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### Increasing Doses of Intraoperative Hydromorphone Do Not Reduce Postoperative Pain

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## Introduction

- Intermediate and long acting opioids are given intraoperatively to reduce pain during emergence from anesthesia.
- Recent evidence suggests that intraoperative opioids have inconsistent effects on nociception and pain in the immediate postoperative period.<sup>1,2</sup>
- Multiple potent, short-acting opioids such as remifentanyl, sufentanyl and fentanyl<sup>1,2</sup> have been shown to produce dose-related increases in pain scores and opioid consumption in the immediate postoperative recovery period.<sup>3</sup>
- Intraoperative doses of longer acting opioids such as morphine<sup>4,5</sup> and methadone<sup>6</sup> have been shown to reduce pain scores and narcotic requirements in the immediate postoperative period.
- Hydromorphone is an intermediate duration narcotic which is commonly used intraoperatively but has not been studied for its potential to reduce pain in the immediate postoperative period.<sup>4-6</sup>

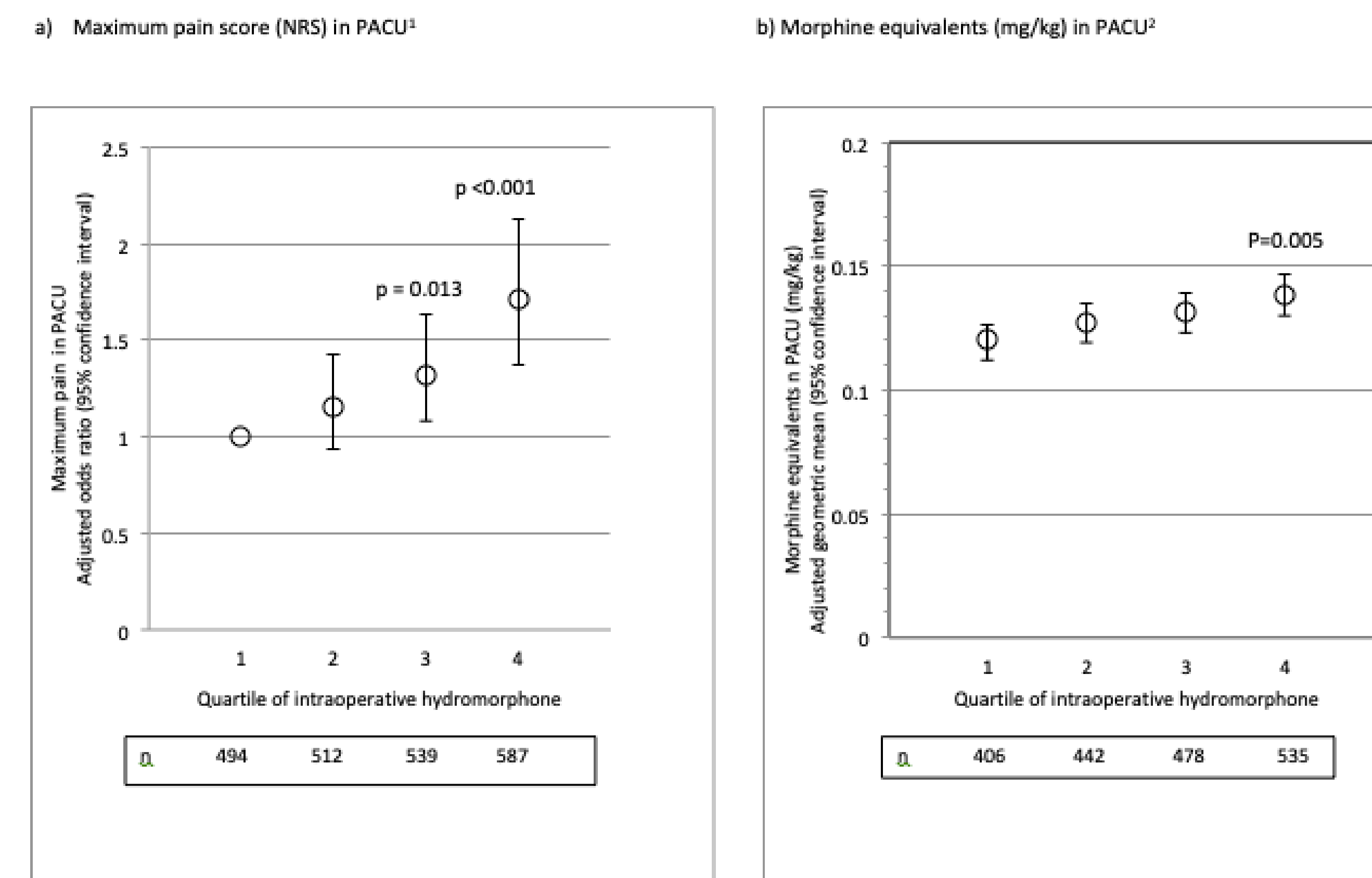
## Methods

- After Institutional Review Board approval, clinical, demographic, and anthropometric data were retrospectively extracted from the electronic health records of all patients who underwent total hip or knee surgery under general anesthesia at Maine Medical Center between 12/3/12 and 5/1/17.
- Patients were grouped into quartiles based on intraoperative hydromorphone dose.
- Pain scores were routinely assessed in the post anesthesia care unit (PACU) using 0-10 numeric rating score (NRS).
- Bivariate analysis was used to identify possible factors associated with pain score and narcotic consumption in the PACU for inclusion in regression analysis.
- Ordinal regression analysis was used for assessing impact on pain score and analysis of covariance was used for assessing impact on narcotic consumption in the post anesthesia care unit (figure 1).

## Results

- 3519 (1023 knee and 2496 hip) cases were found eligible for inclusion.
- The median dose of hydromorphone given during the study period was 8.3 [5.5-11.0] µg/kg.
- Preoperative pain score, age, gender, body mass index, duration of surgery, type of surgery, intraoperative doses of hydromorphone and fentanyl were all found to have significant associations with pain score and narcotic consumption.
- Increasing intraoperative hydromorphone dose had an adjusted dose-related direct correlation with increased postoperative pain scores and narcotic consumption (figure 1).

Figure 1: Adjusted relationships between intraoperative hydromorphone dose, and maximum pain score and total morphine equivalents in PACU



Abbreviations: NRS, numerical rating scale; PACU, post-anesthesia care unit

Quartile 1 2 3 4  
Hydromorphone (µg/kg) 3.95 [0.00-5.54] 6.89 [5.55-8.27] 9.67 [8.29-11.02] 12.97 [11.08-34.45]

- The 3519 surgeries were performed by 3 hip surgeons and 11 knee surgeons; variation in maximum PACU NRS among surgeons was significant in both groups (p<0.001)
- The same variables that were significantly associated with maximum NRS in PACU were also associated with total opiate dose in PACU.

## Discussion

- Most providers use longer acting narcotics such as hydromorphone, morphine or methadone during surgery in part to provide an analgesic effect in the early postoperative period.
- Both morphine<sup>4,5</sup> and methadone<sup>6</sup> have previously been shown to be effective in this regard.
- In our study, increasing intraoperative doses of hydromorphone was independently associated with increased maximum pain score and opioid dosing in the PACU.
- One possible explanation for a lack of effect of hydromorphone may be the timing or the magnitude of the intraoperative doses. It is possible that the hydromorphone was given too early or in too small a dose and the analgesic effect had worn off. This would not explain the paradoxical effect.
- This paradoxical effect could represent acute tolerance (AT) or opioid-induced hyperalgesia (OIH). Each phenomena is associated with higher than expected pain levels and opioid requirements following acute opioid administration.
- This is an observational study limited by its retrospective nature. The findings were of a very small effect of intra-operative hydromorphone dose on post-operative pain scores and opiate consumption that reached statistical significance through the large number of cases examined.

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