The characterisation of unexplained pain after knee replacement

Jonathan RA Phillips, Beverley Hopwood, Rowenna Stroud,
Paul A Dieppe and Andrew D Toms

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Abstract

Background: The aims of this study were to characterise the pain experienced by patients with chronic pain after knee replacement (KR), in whom no apparent 'orthopaedic' problem could be identified, and to establish how many have pain sensitisation problems (including neuropathic pain).

Methods: A total of 44 patients were prospectively evaluated at a multidisciplinary tertiary referral clinic by an orthopaedic surgeon, pain specialist, rheumatologist and physiotherapist. These patients had been pre-screened by an orthopaedic surgeon to remove cases where there was an obvious cause of pain that could be treated with revision surgery. They were then followed up to find out whether any subsequent interventions had occurred.

Results: The mean time since surgery was 29 months (range: 3–108 months), and 18% were revision KR. Patients were evaluated for symptoms of nociceptive pain, allodynia, pains elsewhere and psychosocial factors. The patients were categorised into nociceptive pain 43% (n = 19), pain sensitisation 25% (n = 11) and mixed pain 32% (n = 14). Mean Visual Analogue Score (VAS) pain scores were 6.7/10 with high scores for both constant (66%) and intermittent (70%) pain elements, and pain caused high levels of interference with life. Fifty percent suffered depression and 25% suffered widespread pains (more than three pains elsewhere in the body). Patients with widespread pains suffered more pain ($p = 0.01$) and higher rates of both pain sensitisation ($p = 0.07$) and thermal allodynia ($p < 0.04$).

Conclusion: Patients after KR can experience severe pain that interferes with their lives, depression and many have pain sensitisation problems rather than any local, nociceptive cause. We advocate screening patients with unexplained pain after KR for pain sensitisation problems, pains at other sites and depression. Appropriate further treatment and multidisciplinary interventions can then be arranged.

Keywords

Pain after total knee replacement, nociceptive, sensitisation or mixed types, associated with widespread pains, associated with depression, multidisciplinary approach

Introduction

Knee replacement (KR) is an effective and cost-effective treatment for severe osteoarthritis, and the numbers of these replacements being carried out each year in the developed world are rising.^{1,2} In the United Kingdom, the latest report of the National Joint Replacement Registry (NJR) shows that over 94,000 KR procedures were undertaken in England and Wales in 2015, a 3% increase from the previous year.³

The main indication for KR is pain uncontrolled by conservative measures, and the majority of patients

achieve a good outcome.^{4–6} However, not all patients undergoing KR have a satisfactory outcome. A recent systematic review of the literature indicates that about

Royal Devon and Exeter Hospital, Exeter, UK

Corresponding author:

Jonathan RA Phillips, Royal Devon and Exeter Hospital, Barrack Road, Exeter EX2 5DW, UK.
Email: jonphillips@nhs.net

20% of patients have moderate or severe chronic post-operative knee pain.⁷ This accords with data from the NJR and other sources, which indicate that about 20% of patients are not satisfied with their surgery.^{8,9} Thus, in the United Kingdom alone, there will be some 18,000 patients per annum left with chronic knee pain and unsatisfied after a KR, representing a significant health problem.

The evaluation of these patients is challenging, but the problem has received relatively little attention from the orthopaedic community. Most of the available literature concentrates on mechanical problems within the knee joint (such as instability, malalignment, wear and loosening), infection in or around the knee joint, or referred causes of knee pain such as hip pathology, nerve entrapment and pain of vascular origin.¹⁰ Unfortunately in clinical practice, it is often impossible to label a patient with chronic post-KR knee pain with any of these specific diagnoses, and revising the prosthesis has been shown to lead to poor outcomes, suggesting that the problem is not always to do with the prosthesis.¹¹

As a result of extensive clinical experience with this patient group, the authors of this study came to the view that they needed to approach this cohort of patients in the same way as any other patient with a chronic pain problem rather than from a purely orthopaedic perspective. Pain specialists divide chronic pain into nociceptive (pain arising from a local source of tissue damage activating pain nociceptors) or pain sensitisation categories.^{12,13} Pain sensitisation can occur at both local (around the knee) and distant (in the spinal cord or brain) levels. Severe pain sensitisation is described as neuropathic pain.^{12,14} The diagnosis of neuropathic pain is purely a clinical one, rather than being based on any pathological findings. It is characterised by certain qualities of the pain experience that can be captured by standardised questionnaires such as painDETECT®, and the key examination finding is allodynia.¹⁵ It needs to be distinguished from chronic regional pain syndrome (CPRS) which has a specific set of diagnostic criteria.¹⁶ Pain specialists also recognise the extent to which psychosocial factors can influence all types of pain, and that treatment of these and other co-morbidities can help relieve pain.^{17,18}

The aim of this study was to characterise the pain experienced by patients with chronic post-KR knee pain, in whom no apparent local 'orthopaedic' problem could be identified, and specifically to try to establish how many of these patients have a pain sensitisation problem, rather than a local nociceptive cause for their pain problem. We also wished to establish the likely role of depression or other psychosocial problems.

Patients and methods

A tertiary referral, multidisciplinary clinic was set up in the Royal Devon and Exeter Hospital in the United Kingdom. The team consisted of an orthopaedic surgeon with a specialist revision KR practice (A.D.T.), a professor of rheumatology with a specialist interest in arthroplasty (P.A.D.), an anaesthetist with an interest in pain medicine (B.H.) and a senior extended scope physiotherapist with an interest in arthroplasty (RS).

All patients were pre-screened by the consultant orthopaedic surgeon (A.D.T.), who also reviewed all the radiographs, to remove cases where there was an obvious cause of pain that could be treated with revision surgery. All patients attending this clinic had unexplained chronic knee pain after a KR. The other members of the team then saw these patients together.

Demographic data were collected, including details of their primary knee surgery and any subsequent interventions. Information was collected on their medical co-morbidities, including symptoms and problems relating to their painful joint, pains affecting other joints and other painful conditions. Social and psychosocial issues were recorded, and a drug history (including pain medications) was taken.

The patients were asked to fill in the following questionnaires while waiting to be seen by the team: PainDETECT score for the assessment of neuropathic pain, the Intermittent and Constant Osteoarthritis Pain Score (ICOAP, Knee version), a two-question depression screening tool, the Brief Pain Inventory (BPI) score and a 10-cm Visual Analogue Score (VAS) for pain severity.^{15,19–22}

Clinical examination of the knee was undertaken. This included the following specific tests:

Touch allodynia was tested using a specialist brush (Senselab brush 05, Somatic); this was placed in contact with the skin so that the filaments slightly bend and a 1-second, 40 mm stroke was performed. If this action caused pain, the patient experienced touch allodynia. The brush was also used to detect areas of hyper- and hyposensitivity of the skin around the knee joint. Initially, the whole knee was examined to identify areas of sensitivity. The area of sensitivity was then mapped out and recorded with reference to the distance from the mid-point of the wound scar.

Thermal allodynia was assessed using hot and cold rollers (Rolltemp, Somatic); the roller was rolled gently over the affected area, looking for areas of altered temperature sensation and severe pain (allodynia). This area was also mapped in relation to the mid-point of the wound scar.

Patients were then followed up via a postal questionnaire to find out whether any subsequent interventions had occurred.

Categorisation of patients

The team discussed each patient after taking the history and examining them, and agreed on an a priori categorisation of their pain problem as either:

Group 1: Predominantly nociceptive pain. Patients in whom the team thought that the pain was probably coming largely from problems in or around the knee.

Group 2: Predominantly pain sensitisation. Patients who were thought to have a pain sensitisation problem, including those who could be classified as having neuropathic pain.

Group 3: Mixed pattern. Patients who were thought to have clinical features of both nociceptive problems and pain sensitisation, and often had other complex medical, psychological or social problems that might be contributing to their pain.

Subgroup: Widespread pains. Patients were also further subdivided into groups according to the number of other pains experienced. These were groups of 'no other pains', 'one to two other pains', 'three to four pains' and multiple (≥ 5 pains). The purpose of this separate categorisation was to identify patients with widespread pain issues for further subgroup analysis.

Patients were categorised into these groups after the history and examination were performed. This was then discussed by all of the members of the multidisciplinary team and the categorisation was performed. The presence of features of pain sensitisation as demonstrated by positive clinical tests for allodynia as well as high painDETECT scores was categorised into the 'pain sensitisation group', while the absence of these findings with more nociceptive symptoms was categorised into the 'nociceptive group'. It became clear that not all patients nicely fit into these two categories, often associated with medical and psychosocial issues, and these were categorised into the 'mixed group'.

The data were subsequently analysed by an independent researcher (J.R.A.P.) who documented the scores from each of the self-assessment questionnaires and examination findings, and related them to the a priori categorisation of patients made in the clinic. Statistical analysis was performed using GraphPad Prism VX. Parametric continuous data were analysed using paired or unpaired T-tests. Contingency data were analysed using Fisher's exact test.

Results

Data were collected from 44 consecutive patients seen in the clinic. The mean age was 66 years (range: 40–82 years). In total, 45% of ($n=20$) patients were male, and 5% ($n=2$) had problems with both knees. Thirty-four patients had primary total KRs (four of whom had undergone secondary surgery to replace the patella), two patients had primary partial KRs (unicompartmental) and eight patients had undergone revision surgery. A total of 45% ($n=20$) were tertiary referrals from out of the local region. The mean time since their last surgery was 29 months (median: 24 months, range: 3–108 months), with 7% <3 months ($n=3$), 18% 3 months to 1 year ($n=8$), 25% 1–2 years ($n=11$), 39% 2–5 years ($n=17$) and 9% >4 years ($n=4$).

Categorisation of patients

The 44 patients were categorised into nociceptive pain 43% ($n=19$), pain sensitisation 25% ($n=11$) and mixed pain 32% ($n=14$). The patients were further divided into the number of other pains experienced: no other pains 34% ($n=15$), 1–2 other pains 41% ($n=18$), 3–4 other pains 11% ($n=5$) and ≥ 5 other pains 14% ($n=6$).

Table 1 documents the pain scores and prevalence of depression in each of the three main groups of patients. The Pain Detect score was, as expected, highest in the pain sensitisation group ($p<0.001$). There were also higher mean scores for the other pain instruments, and for depression, in the pain sensitisation group, but these differences were not statistically significant.

As shown in Table 2, skin hyperalgesia and touch and temperature allodynia were all common in those classified as having pain sensitisation, indicating that most of this group could be considered to have neuropathic pain. The skin tests were used to assist categorisation into the pain sensitisation group.

It was noticed that skin hyperalgesia and allodynia were more common to occur on the lateral side of the scar. The site of sensitivity was variable among the patients, but patients with higher levels of pain more often had more widespread areas of sensitivity. Interestingly, patients also often seemed to be surprised by their reactions to the tests for light touch and temperature.

Within the nociceptive group, three patients were found to have large warm effusions in the knee and were, thus, thought to have an inflammatory element to their nociceptive knee pain; one of these patients had rheumatoid arthritis. Co-morbidities were common, particularly diabetes and cardiovascular problems, and most patients were taking several different

Table 1. Pain scores and prevalence of depression in each of the three main groups of patients.

	All	Pain sensitisation	Nociceptive	Mixed
n	44	11	19	14
VAS pain	6.7 (SD 1.9)	7.2 (SD 1.9)	6.0 (SD 1.8)	7.0 (SD 1.8)
painDETECT®	16.6 (SD 7.1)	22.1 (SD 6.8)	11.2 (SD 5.1)	19.7 (SD 3.8)
BPI pain	25.8 (SD 7.4)	29.1 (SD 9.8)	25.0 (SD 6.7)	23.8 (SD 5.3)
BPI interference in life	7.0 (SD 2.0)	7.3 (SD 2.6)	6.9 (SD 1.8)	7.1 (SD 1.7)
Depressed (answers both yes; %)	50	70	35	50
Not depressed (answers both no; %)	26	18	41	8
ICOAP	29.9 (68%) (SD 8.1)	31.3 (71%) (SD 8.6)	27.9 (63%) (SD 8.7)	31.2 (71%) (SD 6.7)
ICOAP constant	13.1 (66%) (SD 3.7)	14.1 (71%) (SD 3.6)	12.1 (61%) (SD 4.2)	13.5 (68%) (SD 3.1)
ICOAP intermittent	16.8 (70%) (SD 4.9)	17.2 (72%) (SD 5.5)	15.8 (66%) (SD 5.3)	17.9 (75%) (SD 3.8)

BPI: Brief Pain Inventory; ICOAP: Intermittent and Constant Osteoarthritis Pain; SD: standard deviation; VAS: Visual Analogue Score. Standard deviation in brackets

Table 2. Clinical features of pain sensitisation in each of the three main groups of patients.

	All	Pain sensitisation	Nociceptive	Mixed
n	44	11	19	14
Skin sensitisation	16	9 (82%)	0%	7 (50%)
Touch allodynia	24	10 (91%)	1 (5%)	13 (93%)
Temperature allodynia	19	8 (73%)	1 (5%)	10 (71%)

Figure 1. Categorisation of pain according to the number of other pains experienced.

medications, including analgesics. The team also noted that significant social problems were common in many of the patients seen in the clinic, but no clear relationship with any of the categories used to divide them were apparent. None of the patients were thought to have CRPS.

Figure 1 shows the categorisation of pain group in relation to the number of other pains experienced, indicating that those with pain sensitisation dominated the group with the most pain elsewhere. Table 3 shows the relationship between pain and depression scores and the number of painful sites recorded.

Pain Detect scores were higher in patients with three or more pains elsewhere when compared to patients with two or less pains elsewhere (mean score 20.8 versus 15.4; $p = 0.036$). In addition, ICOAP pain scores were significantly higher in patients with more than two other pain problems than in those with less than two other types of pain (ICOAP constant pain score 62% versus 77%; $p = 0.049$). Patients with widespread pain (three or more pains elsewhere versus two or less pains elsewhere) also experienced higher rates of skin sensitisation (63% versus 27%; $p = 0.07$), touch allodynia (73% versus 49%; $p = 0.29$).

Table 3. Pain scores, prevalence of depression and clinical features of pain sensitisation according to the number of painful conditions experienced elsewhere.

	No pain	1–2 pains	3–4 pains	>5 pains
n	15	18	5	6
ICOAP	31.4 (71%) (SD 5.9)	27.1 (62%) (SD 9.2)	29.0 (66%) (SD 1.4)	35.8 (81%) (SD 7.4)
ICOAP constant	13.5 (68%) (SD 3.3)	11.7 (59%) (SD 3.8)	13.3 (68%) (SD 1.2)	16.4 (82%) (SD 3.4)
ICOAP intermittent	18.0 (75%) (SD 3.3)	15.4 (64%) (SD 5.8)	16 (67%) (SD 0)	19.4 (81%) (SD 4.4)
Depression (%)	50	50	40	60
painDETECT	15.5 (SD 8.9)	15.4 (SD 6.6)	19 (SD 4.6)	20.8 (SD 4.9)
VAS	6.9 (1.6)	5.9 (SD 1.8)	6.8 (SD 1.3)	9 (SD 1.4)
BPI pain	24.8 (SD 7.5)	25.2 (SD 7.5)	24.2 (SD 3.7)	32.5 (SD 9.5)
BPI interference in life	7.1 (SD 2.1)	6.6 (SD 2.3)	7.2 (SD 0.9)	7.9 (SD 2.5)
Skin sensitisation (%)	20	33	40	83
Touch allodynia (%)	47	50	80	67
Temperature allodynia (%)	27	39	80	67

BPI: Brief Pain Inventory; ICOAP: Intermittent and Constant Osteoarthritis Pain; SD: standard deviation; VAS: Visual Analogue Score. Standard deviation of results in brackets.

and thermal allodynia (73% versus 34%; $p < 0.04$). Similarly the VAS and BPI pain scores were higher in those with widespread pain than in those without ($p = 0.01$; Table 3).

Fifty percent of all patients experienced symptoms of depression (two 'yes scores' on the depression-screening tool). Depression scores were higher in the pain sensitisation group (70%) compared with the nociceptive group (35%), although this was not statistically significant ($p = 0.20$). There was no difference in levels of depression according to the numbers of painful sites.

The mean interference of life scores for all patients using the BPI score was 7.0, meaning that this group of patients experiences high levels of interference in activities of daily living (general activity, mood, walking ability, normal work, relations with other people, sleep and enjoyment of life). The mean levels were between 7.0 and 7.7 for all of the activities of daily living, except for 'relations with other people' (mean 5.5). There were no significant differences between any of the interference scores for each of the pain categories or groups with different numbers of pains elsewhere.

Follow-up

All patients were followed up with a postal questionnaire 1–2 years after the initial appointment (mean 35 months), asking whether they had undergone further surgery on their painful KR or other interventions. Eight patients underwent subsequent revision surgery. The reasons for revision surgery were infection ($n = 1$), aseptic loosening ($n = 1$), instability ($n = 1$), stiffness and implant malposition ($n = 1$), stiffness ($n = 1$), inflammatory synovitis ($n = 1$; open synovectomy with tibial insert exchange) and conversion from partial to

total KR for progression of arthritis ($n = 2$). Of the group that underwent revision, four were in the nociceptive group, three in the mixed group and one in the pain sensitisation group. One patient underwent an open arthrolysis for stiffness (pain sensitisation group), and another patient in the nociceptive group underwent open synovectomy, followed by yttrium injections (the patient with rheumatoid arthritis).

Discussion

The aim of this study was to characterise the pain experienced by patients with chronic 'unexplained' pain after KR. Despite approximately 100,000 KR's being performed each year in England, Wales, Northern Ireland and the Isle of Man, very little is known about the types of problems that patients experience after their surgery. Our main findings are that some patients have severe pain that interferes significantly with their lives, and that a large number of them have pain sensitisation problems, many of which can be classified as neuropathic pain, rather than any local, nociceptive cause. However, it was not possible to categorise all patients as having either a local cause for their pain or a pain sensitisation problem, as many had complex unclassifiable causes for pain, including psychosocial problems.

It is clear that the problem of chronic pain after KR is common and important.^{7,23} Very few previous investigations have examined the problem from a pain perspective, rather than an orthopaedic one. A study performed within our unit demonstrated that only a small percentage of patients at 2 years post-KR have neuropathic pain,²⁴ which is further supported by studies performed by Wylde et al.²³ and Buvenenandran et al.²⁵

In our study, we first excluded those who had a clear mechanical or other orthopaedic problem and found that 25% of the remainder had neuropathic-like pain, and many more had pain sensitisation, contributing to the pain problem. This is important, first, as many orthopaedic surgeons are not familiar with how to detect these patients, and second, because there are simple therapies available to treat them.²⁶ Our investigation suggests that screening with the Pain Detect tool and a brush test for local allodynia may be sufficient to detect this important subgroup. Furthermore, asking the patients about pain at other sites in the body could be a useful screening tool, as there was a clear relationship between pain at other sites and pain sensitisation as a cause of knee pain. This simple question could help identify patients with a pain problem as well or instead of an orthopaedic problem.

Psychosocial problems have previously been found to have an impact on pain and function after a knee replacement (KR).^{27–30} We found high levels of depression in our patients, among all subgroups, but it is, of course, impossible to say whether the depression preceded the KR or not, or whether it was the effect of the chronic pain rather than a causative factor. However, it would seem likely that surgeons should be aware of the possibility of depression and other psychological problems in this group and think about treating these issues as part of the overall management strategy. High levels of pain catastrophising pre-operatively have also been found to be associated with persistent pain at 2 years post-operatively.³¹ We were struck by the high prevalence of other co-morbidities, in particular of social and psychological problems in this patient group, but are unable to say how important this was to their pain problems.

The strengths of this study come from the fact that the patients were thoroughly assessed by an experienced multidisciplinary team, and that both pain and musculoskeletal perspectives were considered. In addition, the self-assessment instruments and clinical tests used to assess the pain were all validated, widely used techniques, providing a comprehensive picture of the severity and impact of the pain, and a clear idea of the extent of pain sensitisation in the group. Its main weakness is the relatively small size of the cohort, and the fact that follow-up did not include any further detailed history or examination of the patients, preventing us from being able to say much about the natural history of this patient group. However, the fact that the majority of those who underwent further surgical intervention were in the group thought by the team to have a local pain problem suggests that they were able to classify patients appropriately using the relatively simple history and examination methods described.

Further studies of this problem are clearly needed, and the development of simple bedside screening tools

for the detection of pain sensitisation and psychological problems that can be treated to help relieve pain, and to help indicate which patients should be referred to a pain clinic, would be of great help to surgeons confronted with this difficult problem.

Importantly, surgeons dealing with patients with significant and persistent knee pain following KR should assess levels of neuropathic pain, pain at other sites and depression. We believe that patients with symptoms suggestive of neuropathic pain would benefit from scoring using the painDETECT score and should be assessed for allodynia. Appropriate further treatment and multidisciplinary interventions can then be arranged for patients with a painDETECT score of 19 or over (suggesting probably neuropathic pain), or the presence of features of allodynia. We would recommend that referral for additional pain management be performed before any revision knee surgery is considered.

In conclusion, we believe that this study indicates that the chronic pain is often multifactorial, and that specialists in pain should be involved in the assessment and management of patients who continue to suffer significant pain after total KR.

Conflict of interest

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