Use of pain medication before and after lumbar discectomy: Longitudinal analysis of a nation-wide cohort

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ABSTRACT

BACKGROUND:

Previous studies have suggested that variation in results of lumbar discectomy depends on careful selection of patients. Numerous factors have been suggested to explain this variation with no direct examinations on this issue. The objective was to examine the use of pain medication before and after lumbar discectomy in patients with back pain.

METHODS:

Prospective occupational cohort study (n=151 618) with linkage to national registers. Of the cohort members, 1 538 (age 44 years) underwent discectomy. Records from purchases of pain medication were obtained during a 3-year period before and after hospital discharge.

RESULTS:

Purchases of pain medication increased during the follow-up period from 9.7 (SD=28.7) to 17.3 (SD=17.3) defined daily doses. Three groups were identified: 1) with constant, relatively low pain medication use; 2) with high use combined with further increases in purchases until the time of surgery and only a slight decrease thereafter; and 3) with a sharp rise in medication use before surgery and a return to no pain medication use approximately six months after the discharge. Non-manual profession (OR 1.34, 95% CI 1.06 to1.69) and open surgery technique increased (OR 1.32, 95% CI 1.04 to 1.67) the probability of being included into the third group.

CONCLUSIONS:

The greater decline in the use of pain medication after discectomy was associated with a sharp rise of that use within six months before surgery. This suggests that lumbar discectomy may benefit especially those with acute or subacute pain within the six-month window.

KEYWORDS

Longitudinal analysis, disc herniation, pain medication

STRENGTHS AND LIMITATIONS OF THIS STUDY

- These results must be interpreted with caution when generalizing them outside the studied sample including only people of working age employed in the public sector.
- Due to limited access to the national registers, some potentially relevant data on the exact indications for surgery, the number of operated levels, the length of operation and stay in a hospital, co-morbidity, and more details on open vs. microscopic surgery could not be included into analysis.
- There were no data available on the duration of symptoms before the surgery, radiologic diagnoses, the level of surgery, possible trauma associated with the onset of pain, or history of addiction.
- It is unclear whether the participants used pain medication for reasons other than back pain, or simply could have refilled a prescription without ever using the medication.
- This is the first study that provides a quantitative evidence on the timing of lumbar discectomy.

FUNDING STATEMENT

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COMPETING INTERESTS STATEMENT

None declared

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DATA SHARING STATEMENT

Due to the national restriction policy, dataset containing register data is not available. Statistical code is partially available on request from the corresponding author.

AUTHORSHIP STATEMENT

MS, KL, JR, ZM, RM, VA, MK and JV contributed substantially to the conception, design and the interpretation of data for the work. VA, MK and JV took the main response for the acquisition of data for the work. MS and VA took the main response for the statistical analysis. MS drafted the work. KL, JR, ZM, RM, VA, MK and JV revised it critically for important intellectual content and finally approved the version to be published. MS, JR, KL, ZM, RM, VA, MK and JV agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

INTRODUCTION

Lumbar discectomy has been a common surgical procedure for several decades with 300 000 procedures conducted in the United States annually [1]. The clinical benefits of discectomy vary greatly, and previous studies have suggested that success of lumbar discectomy depends on careful selection of patients. In some cases, the goal of discectomy is prevention of progressive loss of lower extremity motor function and/or cauda equina syndrome. However, such indications for discectomy are rare compared to the indication of pain and functional improvement in cases of refractory radicular symptoms. Clinical guidelines recommend elective discectomy for patients with remarkable symptoms and signs of radiculopathy with concordant disc herniation identified on imaging, and no response after several weeks or months of conservative therapy [2].

Evidence on factors that predict a successful outcome after lumbar discectomy is increasing. Younger age, sequestered disc fragments, lower level of disability, lack of significant psychological co-morbidity, and unemployed work status have been found to be associated with greater relative advantage from lumbar discectomy [3] [4]. However, the predictive value of pain intensity is unclear as higher preoperative pain intensity has been reported to predict both better and worse outcomes after the surgery [3] [4]. Intact annulus fibrosus (smaller herniation), prolonged sick leave, worker's compensation, and greater severity of preoperative symptoms have been associated with poorer surgical outcomes [4]. The role of side and level of disc herniation, motor weakness, and gender is unclear [4]. The evidence on the superiority of specific discectomy techniques and proper timing for discectomy is inconsistent [5 6 7]. Some reports suggest that prolonged symptom duration is linked to positive outcomes of surgery, while other studies found a positive effect with shorter durations of symptoms [3 4]. It has been suggested that these inconsistencies result from the heterogeneity of surgical timing after the onset of symptoms in the published literature [8], but there are no direct examinations on this issue.

Reduced pain is an important outcome of successful discectomy. To evaluate timing of changes in pain, we examined changes in the amounts of pain medication purchases during a 3-year period before and after lumbar discectomy. We sought to identify different trajectories of pain medication use and examined whether such differences were associated with demographic characteristics or occupation.

MATERIAL AND METHODS

Study population

This study was part of the Finnish Public Sector Study, which is an on-going prospective cohort study of employees working in 10 municipalities and 21 hospitals [9]. This cohort is comprised of 151 618 employees with a job contract of ≥6 months in any year between 1991 and 2005. The participants have been linked to surgical data due to intervertebral disc herniation from the National Care Register for Health Care, maintained by the National Institute for Health and Welfare as well as records of national health registers on purchased prescribed pain medications, maintained by the Social Insurance Institution of Finland. The ethics committee of the Hospital District of Helsinki and Uusimaa approved the study.

Type of surgery and patient characteristics

From the National Care Register for Health Care, we identified all 1 538 cohort members who underwent surgery due to an intervertebral disc herniation between 1996 and 2011. The respondents have been followed also after the termination of their employment contracts. The type of surgery was defined as either microdiscectomy (minimally invasive with a small incision and dilatators) or open lumbar discectomy according to the NOMESCO Classification of Surgical Procedures Version 1.14 by the Nordic Medico-Statistical Committee – ABC 16 and ABC 26, respectively [10]. Age was defined in full years at the time of the surgery. Occupational status was defined according to the International Standard Classification of Occupations[11] and then dichotomized to 'manual' versus 'non-manual'. There have not been any significant change in sick leave regulations during the period of follow-up.

Assessment of pain medication use

National Health Insurance provides coverage for prescription drugs to all (about 5.4 million) residents living in the community. All reimbursed prescriptions are registered in the Finnish Prescription Register managed by the Social Insurance [12]. For each drug, the dispensing date, the World Health Organization Anatomic Therapeutic Chemical (ATC) code and the average daily dosages (Defined Daily Dosages, DDD) are recorded [13]. The following pain medication groups were included into analysis: non-steroid anti-inflammatory drugs (ATC-codes M01A, M01B), paracetamol (N02BE01), opioids (N02A), and some drugs for treating neuropathic pain (gabapentin (N03AX12), pregabalin (N03AX16), and amitriptyline (N06AA09)). Anti-inflammatory drugs specifically for treating rheumatoid arthritis, "osteoarthritis drugs" (e.g. glucosamine), transdermal pain medications, drugs used for treating psychosis and depression other than tricyclic antidepressants, and carbamazepine were excluded. Using 'average daily dose' as a unit, we applied a refill-sequence model to quantify the total duration of the sequence of all refills of pain medication treatment, using 100 DDDs as a maximum for a refill [14 15].

The purchases of pain medication were measured during the following 3-month intervals before and after the day of discharge from the hospital after the lumbar discectomy (‘day 0’):

1) day 0 to 89th day
2) 90th to 179th day
3) 180th to 269th day
4) 270th to 359th day
5) 360th to 449th day
6) 450th to 539th day

Statistical analysis

Group-based trajectory modeling was used to investigate the developmental trajectory (a course of outcome over time) of the pain medication used before and after the surgery. This method is a form of finite mixture modeling for analyzing longitudinal repeated measures data[16-18]. While conventional statistics show a trajectory of average change of outcome over time, group-based trajectory modeling is able to distinguish and describe subpopulations (clusters) existing within a studied population. The trajectories of such subpopulations may differ substantially from each other and from the average trajectory of the entire population. In this study, the procedure consisted of the below steps, described in detail, such that other investigators can easily repeat such analysis:

1) The values of purchased pain medications were skewed due to the overrepresentation of zeroes. Therefore, the values were converted into

their normal logarithms. Further analysis was conducted on that lognormal distribution.

2) Censored (known also as ‘regular’) normal modeling was used with minimum and maximum values set just below the lowest and, respectively, just above the highest values that occurred in the data.
3) The number of subpopulations (clusters) was defined by running the procedure several times with a number of subpopulations from two to six, and choosing the model that demonstrated significant results in at least one regression (linear, quadratic, cubic, etc.) while remaining logically plausible. The graphs of the analyses with a different number of clusters were analyzed visually, checking for the substantial overlap of their 95% CIs. Additionally, the Bayesian Information Criterion (BIC) was used as a criterion to confirm the choice of the quantity of subpopulations considering the lesser BIC appointed to a better model.
4) The order of regression for each subpopulation was defined starting from the second order (quadratic regression) down to the first-order polynomial (linear regression). The highest order was set at the quadratic level based on the assumption that the amount of pain medication may change substantially only once (if at all) during the follow-up – at the time around the surgery. For each subpopulation, the highest-order polynomial with a significant p-value ($\leq$0.05) was retained for further analysis.
5) To assess the probability of group membership by type of surgery and patient characteristics, we used a multinomial logistic regression model

with all predictors – age, occupational status (manual vs. non-manual professions), gender (men vs. women), the year of surgery and type of surgery (microdiscectomy vs open lumbar discectomy) – analysed. The cluster with the largest number of the patients served as the reference category when calculating odds ratios (OR) and 95% confidence intervals (CI).

6) To ensure that a proposed model described the real data reliably, posterior probabilities for assignment to subpopulations were calculated. In other words, we tested the degree of probability that an individual patient – in this real studied population – is assigned to one of the subgroups when using the theoretical model proposed.
7) The baseline characteristics of the subpopulations were compared using the Chi square test for ordinal variables (gender, occupational status, type of surgery) and the Kruskal-Wallis test for a continuous variable (age).

Age was reported as the mean and standard deviation. Occupational status and gender was reported as percentages. All the p-values were reported as 2-tailed values with the level of significance considered to be $\leq$0.05. All the analyses were carried out using Stata/IC Statistical Software: Release 14. College Station (StataCorp LP, TX, USA). The additional Stata module 'traj' was required to conduct group-based trajectory analysis. The module is freely available for both SAS® and Stata software [19].

RESULTS

The 1 538 patients were on average 43.7 (SD 10.8, range 18 to 78) years of age at the time of surgery, and 33% were men and 67% women (Table 1). Forty-seven percent (47%) were employed in non-manual jobs and 53% in manual jobs. There was no loss-to-follow-up, as the data were obtained from a comprehensive national register. On average, the purchase of pain medications increased during the follow-up period from 9.7 (SD 28.7, range 0 to 351.3) to 17.3 (SD 17.3, range 0 to 693.2) defined daily doses (Figure 1). In 1996 (the first year of follow-up), the percentage of microscopic surgery was 16% (10 cases). From 1997 to 2000, the respective percentage was between 46% and 54%. After that, between 2001 and 2011, the share of microscopic surgery increased varying from 57% to 76%.

For different numbers of possible subpopulations (from two to six), BIC estimates varied only slightly from -23,567 to -22,845. A 3-cluster model demonstrated significant p-values for quadratic polynomial with 95% CIs overlapping only slightly on the graph. Thus, further analyses were conducted using 3-clusters (named here ‘A’, ‘B’, and ‘C’ for convenience) with quadratic regression. Of the respondents, 29% belonged to the A cluster, 55% to the B cluster, and 16% to the C cluster (Figure 2). The distribution of the risk factors within the clusters is presented in Table 2. Our model was robust with high average posterior probabilities for all three clusters from 0.89 to 0.95 (Table 3). The odds of correct classification ranged from 16 to 56.

The shapes of trajectories for clusters B and C were very similar, differing from each other only by a variance between the amounts of medication purchased at the beginning and at the end of the follow-up period. Otherwise, they followed the same pattern – mild ascension towards the time of surgery and mild descent thereafter. The shapes of these two trajectories also resembled the shape of the average trajectory for medication purchase in the entire sample. Cluster A showed dissimilar behavior in its trajectory – a sharp rise of medication purchase from a level of zero approximately six months before surgery and an abrupt return to the zero level around six months after the discharge from the hospital.

In the analysis of risk factors, we compared group assignment into A (steep increase and decrease) or C (constantly high medication use) clusters with cluster B (constantly low medical use) as the reference (Table 4). Non-manual profession (OR 1.34, 95% CI 1.06 to1.69) and open surgery technique increased (OR 1.32, 95% CI 1.04 to 1.67) the probability of being included in cluster A. Female gender increased (OR 1.47, 95% CI 1.06 to 2.05) the probability of being included into cluster C. Based on the year of surgery, the patients who underwent the surgery earlier had higher probability to be included into the cluster A. Respectively, those who were operated later belonged more often to the cluster C. The patients belonged to the cluster A were younger while those who were included into the cluster C were older compared to the largest cluster B.

DISCUSSION

In this longitudinal register-linkage cohort study of 1,538 working-aged patients who underwent a lumbar discectomy, three distinct trajectories for purchasing pain medications around the time of surgery were identified: constantly low pain medication use, constantly high pain medication use, and a steep increase and decrease in use of pain medication around the surgery, but not after. Surprisingly, compared to microdiscectomy, open surgical technique increased the likelihood of presenting pain medication according to the trajectory with a steep decrease in use of pain medication after the surgery.

These results must be interpreted with caution when generalizing them outside the studied sample. Due to limited access to the national registers, some potentially relevant data on the exact indications for surgery, the number of operated levels, the length of operation and stay in a hospital, co-morbidity, and more details on open vs. microscopic surgery could not be included into analysis. There were also no data available on the duration of symptoms before the surgery, radiologic diagnoses, the level of surgery, possible trauma associated with the onset of pain, or history of addiction. It is also unclear whether the participants used pain medication for reasons other than back pain, or simply could have refilled a prescription without ever using the medication. In addition, the sample included only people of working age employed in the public sector.

Despite these weaknesses, the study may provide important and novel insight into factors related to different patterns of pain chronicity as reflected by medication use in patients undergoing lumbar discectomy [20]. The least successful outcome related to individuals who used pain medications long before the surgery and who continued using analgesics well after the surgery. Women were more likely to belong to this group than men. We also identified a group of patients who used pain medication at the time of surgery, but not six months before or six months after. It can be assumed that pain escalated within six months of surgery, and then the pain decreased over the subsequent six months after the discectomy. Because the peak and the abrupt descent in the purchase of pain medications was positioned at the time of surgery, the surgery was likely to cause the pain and the outcome appeared to be successful. That the use of pain medication was not anymore needed after six months from the surgery is consistent with previous studies suggesting superior outcomes after lumbar discectomy amongst patients with acute or sub-acute pain [8 21-31]. The unexpected finding was that this pattern was observed more commonly in relation to open rather than microscopic surgery, and it characterized patients with manual rather than non-manual occupations. It is uncertain why more traumatizing open technique produced a better outcome than a less injuring microsurgical procedure. It also remained unclear why individuals employed in non-manual jobs seemed to recover faster compared to those engaged in non-manual occupations.

The data studied reflected the situation until 2011. Further analysis including data gathered after 2011 may alter the conclusions about casual effects.

Conclusions

The present data indicate that a subpopulation of individuals who undergo lumbar disc surgery demonstrate a rapid increase and subsequent decrease in the purchase of pain medication. This suggests that lumbar discectomy may benefit especially those with acute or subacute pain within the six-month window. In the studied cohort, open surgical technique and a non-manual profession seem to increase such positive outcomes. Constant high pain medication use before and after surgery, an unsuccessful outcome, was more common in women than in men.

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FIGURE/TABLE LEGENDS

Figure 1. Mean trajectory of purchase of pain medications before and after the surgery in the total population.

Pain medication purchases are shown on a lognormal scale.

Figure 2. Group-based trajectory analysis of the purchases of pain medication before and after the surgery for an intervertebral disc herniation.

The 95% confidence intervals are shown as tiny dash lines. Pain medication purchases are shown on a lognormal scale.

Table 1. Distribution of the risks within the sample.

Table 2. Distribution of the risks within the identified clusters

Table 3. Posterior probabilities for belonging to the identified clusters

Table 4. Probability of group membership depending on age, gender, occupation, year of surgery, and surgery technique.

Odds ratios (OR) and 95% confidence intervals (95% CI) derived from a multinomial logistic regression model with all parameters adjusted for each other. The reference group is cluster B (55% of the entire sample).