

Persistent pain following knee arthroplasty

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Background and objective The prevalence of persistent pain after orthopaedic surgery has been the subject of only few studies and the risk factors for persistent pain have been evaluated even more rarely. The purpose of the present study was to evaluate the degree and the risk factors of persistent pain after knee arthroplasty.

Methods The prevalence of persistent postoperative pain after knee replacement was evaluated with a questionnaire in a large, register-based cross-sectional prevalence study. The main hypothesis was that the type of operation (primary, bilateral, revision) would influence the prevalence of persistent postoperative pain. Logistic regression analysis was performed to test the hypothesis and to find other possible risk factors for the development of persistent pain.

Results The total number of patients was 855. The operation was a primary arthroplasty in 648 patients (75.7%), a bilateral arthroplasty in 137 patients (21.1%) and a revision arthroplasty

in 70 patients (8.2%). The response rate was 65.7%. The type of operation was not associated with the prevalence of persistent pain, but the degree of early postoperative pain was the strongest risk factor. If the degree of pain during the first postoperative week was from moderate to intolerable, the risk for the development of persistent pain was three to 10 times higher compared with patients complaining of mild pain during the same period. Other risk factors were the long duration of preoperative pain and female sex.

Conclusion Intensity of early postoperative pain and delayed surgery increase the risk of the persistent pain after knee arthroplasty.

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Introduction

Persistent postoperative pain, which is defined as pain lasting for more than 3 months, is today a well known problem independent of the type of surgery.^{1–3} The highest prevalences are reported after leg amputation (60–80%),⁴ thoracotomy and sternotomy (20–50%).^{5–9} Furthermore, routine operations such as mastectomy,¹⁰ hernioplasty,^{11–13} cholecystectomy¹⁴ and caesarean section¹⁵ may also lead to persistent pain in approximately 12–30% patients.

The prevalence of persistent pain after orthopaedic surgery has been the subject of only few studies^{16–24} and the risk factors for persistent pain have been evaluated even more rarely.^{17,18,21–23} The purpose of the present study was to evaluate the degree and the risk factors of persistent pain after knee arthroplasty with a questionnaire in a large, register-based cross-sectional prevalence study. Primary injury influences the intensity of forthcoming pain.^{25,26} The main hypothesis, therefore, was that the type of operation (primary, bilateral, revision) would influence the development of persistent postoperative pain.

Patients and methods

Patients who had undergone knee arthroplasty during the period from 1st September 2002 to 28th February 2004

were recruited from the arthroplasty registry of the arthroplasty specialized hospital. The study was approved by the Ethic Committee of the hospital. Written informed consent was obtained from each patient. The total number of patients was 855. The operation was a primary arthroplasty in 648 patients (75.7%), a bilateral arthroplasty in 137 patients (21.1%) and a revision arthroplasty in 70 patients (8.2%). If a patient was operated several times, the last operation was taken into account. The preoperative pain intensity was evaluated by a surgeon and taken from the hospital registry (none, mild, moderate, severe). All patients were operated on spinal anaesthesia and an epidural catheter was inserted for postoperative pain relief. Epidural analgesia was discontinued on the first postoperative day to ensure early rehabilitation. The early complications such as deep infection and/or dislocation of prosthesis during first 2 months were taken from the hospital registry.

A questionnaire and a consent form with a prestamped return envelope were mailed to all patients in July 2004. In the case of no reply, a reminder was sent once. The time interval between the performed operation and the questionnaire was minimum 4 months and maximum 22 months. The demographics were asked. All the other questions considered preoperative and postoperative pain. The duration of preoperative pain and the intensity of postoperative pain during the first week (mild, moderate, severe, unbearable) were asked. If the patient still was suffering any pain in operated knee while receiving the questionnaire, the pain intensity during rest and exercise was evaluated. The degree of disturbance of daily life and sleep due to pain (none, mild, moderate,

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severe) and the consumption of analgesics for persistent pain at the operated knee were asked.

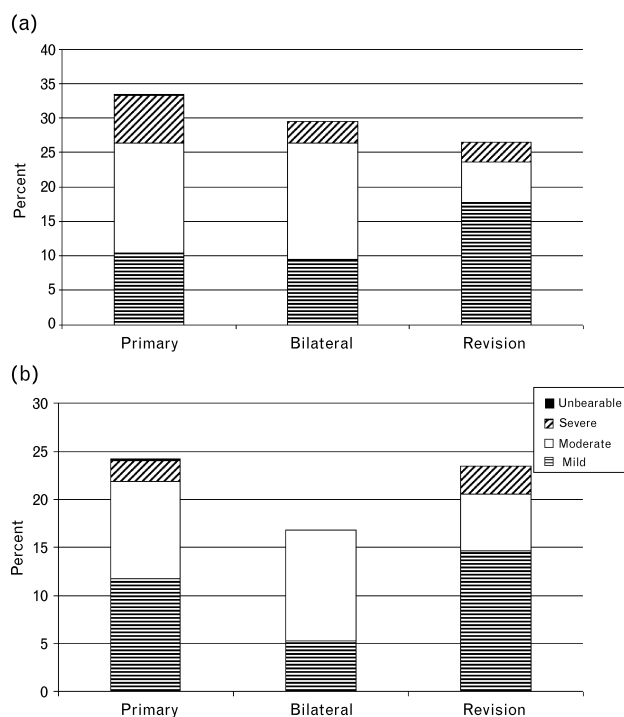
The data from the returned questionnaires and from the hospital registry were analysed using multiple logistic regression analysis. The dependent variable was the pain at the time of the questionnaire. The explanatory variables were treatment, age (centred at the age of 70 years and including a quadratic term), sex, BMI, pain score and duration prior to surgery, pain score during the first week after operation, type of prosthesis and diagnosis. The numeric variables are reported by means with standard deviations (SD) and the categorical variables are presented as absolute and relative frequencies. The results of the univariate and multivariate logistic regressions are presented as odds ratios (ORs) with 95% confidence intervals (CI). *P*-values are also given for univariate analysis. Logistic regression was used instead of linear regression because the object of the study—persistent pain or not—was binomial.

All computations have been made by using R.²⁷

Results

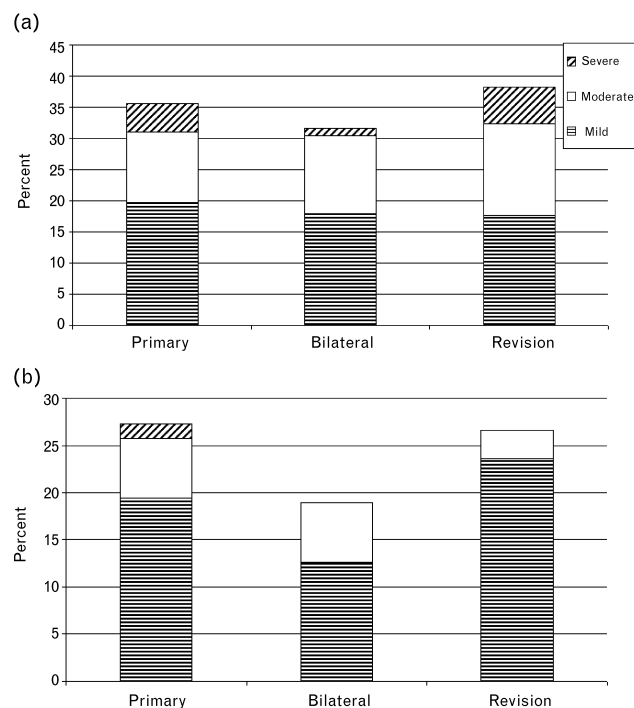
The response rate of the questionnaire was 65.7% in total; 66.8% in the primary arthroplasty group, 69.3% in the bilateral arthroplasty group and 48.6% in the revision arthroplasty group. Pain was not experienced only during exercise (Fig. 1a) but also during rest (Fig. 1b). Thirty-five

Fig. 1



Persistent pain during exercise (a) and rest (b) in primary, bilateral and revision arthroplasty groups. *P*-value is 0.32 (a, b).

Fig. 2



Disturbance of daily life (a) and sleep (b) because of persistent pain in primary, bilateral and revision arthroplasty groups. *P*-values are 0.52 (a) and 0.70 (b), respectively.

percent of patients suffered from daily life disturbing pain (35.6% in primary, 31.6% in bilateral and 38.2% in revision arthroplasty groups, respectively) a minimum of 4 months after the operation (Fig. 2a). Twenty-five percent of patients had disturbances of sleep due to pain (Fig. 2b). The intensity of pain was mostly mild or moderate. The proportion of patients who still used analgesics because of pain in the operated knee was 45.5% after primary arthroplasty, 43.2% after bilateral arthroplasty and 41.2% after revision arthroplasty ($P=0.86$).

The variables listed in Table 1 were all assumed to be risk factors for persistent pain. The results of univariate logistic regressions are presented in Table 2. Backward selection in the multivariate logistic regression left only age and its quadratic term, sex, the duration of pain prior to surgery and early postoperative pain in the final model. Age was entered in the model also quadratically and a possible interaction between age and treatment was considered. According to the primary hypothesis, the operation itself, primary, bilateral or revision arthroplasty and the type of prosthesis, demi-arthroplasty or total arthroplasty, were still left to the final model. The surgical complications checked from the registry were so few that they were left out from the regression analysis. Following Harrell,²⁸ Somer's D_{xy} rank correlation of the final model was 0.50, which corresponds to a value of the area under the Receiver Operating Characteristic

Table 1 Variables evaluated for persistent pain

	Primary N=433	Bilateral N=95	Revision N=34
Age (years; mean±SD)	69.2 (8.9)	65.1 (8.9)	71.2 (10.3)
BMI (kg/m ² ; mean±SD)	29.5 (4.7)	29.6 (4.5)	28.1 (4.0)
Sex F/M (N)	304/129	64/31	28/6
Diagnosis OA/RA (N)	412/12	93/2	30/4
Presurgical pain score N (%); no pain/mild pain	29 (7.0)	4 (4.0)	7 (21.0)
Moderate, occasional pain	219 (51.0)	39 (41.0)	13 (38.0)
Moderate, continuous pain	149 (35.0)	42 (45.0)	9 (26.0)
Severe pain	30 (7.0)	9 (10.0)	5 (15.0)
Presurgical duration of pain	N=419	N=94	N=30
≤12 months N (%)	43 (10.0)	3 (3.0)	5 (17.0)
>12 months N (%)	377 (90.0)	91 (97.0)	25 (83.0)
Early postsurgical pain	N=417	N=93	N=34
Mild N (%)	111 (27.0)	26 (28.0)	14 (41.0)
Moderate N (%)	194 (45.0)	36 (39.0)	14 (41.0)
Severe N (%)	104 (24.0)	26 (28.0)	5 (15.0)
Unbearable N (%)	18 (4.0)	5 (5.0)	1 (3.0)

F, female; M, male; OA, osteoarthritis; RA, rheumatoid arthritis.

(ROC) curve of 0.75. The indices of unreliability and discrimination were $U = -0.0039$ and $D = 0.1443$.

The results of the multivariate logistic regression (OR with 95% CI) are shown in Table 3. ORs for continuous variables refer to one unit changes.

Discussion

The aim of the present study was to find out whether the magnitude of the primary injury, the type of surgery, influences the development of persistent postoperative pain. Logistic regression analysis was chosen to test our hypothesis and to find any other risk factors for the development of persistent pain. Persistent pain after knee arthroplasty was relatively common (35.0%), but the type of surgery did not correlate with pain. Instead, female sex, long duration of pain prior to surgery and high intensity of pain during the first postoperative week led to persistent pain.

Pain is the main indication for knee arthroplasty and pain relief is the most important postoperative outcome. However, there are only few studies concerning persistent pain as an outcome measure after knee arthroplasty,^{16–18,20–22,24} although most studies focus on the survival of prosthesis.

The prevalence of persistent pain in the present study was significantly higher than in the majority of the earlier studies. The study of Brander *et al.*¹⁷ reported 22.6% prevalence of significant pain [Visual Analog Scale (VAS) >4] at 3 months, 18.4% at 6 months and 13.1% at 1 year. In another study the prevalence of moderate pain was 10%, but their time point was at 7 years.²⁰ Lundblad *et al.*²³ reported prevalences that are more in line with our study. The prevalence of persistent pain was 24% at rest and 66% with movement at 18 months after operation.²³

The differences between the studies may be explained by study methods. Pain was not assessed by clinician such

Table 2 Results of univariate logistic regression analysis

Variable	Persistent pain Yes/No (N)	OR	95% CI	P
Treatment; primary	101/304			
Treatment; bilateral	22/70	0.9460	0.5473–1.5844	0.8370
Treatment; revision	7/22	0.9577	0.3695–2.2048	0.9230
Age	130/396	0.9792	0.9580–1.0007	0.0577
BMI	127/388	1.0126	0.9686–1.0580	0.5779
Sex: Male	25/128			
Sex: Female	105/268	2.0060	1.2530–3.3124	0.0049
Diagnosis; RA	6/18			
Diagnosis; OA	124/378	0.9841	0.4026–2.7638	0.9736
Presurgical duration of pain; ≤12 months	5/42			
Presurgical duration of pain; >12 months	122/342	2.9965	1.2677–8.8217	0.0236
Presurgical pain score; no pain or mild	7/31			
Moderate, occasional	59/196	1.3331	0.5876–3.4339	0.5173
Moderate, continuous	48/139	1.5293	0.6639–3.9819	0.3459
Severe	15/24	2.7679	1.0021–8.2608	0.0558
Early postsurgical pain score; mild	11/128			
Moderate	50/179	3.2504	1.6861–6.8002	0.0008
Severe	56/74	8.8059	4.4952–18.6975	<0.0001
Unbearable	13/11	13.7521	5.0873–39.0962	<0.0001

CI, confidence interval; OA, osteoarthritis; OR, odds ratio; RA, rheumatoid arthritis.

Table 3 Results of multivariate logistic regression analysis

Variable	OR	95% CI
Bilateral versus primary arthroplasty	0.8864	0.4802–1.5875
Revision versus primary arthroplasty	1.0904	0.3650–2.8885
Duration of presurgical pain >12 months	2.8431	1.1448–8.6517
Age, centred at 70 years	1.0141	0.9855–1.0434
Age, squared and centred at 70 years	1.0027	1.0007–1.0048
Sex, female	1.9084	1.1434–3.2787
Moderate postsurgical pain versus mild	3.1135	1.5857–6.6186
Severe postsurgical pain versus mild	8.1686	4.0428–17.8303
Unbearable postsurgical pain versus mild	10.6857	3.6304–32.6282

CI, confidence interval; OR, odds ratio.

as in some earlier studies.^{17,20} The patients were able to express their feelings confidentially by the questionnaire used, which might have increased the prevalence of pain. Pain was not graded by VAS^{17,23} but by verbal terms. Mostly patients suffered from mild to moderate pain. The percentile from severe and unbearable pain (up to 21.4%) was more consistent with the study by Brander *et al.*¹⁷

Our strongest risk factor for persistent pain was the intensity of early (the first week) postoperative pain. Earlier studies with knee replacement have not included the intensity of early postoperative pain to their risk analysis, which has left the intensity of preoperative pain as a risk factor.^{17,23} Instead, the study with total hip arthroplasty revealed that persistent postoperative pain was related to the recalled intensity of early postoperative pain rather than the intensity of preoperative pain.²²

Women had an increased risk for persistent pain, which is related to many biological and psychosocial factors as discussed previously elsewhere.^{29,30}

Advanced age seems to reduce the risk of persistent pain after general surgery.^{31–33} In our study, age was not a linear risk factor for persistent pain, which is in line with other orthopaedic studies.^{17,23}

Other factors associated with increased postoperative pain are anxiety and undiagnosed depression,¹⁷ but our questionnaire was not designed to diagnose depression or anxiety.

The hypothesis of this study was that the larger the tissue injury (bilateral versus unilateral arthroplasty group), the higher the prevalence of persistent pain. Surprisingly there was no association in this respect. These results are in line with a previous study³⁴ and support the consensus to offer bilateral knee arthroplasty when needed.

The retrospective nature of data, the response rate (65.7%) and the variable time period from surgery to the questionnaire were the major limitations in the present study. To minimize the effect of retrospectivity, the original size of the study was designed to be large enough to draw conclusions. The response rate can be considered sufficient, but a higher response rate may have been obtained with several reminders. This in turn

would have increased the power of the results. Especially the patients after revision knee arthroplasty were less likely to answer than others and the response rate 48.6% among them could not be regarded high enough. Anyway, the original size of study sample was 855 patients, which is enormous compared with previous prevalence studies.^{17,20,23}

The time interval from surgery to the questionnaire varied from 4 to 22 months. Thus, definition for persistent postoperative pain is filled.³ However, the long time interval for some responders may have affected the memory for preoperative pain. This problem was addressed by gaining the scores for preoperative pain scores from the hospital registry. Moreover, a long interval usually increases the possibility of false negatives,³⁵ which in turn underlies the significance of postoperative pain score as a risk factor for persistent postoperative pain. Altogether a fixed time interval between surgery and the questionnaire would have increased the quality of this study.

Although we found that the intensity of postoperative pain was a strong risk factor for persistent pain, a prospective study with observed pain intensities and the amounts of used analgesics should be carried out to confirm this finding.

Persistent pain after knee arthroplasty seems to be a far more frequent problem than assumed. The preoperative duration of pain and the intensity of early postoperative pain are the risk factors that we are able to influence by our own practice.³ Surgery should be planned before the patients develop long lasting pain conditions and pain management during postoperative period and early rehabilitation should be considered as a challenge for the entire team. Prioritization according these findings is suggested in the healthcare system.

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Appendix

Background:

1. Weight _____ kg
2. Height _____ cm

Pre/Post-surgical status

3. How long did you suffer from pain at the operated knee before surgery? _____ months
4. How much did this pain disturb your daily life?
 - 1 not at all
 - 2 little
 - 3 to some extent
 - 4 a lot
5. How long did you have pain after surgery? _____ weeks/months
6. How would you describe the pain during the first week after the operation?
 - 1 mild
 - 2 moderate
 - 3 severe
 - 4 unbearable

At present

7. Do you still have pain at your operated knee?
 - 1 yes, move to the question 9
 - 2 no (no further questions)
8. Do you have pain at rest?
 - 1 yes
 - 2 no
9. How would you describe the degree of pain at rest?
 - 1 mild
 - 2 moderate
 - 3 severe
 - 4 unbearable
10. Do you have pain at exercise?
 - 1 yes
 - 2 no, move to the question 12
11. How would you describe the degree of pain at exercise?
 - 1 mild
 - 2 moderate
 - 3 severe
 - 4 unbearable
12. How much does this pain disturb your daily life?
 - 1 not at all
 - 2 little
 - 3 to some extent
 - 4 a lot
13. How much does this pain disturb your sleep?
 - 1 not at all
 - 2 little
 - 3 to some extent
 - 4 a lot
14. Do you still use any medicine against post-surgical knee pain? Which? _____