Prolonged opioid use after single-level lumbar spinal fusion surgery in a Belgian population: a multicentric observational study

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Title:

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Abstract:

Purpose:

Lumbar spinal fusion surgeries are increasingly being performed in spinal degenerative disease, often accompanied by perioperative opioid prescriptions. The aim of this study is to analyze prolonged postoperative opioid use following a standardized opioid prescription after single-level lumbar spinal fusion surgery in a Belgian population

Methods:

This prospective, multicentric observational study included patients undergoing single-level lumbar fusion surgery for degenerative disease. A standardized postoperative opioid protocol (Targinact 2x10mg/5mg, Paracetamol 4x1g and Ibuprofen 3x600mg) was applied uniformly. Prolonged opioid use was defined as continued opioid use six months after surgery. Patient data were collected using the Back-App®.

Results:

Among 198 participants, 32.8% continued opioid use six months post-surgery, with 8% utilizing strong opioids. Prolonged opioid use correlated with lower pre-operative back pain. Patients with prolonged opioid use and strong opioid use at six months show less improvement in disability compared to patients without prolonged opioid use. Moreover, patients with prolonged strong opioid use tend to have lesser improvement of the low back pain. The odds for prolonged opioid use decrease with the increase of the improvement in ODI.

Conclusion:

1 in 3 patients undergoing single-level lumbar spinal fusion surgery is at risk for prolonged opioid use. The study underscores the importance of tailored pain management strategies, particularly given the rising prevalence of spinal fusion surgeries. The association between pre-operative low back pain, post-operative improvement in functionality (ODI), and prolonged opioid use emphasizes the need for judicious opioid prescribing practices and highlights the role of functional outcomes in treatment goals.

1. Introduction

Low back pain (LBP) is a major public health issue affecting more than 90% of humanity at some point during their lives [1, 2]. A considerable number of patients continue suffers from chronic LBP [3]. In case of lumbar disc degeneration and/or degenerative spondylolisthesis lumbar spinal fusion surgery can be considered to improve back pain [4]. Pre-operatively pain management can be challenging. Some physicians have the tendency to prescribe opioids for chronic (non-cancerous) LBP. Based on Cochrane meta-analytic data there is only very low to moderate-quality research describing the short-term efficacy of opioids compared to placebo for chronic LBP [5].

A task force of the European Pain Federation (EFIC) concludes that Europe is not facing an opioid epidemic [6]. Although opioid prescription has been increasing in Europe, the increasing use has not yet reached the proportions observed in the United States and Canada. However, in a report published by the Organisation for Economic Co-operation and Development (OECD), Belgium is the country with the third highest daily use of opioids per million inhabitants within Europe. In 2018, 10% of the Belgian population used one of the following opioid analogs: tramadol, tilidine, oxycodone, fentanyl or piritramide [7].

Since the amount of spinal fusion surgery is increasing with less invasive procedures and extending surgical indications, the use of opioids in preoperative and post-operative pain management is questionable. Spinal fusion surgery might be associated with high risk of persistent postoperative opioid use [8, 9]. A recent systematic review concluded that preoperative opioid use is associated with negative surgical and functional outcomes, including postoperative opioid use [10]. Furthermore, more patients receive long-term opioids after spinal surgery than before surgery [11].

When surgery is considered in chronic LBP patients, the primary goal for the patient and the physician is to reduce pain and regain functionality. A reduction of pre-operative pain medication should be a related goal, in particular a reduction in opioid use. Long-term efficacy has not been proven, nor is it advised in current guidelines for non-cancerous LBP [5, 12].

The aim of this study is to evaluate post operative opioid use after a standardized opioid prescription following single-level lumbar spinal fusion surgery in a Belgian population. These results will provide insight in the opioid use/disuse in spinal fusion surgery in a Belgian population in which, based on the OECD report, opioid usage is concerningly high.

2. Methods

2.1. Study design and population

This study is a prospective, multicentric observational study, part of the ongoing real world data collection in spinal pathology. Patient population was selected in three Belgian neurosurgical centers. Patients were included if they met the following criteria: (a) 18 years or older, (b) selected for single-level posterior lumbar fusion surgery (PLIF, MPLIF or TLIF) after failure of conservative measurements for lumbar degenerative disease and (c) capable of giving written informed consent. The exclusion criteria included multiple level spinal surgery, minimally invasive spine surgery (XLIF, DLIF or OLIF), spinal fractures, spinal infections, cancer related fusion surgery and opioid use for another condition than spinal degenerative disease.

2.2. Data collection and outcome measures

Patients from daily practice, undergoing single level lumbar spinal fusion surgery, were informed and requested to participate study. Patient characteristics and outcome measures were collected by a patient driven application, the Back-App®. This application allows to collect both general information and specific questionnaires from patients at the spine unit before their appointment with the physician. The informed consent is signed electronically on a tablet. General patient characteristics recorded consist of age, gender, employment status, duration of symptoms and the use of pain medication (WHO classification).

Pain scores were measured with a visual analogue scale (VAS) for back and leg pain. Additionally, the pain-catastrophizing scale (PCS) was used to evaluate the catastrophizing impact of the experienced pain. The pain vigilance and awareness questionnaire (PVAQ) was used to measure preoccupation with pain. The Oswestry Disability Index was used to investigate the sciatica-related disability [13]. The health-related quality of life was measured using the EuroQol 5-dimensions questionnaire (EQ-5D) [14].

Six months after spinal fusion surgery patients were asked about their pain (VAS back and leg), functioning (ODI) and quality of life. The use of pain medication was documented. Tramadol was defined as weak opioid. Oxycodon and/or other opioid equivalents were reported as strong opioids. Improvement in VAS score was calculated as pre-operative VAS minus post-operative VAS. Improvement in ODI was calculated as pre-operative ODI minus post-operative ODI. QOL was calculated as post operative EQ-5D minus pre-operative EQ-5D.

The primary outcome in this study is long-term opioid dependance. Long-term opioid use is defined as continued intake of opioids (strong and/or weak opioids) after 6 months of follow-up. All variables influencing this long-term dependance will be evaluated to identify risk factors of chronic opioid use after single-level spinal fusion surgery and a standardized post operative opioid prescription protocol.

2.3. Post operative opioid protocol

All patients were prescribed a standardized pain protocol post-operatively. The protocol consists of Paracetamol 1000mg 4x/day, Ibuprofen 600mg 3x/day and Targinact 10mg/5mg (oxycodon 10mg/naloxone 5mg) 2x/day. Oxynorm (oxycodon hydrochloride) 5mg subligual tablets are prescribed as rescue medication. Patients were educated on the use of opioids and the need to reduce the use at home during the recovery period. All treating physicians share the same objective to reduce medication (opioid) post-operatively as soon as reasonably possible.

2.4. Statistical analysis

All statistical analyses are conducted with IBM SPSS Statistics or an equivalent validated statistical analysis software.

Continuous variables are reported as mean and standard deviation and discrete variables as numbers and percentages.

The Shapiro-Wilk test was used to validate a normal distribution of the data. Unpaired two-sample t-tests were used for normally distributed data. If not, the Mann-Whitney U test was used. The Pearson's Chi squared test was used for categorical variables. Baseline variables and outcomes after six months are compared for patient with prolonged opioid use in comparison with patients without prolonged opioid use to identify risk factors.

A logistic regression was conducted analyse the association between chronic opioid use. Results will be corrected for confounding by standard model building.

Significant findings are reported and include p-values (p<0,05) and confidence intervals as appropriate.

2.5. Ethics

Each participating center's institutional ethics committee approved the study. The study is conducted in accordance with good clinical practice (GCP) and the ethical principles in the Declaration of Helsinki adopted by the 18th World Medical Assembly in Helsinki, Finland in 1964 and amended by subsequent assemblies. Subjects were free to withdraw at any point in the study.

3. Results

In total 198 patients undergoing single-level spinal fusion surgery were included in this study. The mean age was 54 (±13) and 68,7% of the study population was not working at the time of inclusion. Females comprised 51% of the patients. Mean pain scores for back and leg pain were 6,6 (± 2,3) and 6,2 (±2,4) respectively. The mean ODI was 19,51 (±9,1) with a quality of life of 0,51(±0,3) on the EQ-5D.

Six months after spinal fusion surgery 65 patients (32,8%) continued using opioids (weak and strong opioids). 8% (16) of the patient population or 24,6% of the patient with prolonged opioid use remained using strong opioids.

Patients with prolonged opioid use (weak and strong) and prolonged strong opioid use had a lower pre-operative VAS for backpain. These results are summarized in table 1.

When comparing the improvement after spinal fusion surgery, patient with prolonged opioid use (weak and strong opioids) had significantly less improvement in back pain and disability (ODI). In the group with prolonged strong opioid use mean improvement in ODI showed an

increase of disability after six months (+4,75±15,76), compared to a decrease in ODI in patients without prolonged opioid use (-4,54±9,97). In this group the improvement in back pain was also less than compared to the patients without prolonged opioid use.

There was no difference in pre-operative opioid use between patients with or without prolonged opioid use. 49,2% of patients who continued the use of both weak and strong opioids were taking opioids pre-operatively. In the group with prolonged strong opioid use, no patient was using strong opioids pre-operatively. As a result, 10% (16/158) of patients without pre-operative exposure to strong opioids have prolonged strong opioid use after 6 months.

Table 2 gives an overview on the odds ratio derived from a logistic regression on prolonged opioid use and prolonged strong opioid use. A multivariate analysis revealed no interacting or confounding variables. The odds ratio for prolonged opioid use and prolonged strong opioid in association with the improvement in ODI was 0,95 (95% CI: 0,92 – 0,98) and 0,92 (95% CI: 0,88 – 0,97) respectively. This indicated that an improvement in ODI reduces the odds (factor 0,95 and 0,92) of continuing opioids or strong opioids after six months.

When investigating the relationship between the quality of life (QOL) and the likelihood of prolonged strong opioid use, we observed an odds ratio of 0.20 (95% CI: 0,04 – 0,93). This result suggests that for every one-unit increase in the EQ5D score, the odds of prolonged strong opioid use decreased by a factor of 0.20.

Based on this logistic regression figures 1 and 2 illustrate the predicted probability of prolonged opioid use and prolonged strong opioid use based on the ODI improvement after six months after spinal fusion surgery.

4. Discussion

The current study analyzes the incidence and risk factors for prolonged opioid use after standardized opioid prescription after single-level spinal fusion surgery. Overall, 32,8% of the study population continued both weak and strong opioid use until six months after surgery. About one out of four patients with prolonged opioid use or 8% of the study population is using strong opioids at six months.

The risk for prolonged opioid use seems to be associated with pre-operative LBP and post operative improvement in LBP and disability (ODI). Patients with prolonged opioid use and strong opioid use at six months show less improvement in post operative disability compared to patients without prolonged opioid use. Moreover, patients with prolonged strong opioid use tend to have lesser improvement of the LBP.

The odds for prolonged opioid use after six months decrease with the increase of the improvement in ODI based on logistic regression. The odds for prolonged strong opioid use also decrease with the increase of the improvement in ODI and QOL.

Belgium is the country with the third highest daily use of opioids per million inhabitants in Europe [7]. This should make surgeons think about the responsible use and prescription of opiates for spinal fusions. Fusion surgery may be associated with significant post operative pain due to tissue/muscle dissection, vertebrae manipulations and placement of implants [15]. These patients require adequate post operative pain management, in which opioids are

often being prescribed [12]. Moreover, patients undergoing fusion surgery are often being treated with opioids pre-operatively for their chronic back pain.

In a recent systematic review and meta-analysis several pre-operative risk factors for prolonged opioid use after fusion have been identified. Post-operative opioid use tends to be associated with pre-operative opioid use, drug and alcohol abuse, psychiatric disorders, depression, history of smoking and female gender. Overall this meta-analysis reports a pooled prevalence of prolonged opioid use of 40,23% [16]. This is somewhat higher than 32,8% in our study. The definition of prolonged opioid use differs amongst the different studies included and ranges from three months to one year of follow-up [16]. These rates of chronic opioid use after lumbar spine surgery are considerably higher than the overall estimated risk of 6,7% for prolonged opioid use after all surgeries. One could hypothesize that patients with low back pain are more likely to develop pain catastrophizing behavior with central sensitization as a risk factor for opioid abuse and dependence [17, 18]. Studies have shown that patients with chronic pain and central sensitization are more likely to experience persistent postoperative pain and may have a higher risk of prolonged opioid use. [17, 19] However, the current data shows no association between pre-operative pain catastrophizing or awareness (i.e. suffering) and post-operative opioid use after six months.

Pre-operative opioid use has been designated as major risk factor for prolonged post-operative opioid use, with an estimated 6-fold risk [11, 16, 20-22]. Chronic pre-operative opioid use is also associated with less likelihood to return to work and an increased length of stay [23]. Deyo et al. estimates that 77% of patients with long-term pre-operative opioids continued opioid use long-term post-operatively. [11] In comparison, 57% of our patients

with pre-operative opioid use (weak and strong) continued opioid use after six months. However, the current data indicates that pre-operative opioid use is not associated with prolonged post-operative opioid use. Hence, in the group with prolonged strong opioid use, all patients had no pre-operative use of strong opioids. They represent 10% of all strong opioid-naïve patients. Cook et al. reported comparable rates of the development of chronic opioid use, with 15-18% in opioid-naïve individuals and 50-64% in chronic opioid users [24]. The finding that all patients with prolonged strong opioid use had no pre-operative use of strong opioids suggests that other factors, besides prior exposure, may play significant roles in the dependence on stronger opioids postoperatively. Possible explanations could include inadequate pain control with weak opioids, the availability of strong opioids in this standard protocol or higher levels of post operative pain.

Previous studies focused on sociodemographic and comorbidities as risk factors. The current study is innovative as it included a variety of patient reported outcomes (PROMs) at baseline and after treatment to investigate associated risk factors. Pre-operative back pain was lower in patients with prolonged opioid use, as was the improvement in back pain after surgery. The difference in back pain between these groups might be significant, but not clinically relevant as the difference is less or just equal to the minimal clinically important difference (MCID) threshold in patient with chronic back pain [25]. On the other side, patients with less pre-operative back pain might be used to less pain and as a result use more opioids post operative. Next, the improvement of functionality (ODI) plays an important role as a risk factor for prolonged opioid use. In a recent patient profile analysis by Raymaekers et al. in patients with lumbar disc herniation, a decrease in functionality (ODI) was also associated with an increase in the use of opioids. Therefore, the registration of PROMS could guide

physicians in establishing treatment for their patients. Based on this data, preserving and/or improving patients' functionality could be an effective prevention measure for chronic postoperative opioid use.

Moreover, surgeons should adopt several strategies to minimize the likelihood of long-term opioid use. Preoperative patient education about the expected course of pain and recovery, setting realistic expectations about postoperative pain can reduce post operative opioid use [26]. Next, implementing a multimodal pain management approach that combines non-opioid medications (e.g., acetaminophen, NSAIDs), regional anesthesia techniques, non-pharmacologic interventions (e.g., physical therapy, cognitive-behavioral therapy) and neuromodulation techniques can effectively control pain while minimizing opioid consumption [27, 28]. Hence, attention should be given to opioid-sparing medications, such as gabapentin or nerve blocks, that can provide effective pain relief without the need for long-term opioids. These medications can be part of the perioperative pain management plan, reducing the initial and sustained need for opioids [28, 29]. Post operatively the treating physician should develop a structured opioid tapering plan that gradually reduces opioid dosage [30]. In each stadium of pain management in spinal pathology, involving a multidisciplinary pain team, including pain specialists, psychologists, and physical therapists, can provide comprehensive pain management and support the transition away from opioids [31].

The results should be interpreted considering the studies limitations. Firstly, the study is an observational study without a control group. Secondly, the study focusses on a Belgian population. This study's findings may not be directly generalizable to all European countries due to variations in opioid prescribing practices and differences in pain management.

However, the results can serve as a relevant example for countries with opioid use patterns similar to Belgium. Additionally, these findings can act as a cautionary indicator for countries where opioid use has not yet reached comparable levels, emphasizing the need for proactive measures to prevent a potential rise in opioid dependency. Lastly, the study's follow-up period of six months may not capture long-term trends or fluctuations in opioid use beyond this timeframe. However, chronic opioid use has been defined as the use beyond three months in literature [32].

5. Conclusion

A significant portion of patients (32,8% and 8% for both weak and strong opioid or strong opioids respectively) is at risk for prolonged opioid use after single-level lumbar spinal fusion surgery in Belgium.

The study emphasizes the necessity for cautious opioid prescription practices amid the rising number of spinal fusion surgeries. The association between pre-operative LPB, post-operative improvement in functionality (ODI) and prolonged opioid use emphasizes the importance of tailored pain management strategies. Therefore, all spine surgeons have an obligation to reduce the use of opioids when reasonably possible and guard the patients functionally before and after surgery.

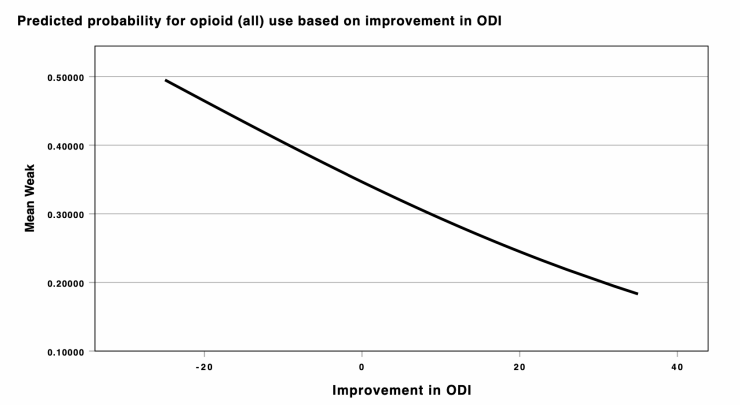

Figure 1: predicted probability of prolonged opioid use (weak and strong) based on logistic regression.

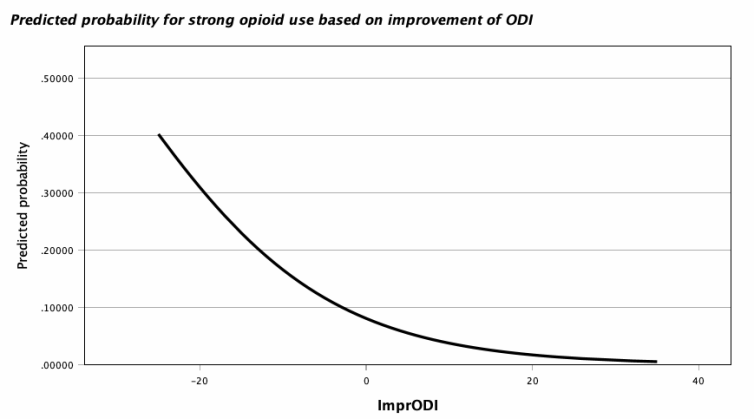

Figure 2: predicted probability of prolonged strong opioid use based on logistic regression

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