Impact of COVID-19 on opioid use in those awaiting hip and knee arthroplasty: a retrospective cohort study

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ABSTRACT

Background COVID-19 has had a detrimental impact on access to hip and knee arthroplasty surgery. We set out to examine whether this had a subsequent impact on preoperative opioid prescribing rates for those awaiting surgery.

Methods Data regarding patient demographics and opioid utilisation were collected from the electronic health records of included patients at a large university teaching hospital. Patients on the outpatient waiting list for primary hip and knee arthroplasty as of September 2020 (COVID-19 group) were compared with historical controls (Controls) who had previously undergone surgery. A sample size calculation indicated 452 patients were required to detect a 15% difference in opioid prescription rates between groups.

Results A total of 548 patients (58.2% female) were included, 260 in the COVID-19 group and 288 in the Controls. Baseline demographics were similar between the groups. For those with data available, the proportion of patients on any opioid at follow-up in the COVID-19 group was significantly higher: 55.0% (143/260) compared with 41.2% (112/272) in the Controls (p=0.002). This remained significant when adjusted for confounding (age, gender, Scottish Index of Multiple Deprivation, procedure and wait time). The proportion of patients on a strong opioid was similar (4.2% (11/260) vs 4.8% (13/272)) for COVID-19 and Controls, respectively. The median waiting time from referral to follow-up was significantly longer in the COVID-19 group compared with the Controls (455 days vs 365 days; p<0.0001).

Conclusion The work provides evidence of potential for an emerging opioid problem associated with the influence of COVID-19 on elective arthroplasty services. Viable alternatives to opioid analgesia for those with end-stage arthritis should be explored, and prolonged waiting times for surgery ought to be avoided in the recovery from COVID-19 to prevent more widespread opioid use.

INTRODUCTION

Hospitals worldwide were forced to restructure when the COVID-19 pandemic called for an immediate significant shift towards prioritisation of acute care.[1] This led to widespread postponement of elective orthopaedic procedures in concordance with the need for resource reallocation, as well as concerns over risk of nosocomial infection transmission and the impact of COVID-19 on surgical risk.[2]

While these changes have served to 'flatten the curve' and reduce some of the harm associated with COVID-19 infection, there has undoubtedly been an impact on patients whose elective procedures were postponed. Patients awaiting hip and knee arthroplasty, as one of the most common elective procedures, have been disproportionally affected.[3] It has been estimated that over 6 million elective orthopaedic procedures were cancelled worldwide during the first peak of the pandemic.[4] With continued delays in the provision of timely total hip and knee arthroplasty expected for some time due to the considerable backlog of patients awaiting surgery, patients will need to seek alternative treatment options to manage their symptoms.

Opioids are often used as a last line for symptomatic pain management in end-stage osteoarthritis.[5] However, there is increasing evidence for limited benefit[6] and long-term detriment to health,[7] especially in older adults.[8] More specifically within the arthroplasty population, long-term opioid use preoperatively has been associated with increased risk of perioperative complications,[9 10] poorer functional outcome[11 12] and ongoing opioid dependence postoperatively.[13 14]

Increased risk of opioid harm has been identified in unscheduled care clinical settings associated with the COVID-19 pandemic,[15 16] but it is currently not understood how the associated increase

in waiting times for surgery has influenced routine preoperative opioid prescribing for patients awaiting elective operations.

We have therefore set out to address this important clinical question through a comparative study of opioid utilisation presurgery in a historical cohort versus patients on the waiting list for primary hip and knee arthroplasty whose surgery has been delayed secondary to COVID-19.

With evidence that surgical delay associated with the COVID-19 pandemic has led to a deterioration in arthritis severity, associated pain and reduced quality of life,[17] we hypothesise that this will be associated with increasing use of opioid analgesia within the population awaiting surgery to manage this exacerbation of symptoms preoperatively.

METHODS

Study design, setting and participants

We undertook a retrospective cohort study of patients awaiting primary hip and knee arthroplasty at a large university teaching hospital in Scotland. Using a theatre management system (Centricity Opera, GE Healthcare, Chalfont St Giles, UK), two groups were identified: those on the outpatient waiting list for surgery (as of September 2020) who had their operation delayed due to COVID-19 (COVID-19 group) and a historical comparison of patients that had previously been on the outpatient waiting list and had been operatively managed between 2016 and 2017 (Controls). Patients in the COVID-19 group had been added to the waiting list between May 2019 and April 2020, whereas patients in the Controls were added between December 2014 and August 2017. The timeframe for the Controls was chosen due to feasibility of data access and availability. Previous analysis of unpublished data had not identified a temporal trend in incidence regarding opioid prescription for arthroplasty patients prior to the COVID-19 pandemic (online supplemental table 1). Exclusion criteria included patients undergoing other types of arthroplasty operation (eg, unicompartmental arthroplasty, revision arthroplasty or arthroplasty at other anatomical sites), patients in the Controls who did not undergo operative management and patients in the COVID-19 group that had been added then removed from the waiting list as of September 2020 (start of data collection period). No patient in the COVID-19 group had yet undergone surgery at the time when data collection was performed (September 2020–October 2020).

Standard practice at the study centre pre-COVID was that patients would be referred from general practice and then reviewed by orthopaedic surgeons to determine their eligibility for arthroplasty surgery. Patients would then be added to the waiting list for surgery if eligible. A further pre-assessment clinic review was then performed 2–4 weeks prior to surgery. The timeframe from date of referral from general practice to orthopaedic review was typically 3–6 months. The timeline from addition to the waiting list to date of surgery was usually about a further 3–9 months, dependent on individual surgeon waiting list length.

Data collection

A preformatted data collection proforma was used for data extraction. Data were obtained from the patient electronic health record, which included patient demographic data, waiting list details, clinical letters (including referral details), linked primary care prescribing records (Scottish National Prescribing Information System) and pre-assessment documentation (where applicable).

Variables included in the data collection proforma were as follows:

Demographic

This includes age, gender and Scottish Index of Multiple Deprivation (SIMD).

Pharmacological

On opioid at referral, on opioid at follow-up, type of opioid (strong (morphine/diamorphine/fentanyl/oxycodone/buprenorphine/hydromorphone/tapendadol/methadone) vs weak (codeine/dihydrocodeine/tramadol)), as defined in the British National Formulary.[18] All combination productions containing any of the above-described medications were also classified as opioids.

Process of care

This includes date of referral, date of follow-up (presurgery) and time from referral to follow-up.

Medical

This includes history of anxiety or depression and site of operation (hip vs knee).

Sample size calculation

An a priori sample size calculation was performed using a freely available online tool.[19] A sample size calculation indicated a minimum of 452 patients were required to detect a 15% difference in opioid prescription between groups at $p<0.05$% and 90% power with a baseline expected outcome proportion of 50% in the Controls. The expected proportion of opioid prescription in the controls was extracted from the unpublished data outlined in online supplemental table 1, where a mean proportion of 55% for any opioids was observed between 2012 and 2017. A slightly lower value was chosen to avoid overestimation given the opioid prescription proportion was lower in the latter half of this study period.

Statistical analysis

Initial data scoping was performed to identify the presence and type of missing data extracted. Missing

data were present in <0.5% fields with no evidence of missing data not at random; therefore, a decision was made that no formal data imputation techniques were required. Pairwise deletion was used to manage missing data fields, with no patient excluded due to missing data.

Baseline assessment of covariates was then performed using a Student's t-test for normally distributed continuous data, a Mann-Whitney U test for non-normally distributed continuous data and a χ^2 test for categorical data.

Comparisons between waiting time from referral to follow-up was also performed. For patients in the COVID-19 group, this was the date of referral from the general practitioner to the time of individual patient data collection (September–October 2021). For patients in the Controls, this was the date of referral from the general practitioner up to the date of surgery. Waiting times were identified as non-normally distributed from a Shapiro-Wilk test, and therefore, a Mann-Whitney U test was performed.

Finally, comparative analysis between the number of patients on an opioid at referral and at follow-up was performed using a χ^2 analysis. Multivariable logistic regression was used to assess the potential impact of preidentified confounders (age, gender, SIMD, procedure, history of anxiety and depression, and wait time) on the results.

All statistical analyses were performed using SPSS for Windows (V.24.0, SPSS). In all analyses, $p<0.05$ denoted statistical significance.

Ethics

Our study was conducted in accordance with the Declaration of Helsinki 1964 and its later amendments. Given the nature of the study as a retrospective review of anonymised patient data, ethical approval was not required. Data storage and analysis was undertaken in alignment with the Caldicott principles—the data guardianship regulations governing the use of patient data in the UK. There was no external funding source for the study. The study has been reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.

RESULTS

Patients' demographics

A total of 548 patients (58.2% female) was included in our study, 260 in the COVID-19 group and 288 in the Controls. Of those individuals, 295 were listed for primary hip arthroplasty (53.8%) and 253 for primary knee arthroplasty (46.2%). The mean age was 69 years (range 22–95). The median SIMD was 7 (IQR 5–9) (indicating lower than average deprivation compared with national levels). Out of 548 patients, 121 (22.0%) presented with a previous diagnosis of anxiety/depression or both.

Table 1 Comparisons of demographics of the COVID-19 and Controls groups

	COVID-19 (n=260)	Controls (n=288)	P value
Gender			0.11
Female	142 (54.6%)	177 (61.5%)	
Male	118 (45.3%)	111 (38.5%)	
Age, mean	69	68	0.39
Procedure			0.10
TKR	130 (50.0%)	123 (42.7%)	
THR	130 (50.0%)	165 (57.3%)	
SIMD, median	7 (IQR 6–9)	7 (IQR 5–9)	0.77
History of anxiety/depression	48 (18.4%)	73 (25.3%)	0.05

Table created by the authors.
SIMD, Scottish Index of Multiple Deprivation; THR, total hip replacement; TKR, total knee replacement.

The characteristics of the studied patients are summarised in table 1. Overall, both groups shared similar demographics characteristics, although there was a weak association for higher anxiety and depression in the Controls (p=0.05).

Median waiting time

There was a significant increase in the waiting time of patients being referred until presurgical follow-up. Median time for follow-up from referral in the COVID-19 group was 455 days (IQR 368–626) vs 365 (IQR 238–519) days in the Controls, a 90-day difference (p<0.001).

Change in opioid use

Table 2 illustrates the volume of opioids used by patients in the COVID-19 group and Controls at referral and at follow-up. Formal statistical comparisons of the differences between weak and strong opioid groups were not performed due to low absolute numbers. The proportion of patients on a strong opioid at follow-up was however similar (4.23% (11/260) vs 4.80% (13/272)) for the COVID-19 group and Controls, respectively.

At referral, the percentage of patients on any opioid in the COVID-19 group was 12 percentage points lower than in the Controls (40.6% vs 52.6%, respectively, p=0.005). This remained significant when adjusted for potential confounding (age, gender, SIMD, procedure, history of anxiety and depression, and wait time) (online supplemental table 2).

However, at follow-up, the COVID-19 group demonstrated an upward trend in any opioid use, while the Controls showed a downward trend (table 2). Final percentages of opioid utilisation at follow-up were 13.8 percentage points higher in the COVID-19 group versus the Controls (55.0% vs 41.2%, respectively, p=0.002). This again remained

Table 2 Difference in opioid utilisation between the COVID-19 groups and Controls at referral and at follow-up

	COVID-19 (n=260)	Controls (n=288)	P value
Percentage of patients on opioid at referral (95% CI) (n)			**0.005**
Weak opioid	38.6% (32% to 44%)(98/254)	49.8% (44% to 56%)(143/287)	
Strong opioid	2.0% (0% to 4%) (5/254)	2.8% (1% to 5%)(8/287)	
Any opioid	40.6% (35% to 47%)(103/254)	52.6% (47% to 58%)(151/287)	
Percentage of patients on opioid at follow-up (95% CI) (n)			**0.002**
Weak opioid	50.8% (45% to 57%)(132/260)	36.4%(31% to 42%)(99/272)	
Strong opioid	4.2% (2% to 7%)(11/260)	4.8% (2% to 7%)(13/272)	
Any opioid	55.0% (49% to 61%)(143/260)	41.2% (35% to 47%)(112/272)	

Table created by the authors.
The denominator for numbers (n) of patients included at each stage reflects data availability for each specific subgroup.

significant when adjusted for potential confounding (online supplemental table 3).

DISCUSSION

This study suggests a marked negative impact of the COVID-19 pandemic on patients awaiting joint replacement in relation to delay to surgery and opioid use. We identified that patients were required to wait longer for their surgery (88-day difference in median wait time from referral to follow-up), and a significantly larger proportion of patients were prescribed opioid-based analgesia (14 percentage points more in the COVID-19 group compared with our historical Controls) preoperatively, despite a lower frequency of opioid use at referral. Given the previously known associations between preoperative opioid use and poorer perioperative surgical outcomes,[9–14] urgent attention is required to identify alternative effective non-operative treatment strategies or expedite operative intervention for those awaiting arthroplasty surgery. Increasing use of opioid medication routinely within this healthcare setting may also have larger long-term consequences for public health.[20]

The justification for the increasing use of opioid analgesia in those awaiting arthroplasty surgery is limited, although this may be related to the lack of strong evidence for other pharmacological solutions for arthritic pain and/or a response to difficulties in alleviation of patient suffering. There is, however, some evidence that non-steroidal anti-inflammatory medication provide at least similar analgesic efficacy to opioids for osteoarthritis and have a better safety profile, particularly when considering topical formulations.[21] Intra-articular injections are another alternative, with some evidence for short-term pain relief from corticosteroid injection,[22] hyaluronic acid,[23] protein-rich plasma[24] and saline.[25] There are, however, concerns about the potential risks for side effects with these treatments, including deterioration in arthritis severity,[26] and postoperative infection,[27] that limit their use perioperatively.

Non-pharmacological interventions such as physiotherapy,[28 29] use of offloading braces in the knee setting[30] and neurological ablation therapy[31] have also been identified as having a potential role to improve symptoms in end-stage osteoarthritis. High-quality evidence for benefit is however lacking, although the side-effect profile from such interventions is likely different from any pharmacological alternatives.

Given the lack of viable alternative to joint replacement surgery, it is imperative that the recent significant increase in the waiting list is addressed.[32] There is substantial evidence available for the mental, physical and economic negative impact of extended surgical waiting times in arthroplasty patients, in both the short and long term.[33–37] A recent paper by Clement *et al*[17] has shown that a significant proportion of those patients awaiting hip and knee arthroplasty are now classified, according to their self-reported EuroQOL 5 Dimension (EQ-5D) questionnaire scores, as in a health state 'worse than death'; with the vast majority reporting symptom deterioration associated with surgical delays secondary to the COVID-19 pandemic. While restarting elective services has to be taken in the context of overall hospital workflow, there is evidence for the relative safety of undertaking arthroplasty procedures with appropriate protocols in place,[38] and that the majority of patients wish to proceed with surgery in view of the relative benefit and risk involved.[39] Given the vast backlog of patients awaiting surgery accumulated secondary to the pandemic, it will likely take several years of increased activity before a return to normality is realised. This once again therefore highlights the importance of reducing where possible the preoperative opioid prescribing for these patients as evidenced by our research.

The strengths of our study include broadly similar cohorts from before and during the pandemic. We also provide adjustment for known confounders to attempt to ensure the associations seen are a true reflection of clinical practice. The results provided likely represent an underestimate of true effect given that the proportion of patients on an opioid at referral was significantly higher in the Controls, and also the fact that no patients in the COVID-19 group had yet undergone surgery, indicating the potential for further individuals to be started on opioids associated with ongoing delays.

It is, however, possible that the analysis is skewed by unadjusted confounders and accuracy of clinical information recorded within the electronic health record, as well as the possible interference of the COVID-19 pandemic on psychological and social lives of patients. Historical data collection sources, however, retained accuracy due to electronic records' lack of susceptibility to recall bias. Use of a historical cohort may also add potential bias within treatment and group effects, although no previous temporal trends were identified in the supplemental data. No data were available regarding timing of opioid prescription in relation to waiting time which could have helped better define any temporal trends in a relationship between surgical delay and opioid use. It should also be noted that data from the COVID-19 group were truncated (as the patients had not yet undergone surgery), and therefore, these results are an underestimate of the actual difference in median waiting time. We were also unable to examine the doses and strengths of medication prescribed to and consumed by patients to provide a more nuanced reflection on opioid consumption.

Overall, we feel that the sample provides a realistic reflection of current practice that is likely applicable to similar healthcare systems, particularly given that disruption to elective orthopaedic services was a widespread occurrence at a national level during the pandemic. It, however, must be emphasised that due to the nature of the study design no causality can be determined in relation to the associations identified between increasing opioid use and the COVID-19 pandemic.

Further analyses using larger scale national data samples consisting of surgical and prescribing data will be of use to confirm the associations seen here and provide additional insights into the dosage, frequency and type of opioid prescriptions used that we were unable to elicit in our analysis.

CONCLUSION

Despite a suggested reduction in opioid use at referral, COVID-19 has been associated with a higher proportion of patients prescribed opioids that has potential to invoke short-term and long-term patient harm. Viable alternatives to opioid prescription for those awaiting surgery must be urgently identified, with a widespread public health message to prescribers about the negative consequences of long-term opioid prescribing in arthroplasty patients. Prolonged waiting times for surgery should be avoided in the recovery from COVID-19 to prevent more widespread opioid use in this population, particularly in sight of the documented lack of clinical efficacy, large side effect profiles and potential for long-term opioid dependence.

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Contributors LF: Research idea development, data acquisition, data analysis, results interpretation and drafting/revision of the paper. He is the guarantor. WTG: Research idea development, data acquisition, drafting/revision of the paper. CCT: Data acquisition, drafting/revision of the paper. RL: Data acquisition, drafting/revision of the paper. PF: Research idea development, results interpretation, drafting/revision of the paper. GPA: Research idea development, results interpretation and drafting/revision of the paper.

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