthritis (OA) [1-4]. Cemented implants have been available for many decades, however, due to complications associated with loosening and, ultimately, failure over time, uncemented femoral stems were introduced in the early 1980s. Mainly through technical advances, the 10-year survival rate of uncemented THA has improved over the past years [1-6]. Indeed, the number of uncemented THAs performed annually is increasing [7], with young patients (< 65 years) representing the majority (> 50%) of the current and future demand for uncemented THA [8].

Despite the increasing number of uncemented THAs performed annually, activity-limiting thigh pain seems to be a significant post-surgical complication in 2% to 40% of patients and the incidence is increasing in accordance with the increasing use of uncemented stems [9-15]. Patients typically report a dull aching pain in the anterolateral thigh, without a previous history of systemic illness or recent trauma. They can localize the discomfort to a discrete area on the femur (i.e. anterolateral thigh) that correlates with the location of the prosthetic stem tip [14]. The occurrence, temporal characteristics and severity of thigh pain can vary. In most cases, the reported thigh pain is mild to moderate, resolves spontaneously or does not progress, and requires no or minimal intervention [9, 11-13]. However, some patients (4%) do experience persistent severe, disabling thigh pain that can be a source of dissatisfaction post-surgery, which is concerning and requires appropriate treatment [16, 17].

The etiology of thigh pain seems to be multifactorial and linked to the femoral component of the uncemented THA. Possible causes include excessive micromotion at the bone-prosthesis interface, relative difference in structural rigidity between the prosthesis and the surrounding host bone (modulus mismatch), poor host bone quality or unnoticed periprosthetic fractures

[14, 18]. Thigh pain incidence in THA seems to be influenced by the stem material, stem design, stem size and extent of porous coating [14]. For example, titanium implants are associated with less thigh pain compared to cobalt-chromium implants due to their lower structural rigidity [19, 20] and tapered femoral stems have been associated with less thigh pain compared with cylindrical stems [14, 21].

Currently, THA is also a feasible option for the young and more active patients with hip OA [7, 8, 22]. However, especially these patients have increased stress on the implant and a greater risk of future revision, which makes the THA clinically challenging [21]. Uncemented femoral components are manufactured in a variety of shapes and lengths to accommodate to a wide range of femoral canal sizes in patients undergoing THA. Conventional length femoral uncemented stems (minimum 120 mm in length) have several reported disadvantages, including proximal/metaphyseal and distal/diaphyseal mismatch, inadequate bone preservation for potential femoral component revision surgery, no maximal facilitation of less-invasive surgical exposures and no optimal proximal load transfer [21, 23]. Therefore, short stem femoral implants were introduced, which are available in different geometries and designs. Stem lengths in short femoral implants range from 40 to 135 mm [24]. No exact definition exists, but the main characteristic of this kind of implants is that the femoral neck is often preserved and fixation is achieved in the neck or proximal metaphysis. However, some implants have their fixation extending below the lesser trochanter [24]. They are mainly designed with the aim of preserving proximal bone stock for future revisions and improving biomechanical reconstruction (by following the anatomic curvature of the femoral neck, which allows more rotational stability, prevents distal migration and avoids stress shielding). Short stem designs also make tissue-spearing minimally invasive approaches easier and potentially decrease or limit the incidence of thigh pain [21].

Studies with short- and mid-term follow-up (<10y) have shown that short stems lead to similar favourable clinical and radiographic outcomes in terms of pain relief, functional restoration, and stability as conventional length designs [25, 26]. Due to the benefits of soft tissue and bone preservation achieved with short stem implants their usage could be promoted, although currently long term (>10y) functional and radiographic results are unknown [21, 25]. Long-term RCTs to confirm the benefits of short stem THA are thus needed. Additionally, at this moment, it remains unclear whether short stems designs are able to limit thigh pain. Inconsistency is shown in literature, with some studies reporting thigh pain in patients receiving a short stem THA [27-30] and others reporting no thigh pain [31-35]. Literature comparing directly short stems with conventional length stems shows a lower incidence of thigh pain in short stem implants [36, 37], while another recent study indicates more thigh pain with short stem designs compared to conventional length stems [17]. Further research is certainly warranted.

It is clear that improved stem design (e.g. from cemented to uncemented design, from conventional length to short stem design) and stem material have diminished stress shielding and osteolysis with the advantage of preserving proximal bone stock for future revisions and making tissue-spearing minimally invasive approaches easier. Indeed, radiographic results of short stem designs are very encouraging in terms of bone implant fixation and stress shielding [21]. Despite all the aforementioned advantages, post-surgical thigh pain still remains a concern and a clinical challenge with THA.

No revision surgery should be planned before identification of the underlying cause [18]. Understanding the potential etiologies of persistent thigh pain in short stem THA is of the utmost importance for selecting the appropriate treatment strategy. Therefore, this manuscript explores the hypothetical etiologies of persistent thigh pain in short stem THA, including both

peripheral factors (structural or biomechanical causes) and central factors (involvement of the central nervous system).

HYPOTHESES

Short stem uncemented femoral components were developed in order to preserve proximal bone stock for possible future revision, improve biomechanical reconstruction, simplify insertion in less invasive exposures and potentially limit thigh pain. Although the first three mentioned arguments seem logical, it remains unclear whether short stem designs actually do decrease post-surgical thigh pain when compared with conventional length stems. The etiology of persistent post-surgical pain after short stem THA might be complex and multifactorial. We theorize that this persistent post-surgical thigh pain in short stem THA might be related to peripheral and/or central factors.

Peripheral factors

Thigh pain after a short stem THA could be considered as a dominant nociceptive pain, resulting either from activity in neural pathways related to tissue damage or from an inflammatory process linked to the surgical procedure itself. In most cases, the reported thigh pain resolves spontaneously in the months after the THA according to phases of tissue repair as one could expect. However, some patients (4%) still experience persistent thigh pain in the long-term after a THA [14, 16].

In case of persistent thigh pain after short stem THA, several *intrinsic* causes of post-surgical pain should first be ruled out, such as aseptic femoral loosening, prosthetic joint infection, hypersensitivity due to metallosis or prosthetic impingement and instability [14, 18]. A thorough investigation can be helpful to determine the contribution of these factors to the clinical picture. For example, pain present at the beginning of an activity that decreases when activity continues (warm-up phenomenon) should raise suspicion of prosthetic loosening,

whereas pain not relieved with rest but continuing through the night is suggestive of infection. If persistent thigh pain is explained by one of these intrinsic causes, a one or two-stage re-implantation, antibiotic therapy or revision surgery should be considered [18]. Sources of post-surgical thigh pain could may also be *extrinsic* and not directly related to the prosthetic reconstruction, such as muscle pathology (i.e. adductor or quadriceps muscle strain), bursitis (i.e. iliopectineal bursitis) or spinal pathology [14]. Accordingly, a thorough history, physical examination (including neurologic assessment) and radiographic evaluation (plain radiographs of the pelvis, hip and femur), possibly supplemented by other medical imaging techniques (e.g. Magnetic Resonance Imaging or PETscan), should confirm that the THA is well fixed, stable, aseptic and without an extra-articular source of thigh pain [14].

Persistent thigh pain after successfully osseo-integrated uncemented short stem THA remains a clinical challenge in a small percentage of patients. After ruling out loosening, infection or extra-articular sources of thigh pain, other specific causes for thigh pain related to the prosthetic reconstruction should be considered. Short stems have several potential advantages compared with conventional length stems. Their inherent bone-preserving nature wherein a more oval-shaped stem is fixed to the proximal femur allows more rotational stability and prevents distal migration and the absence of a distal portion of the stem helps to avoid stress-shielding [21, 38-40]. However, short stem designs also have potential disadvantages. For example, the definitive alignment of the stem is strongly related to the preparation of the femur. Femoral stems need femoral compaction rasps that are inserted following the curve of the femoral medial cortex, gradually increasing the size until proper fit is achieved. As the rasps are not introduced straight into the femoral canal but should follow the medial curve of the femur, the stem can be placed in a varus position. Coronal *malalignment of the stem*, particularly in varus position, has been reported in several studies related to short stems [31, 35, 41, 42] and has been associated with poor functional outcome [40]. Moreover, incorrect

stem size can cause *unintended subsidence*, making precise stem sizing of short stems more difficult and challenging as compared with conventional stems [29]. Because of these disadvantages, *micro-motion at the bone-prosthesis interface* can occur or periprosthetic fractures might develop, which could explain the presence of post-surgical thigh pain. Persistent thigh pain in short stems may also be related to the *modulus mismatch* between the stem tip and bone at the high stress subtrochanteric region of the femur [17]. In young, vigorous patients with robust, thick diaphyseal cortices and cancellous metaphyses a mismatch of the modulus of elasticity of the short stem implant and the host bone can be present. Moreover, especially in relation to short stems, *proximal femoral fractures* may occur [40], despite they are often overlooked.

In recent years, due to their potential benefits, the number of uncemented THAs with short stem designs performed in young and active patients has increased [22]. Concurrently, scientific literature has shown that post-surgical pain is often experienced by young and active patients after THA [17, 43]. This latter finding seems logical especially if one considers that younger and more active patients put *more stress on the implant* than older and more sedentary patients. In addition, young and active patients might have *unrealistic expectations* from THA surgery and might expect an easy and fast return to high impact activities, such as football or running. These factors might partly explain why short stem designs do not consistently decrease thigh pain when compared with conventional length stems. Patients should be educated away from these unrealistic expectations [44] and encouraged to gradually increase joint loading during rehabilitation.

Central factors

It might be appropriate to interpret the etiology of persistent thigh pain after short stem THA in a broader concept than the pure structural or biomechanical approach. Given our current understanding of chronic post-surgical pain, the involvement of the nervous system should also be taken into account hypothesizing the etiology of persistent thigh pain after short stem THA.

Hip OA accounts for up to 81% of THA, making it the primary diagnosis leading to hip replacement surgery [45]. Historically, OA-related pain and chronic post-surgical pain after joint replacement or revision surgery have been considered a nociceptive pain associated to the degree of structural joint or tissue damage and are still mainly treated on the basis of the biomedical model [46]. This model has favored the formulation of direct associations between structural factors (i.e. joint degeneration) and clinical symptoms. However, pain experience in OA is a multifactorial phenomenon comprising not only structural changes but also psychosocial and pain neurophysiology factors. Indeed, inconsistent results have been shown when associations between structural joint abnormalities, measured by radiography or Magnetic Resonance Imaging, and pain manifestations were investigated [47, 48]. Recently, traditional understanding of OA-related pain and chronic post-surgical pain has been challenged and it seems evident that other factors, such as altered central nociceptive processing, might also be involved in enhancing the nociceptive drive from damaged structures and hence causing more pain than can be accounted for by the damage [46].

Scientific understanding of chronic pain has indeed increased substantially over the past decades and it is now well established that the biomedical model falls short in explaining many chronic pain conditions [46]. Similar to other chronic pain conditions (i.e. whiplash associated disorders [49], rheumatoid arthritis [50]), there is a growing body of research suggesting that in a subgroup (around 30%) of patients with OA, the clinical picture is dominated by sensitization of central nervous system nociceptive pathways (i.e. central

sensitization) rather than by structural damage causing nociceptive pain [51, 52]. Moreover, recent research suggests a relevant role for altered central nociceptive processing in patients with chronic pain after joint arthroplasty or revision surgery [53, 54].

Pathophysiological mechanisms underlying central sensitization are complex and numerous, but the net effect is an amplification of neural signalling within the central nervous system that elicits pain hypersensitivity [55]. It is a broad concept reflecting not only spinal cord sensitization, but also an alteration of sensory processing in the brain [56], loss of descending anti-nociceptive mechanisms [57], enhanced descending facilitatory pain mechanisms [56, 58], increased bottom-up sensitization characterised by enhanced temporal summation or wind-up phenomenon [58] resulting in long-term potentiation of neuronal synapsis in spinal cord and brain regions (e.g. anterior cingulate cortex) [59]. The outcome of the processes involved in central sensitization is an increased responsiveness to a variety of noxious and non-noxious stimuli. When the central nervous system is sensitized, either no or minimal and undetectable tissue damage is sufficient to induce pain.

Obviously the process of central sensitization is a biopsychosocial phenomenon. Enhanced pain facilitation may for example be (partly) the result of 'cognitive emotional modulation'[60], which refers to the capacity of forebrain centers to exert powerful influences on various nuclei of the brainstem, including nuclei identified as the origin of descending facilitatory pathways [61]. Activity in descending pathways can indeed be modulated, for example, by forebrain products such as cognitions, emotions, attention and motivation. Every strongly relevant individual concern, like fear, can thus yield cognitive bias [60]. The presence of catastrophic thinking for example predicts more pain after a THA or total knee arthroplasty [62, 63].

According to the above mentioned discussion, it seems plausible that persistent thigh pain after short stem THA might no longer be considered as a simple transmission of nociception, but as a complex and multidimensional pain experience. It could be that features involved in post-surgical thigh pain are the result of structural or biomechanical abnormalities (e.g. micro-motion bone/prosthesis, modulus mismatch, unnoticed periprosthetic fractures, …) *and* sensitization of the central nervous system (i.e. central sensitization). It is possible that the majority of the nociceptors around the joint prosthesis remaining silent under normal conditions become active when the joint prosthesis is subjected to damaging mechanical deformations with subsequent release of certain chemical substances. The nociceptors then could be sensitized by release of neuropeptides from the nerve endings, leading to peripheral sensitization and hyperalgesia. Continuous and intense nociceptive input from the joint prosthesis may eventually drive central sensitization. So, in some patients the pain system might go through a transition from localized joint hyperalgesia (peripheral sensitization) to spreading hyperalgesia and other symptoms of central hypersensitivity (central sensitization) [64-66]. It is likely that in some patients the reported post-surgical thigh pain is predominantly nociceptive pain (dominated by peripheral factors) while in other patients the persistent thigh pain is dominated by sensitization of the central nervous system.

Recent knee OA studies have shown an enhancement of local and widespread hyperalgesia to pressure pain stimulation in patients with chronic post-surgical pain after total knee arthroplasty compared to patients with chronic knee OA pain [53, 54]. If patients who had pain after the first joint replacement undergo a revision surgery still experience pain, the hyperalgesia could even be further enhanced [53, 54]. In addition, patients with persistent pain after revision joint surgery showed facilitated temporal summation and lower conditioned pain modulation as compared to patients with no pain [53].

IMPLICATIONS

A meta-analysis shows that the risk of chronic post-surgical pain after THA ranges from 7 to 23 % [67], which represents a major clinical problem and highlights the need to optimize our understanding of potential etiologies of persistent thigh pain after THA. A thorough knowledge and insight into these etiologies might offer new opportunities for more appropriate treatment. Revision surgery should not be planned without identification of the underlying cause. So, in case of persistent thigh pain after THA, clinicians' clinical reasoning needs to incorporate the complexity and multidimensionality of pain in order to offer effective treatment.

Over the last 2 decades evidence has emerged of neurophysiological changes within the peripheral and central nervous system (central sensitization) associated with chronic musculoskeletal disorders, including OA and chronic post-surgical pain [68]. As awareness is growing that central sensitization might be important in the presence of persistent thigh pain after short stem THA, it is very important to consider central sensitization before a primary THA or before revision surgery. Revision surgery purely based on the indication pain should certainly be thoroughly reconsidered.

First, it is essential that clinicians are able to identify or recognize central sensitization, based on a thorough history and physical examination, in hip OA patients presenting for treatment. The classification between 'dominant nociceptive pain' and 'dominant central sensitization pain' is clinically very challenging. Recently, clinical classification criteria have been published that can assist clinicians to differentiate and diagnose the dominant pain mechanism in people with chronic musculoskeletal disorders including hip pain [69]. Clinicians are advised to screen their patients for 3 major classification criteria, and use them to complete a classification algorithm for each patient [69]. The first and obligatory criterion for dominant

central sensitization pain entails disproportionate pain, implying that the severity of pain and related reported or perceived disability are disproportionate to the nature and extent of injury or pathology. The two remaining criteria are 1) the presence of diffuse pain distribution, allodynia and hyperalgesia and 2) hypersensitivity of senses unrelated to the musculoskeletal system such as a high sensitivity for noise, heat or cold or bright light (defined as a score of at least 40 out of 100 on the Central Sensitization Inventory [70]).

Patients scheduled to undergo THA should especially be screened for signs of central sensitization. Recognition of subsets of patients with different clinical manifestations and pain mechanisms is important in order to tailor applied interventions and thus improve outcome [71].

In those patients with central sensitisation as dominant pain mechanism, a broader therapeutic approach aiming to desensitize the central nervous system could be adapted (first). Healthcare professionals have at their disposal tools to address centrally-mediated changes in nociceptive processing. Top-down cognitive-based interventions (from higher to lower hierarchical structures within the nervous system) (e.g. pain neuroscience education, cognitive-behavioral therapy (e.g. graded activity and graded exposure), mindfulness meditation, motor imagery) and bottom-up physical interventions (from peripheral to central structures of the nervous system) (e.g. motor learning, peripheral sensory stimulation, manual therapy) can induce neuroplastic changes across distributed areas of the nervous system and can affect outcomes in patients with chronic pain [68].

So, peri-surgical interventions addressed to patients with signs of central sensitization, such as cognitive-behavioral therapy or pain neuroscience education could be valuable in this regard. Evidence supports the use of cognitive-behavioral therapy (graded activity and graded exposure) and pain neuroscience education for patients with chronic musculoskeletal pain

[72-74]. However its use for patients awaiting replacement surgery has been suggested [51], but not yet studied. Further research regarding the use of strategies aiming to desensitize the central nervous system in patients with persistent post-surgical thigh pain after THA is also warranted.

Working within a biopsychosocial approach in orthopaedic surgery, specifically in relation to THA, seems to be very important and may lead to better outcomes. If individuals at risk for post-surgical pain and disability may be identified early, individual's suffering could be prevented or reduced to a significant degree.

TESTING THE HYPOTHESES

In order to test the above outlined hypotheses, further investigation is needed.

Future biomechanical experiments should investigate the internal loading on the short stem femoral implant and surrounding tissues, especially in young and active patients, for example using 3D motion analysis measuring external joint moments. In addition, the relationship between relevant biomechanical/structural parameters (e.g. stem alignment, micro-motion bone-prosthesis interface, modulus mismatch, presence of femoral fractures, …) and patient's symptoms should be investigated. Biomechanical/structural parameters can for example be measured using anterior-posterior pelvic-hip radiographs (stem alignment) [75], series of radiographs (subsidence) [76] or radiostereometric analyses (micro-motion) [77].

Furthermore, research should explore whether patients with persistent thigh pain after a short stem THA show centrally-mediated changes in nociceptive processing compared to patients with no pain after short stem THA and whether signs of central sensitization are associated with post-surgical thigh pain severity. The presence of central sensitization in patients with OA can be assessed experimentally using Quantative Sensory Testing (QST) [78, 79]. Given the complexity of central sensitization, its measurement should preferably be multidimensional by including various stimulus modalities (mechanical, chemical, electrical, etc.) and covering different pain mechanisms (pain and tolerance thresholds measured locally and extrasegmentally, spatial and temporal summation, efficacy of endogenous pain inhibition, etc.) [80]. It might be interesting to investigate whether any correlates or biomarkers of central sensitization (e.g. enhanced temporal summation, inefficacy of endogenous pain inhibition, …) could predict before surgery the development of persistent post-surgical thigh pain [81, 82]. Regarding revision surgery, it might also be interesting to investigate whether signs of central sensitization after primary THA are associated with

change in pain severity from post-surgery (primary THA) to 12 months after revision surgery (how much pain relief patients gained from revision surgery).

In addition, future research should elucidate if top-down cognitive-based interventions and bottom-up physical interventions, used alone or in combination with total hip replacement surgery, might be useful. These interventions aim to desensitize the central nervous system in contrast to therapeutic modalities that are only directed to structural joint pathology.

CONFLICT OF INTEREST STATEMENT

This study was not financially supported by any study sponsor.

The authors declare that they have no conflicts of interest.

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