Pain, Opioids, and Confusion After Arthroplasty in Older Adults

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BACKGROUND: Postoperative confusion is a common complication in older adults, particularly after total joint replacement (arthroplasty). Confusion after surgery can result in slower mobility progression, longer hospital stay, and increased patient distress. Postoperative pain has been shown to be a risk factor related to confusion; however, there is limited evidence regarding pain level, medication use, and confusion development in postoperative arthroplasty patients.

PURPOSE: To evaluate development of postoperative confusion and the current practice of pain management for older adult patients with hip or knee arthroplasty.

METHODS: Two-month retrospective chart review of medical records at a large, Midwestern, private hospital. Pain assessments were performed on a regular basis using self-report 11-point Numeric Rating Scale (0–10). Opioid use was scored using an equianalgesic conversion chart.

RESULTS: Ninety-eight patients met inclusion criteria and 97 received treatment with opioids during the first 48 hours postoperatively. No patients received opioid agents that are contraindicated in older adults. Thirty-three patients had evidence in the medical record of confusion during the first 48 hours postoperatively. Lower equianalgesic dose was significant for increased age and increased confusion on postoperative day 1 (POD 1) and POD 2. Patients with higher equianalgesic scores were less likely to meet benchmark pain scores less than 5 on POD 0, POD 1, and POD 2.

CONCLUSIONS: Patients receiving lower amounts of opioids in the first 48 hours after surgery were more likely to be confused on POD 1(p = .023) and POD 2 (p = .049).

Acute confusion is common among patients undergoing both cardiac and noncardiac surgery (Thornlow, Anderson, & Oddone, 2009). Postoperative confusion is associated with slower hospital discharge, more frequent complications, higher rates of discharge to nursing homes, and higher mortality (Brooks, 2012; Voyer, McCusker, Cole, St-Jacques, & Khomenko, 2007; Wilcox et al., 2010). Rates of confusion have been shown to increase with age as well as other variables such as blood loss and comorbidities (Kalisvaart et al., 2006; Vaurio, Sands, Wang, Mullen, & Leung, 2006).

Pain is also a major issue for older adults following surgery. Postoperative pain is a risk factor for the development of, and slower recovery from, postoperative confusion (Brooks, 2012; DeCrane et al., 2011). Research has shown that postoperative pain scores are a better reflection of risk for delirium development than is opioid use, with higher Visual Analog Scale scores leading to higher rates of delirium among patients with similar doses of hydromorphone (Leung et al., 2009). In patients with hip fracture, severe pain has been found to increase risk of delirium as many as nine times (Morrison, Magaziner, Gilbert, et al., 2003), and avoiding opioids or using very low doses increases the risk of delirium in patients with hip fracture (Sieber, Mears, Lee, & Gottschalk, 2011).

Appropriate assessment and treatment of pain after orthopaedic surgery have been shown to shorten length of stay and improve mobility (Morrison, Flanagan, Fischberg, Cintron, & Siu, 2009; Morrison, Magaziner, McLaughlin, et al., 2003). Greater understanding of the relationship between pain management and cognitive status in older adults is needed, as evidence indicates that nurses' knowledge of and behavior toward pain management are key

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components for successful recovery from surgery (Dihle, Bjolseth, & Helseth, 2006; Ene, Nordberg, Bergh, Johansson, & Sjostrom, 2008; Wilson, 2007).

Conceptual Framework

Delirium is an approved diagnosis of the *Diagnostic and Statistical Manual of Mental Disorders* (American Psychiatric Association, 2000); however, many patients have episodes of mental status disruption after surgery that either resolve prior to physician diagnosis or do not meet the full diagnostic criteria of the *Diagnostic and Statistical Manual of Mental Disorders* (Elie et al., 2000; Inouye, Foreman, Mion, Katz, & Cooney, 2001). This leads to missed or underreported cases that are significant at the clinical, point-of-care level. For this reason, the broader definition of "confusion" is used in the context of this study.

The conceptual framework for this study is the "cognitive reserve" model that uses variability among persons and reduced resilience to changes or stressors to explain confusion episodes in the aging brain (Jones et al., 2010). Pain acts as a stressor or stimulus that disrupts cognitive processing of other information. In addition, several studies have shown that undertreatment of pain is more likely to be associated with postoperative confusion than use of opioids (Lynch et al., 1998; Morrison, Magaziner, McLaughlin, et al., 2003, Morrison, Magaziner, Gilbert, et al., 2003; Sieber et al., 2011). As a result, clinical decision-making by nurses becomes a complex task including understanding the risks and benefits of appropriate medication administration in older adults, as well as patient-specific variables that increase the chances of an adverse event (Thornlow et al., 2009).

Evidence-based guidelines exist for acute pain management in older adults (Herr, Bjoro, Steffensmeir, & Rakel, 2006). These guidelines address many issues that clinicians confront when providing care to older adults as well as a list of opioid analgesics recommended for acute pain, including morphine, hydromorphone, oxycodone, fentanyl (not in patch form), and hydrocodone (Herr et al., 2006; Pasero & McCaffery, 2011). Tramadol may also be used with caution in older adults for mild to moderate acute pain (Herr et al., 2006). Based upon this framework, the purpose of this study was to examine the following aims:

1. Are older adult patients receiving analgesia with recommended opioid medications for use in acute (surgical) pain?
2. What is the incidence of confusion among postoperative hip and knee arthroplasty patients?
3. Is higher equianalgesic dosage of opioids associated with improved pain scores (≤5)?
4. Is lower equianalgesic dosage of opioids associated with more confusion?

Methods

The institutional review board approval was obtained for retrospective access to electronic medical records (EMRs). Medical record staff of a large, Midwestern private hospital identified a 2-month sample (n = 106) of patients with procedure codes for both elective or trauma-related hip or knee arthroplasty. Eight patients were below the age of 50 years and were excluded, making a sample size of 98. An audit form was created for data collection on the basis of literature review and experience of team members. These variables included age, sex, body mass index (BMI), surgery type (hip or knee), transfusions received, American Society of Anesthesiologists (ASA, 2013) physical classification score, and anesthesia type. Age was recorded by category of 50–69, 70–79, or ≥80 years; BMI was recorded as underweight or normal (<25), overweight (25–30), or obese (>30); and ASA score was dichotomous as either I-II or III-IV. Anesthesia type was obtained from the operating room record; all patients had received either general or intrathecal anesthesia.

Patients on the orthopaedic unit who were able to self-report had used an 11-point Numeric Rating Scale (0–10 NRS) with 0 being the absence of pain and 10 being the worst pain possible. For the purpose of this study, pain scores were recorded as a dichotomous variable of less than 5 or 5 or more. All pain scores were recorded for each of three 24-hour postoperative periods: the operative day (POD 0), first postoperative day (POD 1), and second postoperative day (POD 2). Opioid use was recorded for POD 0, POD 1, and POD 2, including medication name, dose, route, and frequency. Confusion was defined as any narrative or mental status assessment in the EMR that indicated a change in mental status or confused behavior/statements. Two members of the research team completed all audits from the data provided. Using an equianalgesic chart (Pasero & McCaffery, 2011), the principal investigator (S.D.) converted opioid doses to equianalgesic units (Pasero & McCaffery, 2011, p. 443) for 24-hour periods on surgical day (POD 0), POD 1, and POD 2. One equianalgesic unit was considered to be morphine 10 mg i.m./s.c./i.v., morphine 30 mg p.o., fentanyl 100 mcg i.v., hydrocodone 30 mg p.o., hydromorphone 1.5 mg i.v. or 7.5 mg p.o., or oxycodone 20 mg p.o.

Data were analyzed using SAS 9.3 (SAS Institute, Inc., Cary, N.C.). Descriptive statistics such as frequency, mean, and standard deviation were computed. Associations between confusion and other variables were performed using bivariate comparison with chi-square tests for categorical variables, Mantel-Haenszel chi-square test for ordinal variables, and Student's t tests under unequal variances for continuous variables. Bivariate analyses were conducted to compare confusion to pain scores on POD 0, POD 1, and POD 2.

To investigate the association of equianalgesic use score by each day, bivariate associations were conducted using chi-square tests or Fisher's exact tests for categorical variables, Mantel-Haenszel chi-square test for ordinal variables, and Student's t tests under unequal variances for continuous variables. Because equianalgesic use score is highly skewed to the right, we also performed Wilcoxon or Kruskal–Wallis nonparametric tests to examine the association between equianalgesic and other variables. P values < .05 (two-tailed) were considered statistically significant.

Results

Descriptive and demographic findings are reported in Table 1. Patients in this study were more likely to be female (67%; $n = 66$) with approximately one third of patients in each age range. The average BMI was 30.5, with nearly half of the sample in the obese category (≥30). Surgery type was fairly equal between hip (55%; $n = 53$) and knee (45%; $n = 44$). Most patients had comorbidities that placed them in ASA category III or IV (70%; $n = 67$). Only 2 patients received postoperative packed red blood cell transfusions, and more patients received intrathecal (77%; $n = 75$) than general (23%; $n = 23$) anesthesia.

To answer the first aim, of 98 patients, 95 (97%) patients received opioids during the first 48 hours after arthroplasty that included morphine, hydromorphone, hydrocodone, fentanyl, and oxycodone; two patients received tramadol as first-line pain management. One patient from the sample of 98 had no evidence in the EMR of receiving pain medication in the first 48 hours. One patient was receiving methadone in addition to short-acting opioids. No patients received contraindicated opioids, including meperidine, pentazocine, nalbuphine, butorphanol, or dezocine (Pasero & McCaffery, 2011).

To answer the second aim, of the sample of 98 patients, 33 (34%) had evidence in the medical record of disrupted mental status during the first 48 hours postoperatively. Of those 33 patients, 20 (60%) had a delirium diagnosis documented in the physician notes. Bivariate comparisons between confusion and other surgical factors were not significant for gender (p = .216), BMI (p = .145), blood loss (p = .372), or postoperative homologous transfusions (p = 1.00). Bivariate comparisons were significant for hip surgery (p = .010), ASA category of III or IV (p = .020), and general anesthesia (p = .008). Bivariate associations related to confusion and pain scores for each surgical day were not significant (POD 0, p = .312; POD 1, p = .595; (POD 2, p = .125). Results of the bivariate comparison values for postoperative confusion are reported in Table 2.

The third and fourth aims, to compare equianalgesic dosage of opioids to other variables in the study, indicated that lower equianalgesic dosage of opioids was associated with more confusion on POD 1 (p = .023) and POD 2 (p = .049). In addition, lower equianalgesic dose was more likely to be associated with higher age at all three time points (POD 0, p = .019; (POD 1, p = .001; (POD 2, p = .019). Pain scores, when compared to equianalgesic dose at each time point, indicated that patients with higher pain scores were more likely to have received more opioids throughout the first 48 hours after surgery. Table 3 displays the results of daily equianalgesic dose on other variables in the study and for each postoperative day (POD 0, POD 1, POD 2).

TABLE 1. SUBJECT CHARACTERISTICS

	N (%) or *M* ± SD
Gender	
Male	32 (33%)
Female	66 (67%)
Age (years)	
50–69	34 (34%)
70–79	35 (36%)
≥80	29 (30%)
Body mass index	30.3 ± 6.9
Underweight or normal (<25)	20 (22%)
Overweight (25–29.9)	27 (30%)
Obese (≥30)	43 (48%)
Surgery type	
Hip	53 (55%)
Knee	44 (45%)
ASA	
I-II	29 (30%)
III-IV	67 (70%)
Transfusions	
Yes	2 (2%)
No	85 (98%)
Anesthesia	
General	23 (23%)
Intrathecal	75 (77%)

Note. $N = 98$. ASA = American Society of Anesthesiologists.

Discussion

The findings of this study suggest that treatment of pain using appropriate opioids in older adult patients is not associated with increased postoperative confusion. In fact, patients who received lower equianalgesic doses of approved opioid medications had higher rates of confusion on POD 1 and POD 2, suggesting that opioids contributed more benefit than harm. There were, however, some interesting limitations that indicate the need for more research. Our finding that lower equianalgesic dose was associated with more confusion could indicate that keeping medication use low may increase the likelihood of postoperative confusion, or that confused patients were less likely to receive opioids. We suspect the possibility of both; in fact, anecdotally we did find orders to "hold" opioids when confusion episodes were reported. More research using prospective designs is needed to determine whether more aggressive management of pain after surgery reduces the incidence of delirium in the first 48 hours.

Our finding that incidence of confusion was not statistically related to higher pain scores of 5 or more for any postoperative day (see Table 2) is possibly related to a design flaw in that we recorded pain as a dichotomous variable of less than 5 or 5 or more. The choice to use dichotomous pain level scoring was determined because less than 5 was the benchmark for pain control for discharge from perianesthesia care units (ASA, 2004), and previous research by members of our team had shown that pain scores of 5 or more were associated with slower recovery from postoperative delirium (DeCrane et al., 2011). Our findings would suggest that opioid consumption and cognitive function impairment

TABLE 2. BIVARIATE ASSOCIATION BETWEEN VARIABLES AND CONFUSION

	Confusion Documented by Nurse, Mean ± SD or N (%)			
Variable	Yes (n = 33)	No (n = 65)	Test Statistic$_{[df,N]}$	p
Gender			$\chi^2_{[1,N=98]} = 1.60$	.216
Male	8 (25%)	24 (75%)		
Female	25 (38%)	41 (62%)		
Age (years)			$\chi^2_{M[1,N=98]} = 4.17$	.041
50–59	8 (24%)	26 (76%)		
70–79	11 (31%)	24 (69%)		
≥80	14 (48%)	15 (52%)		
Body mass index			$\chi^2_{[2,N=90]} = 3.86$	.145
Underweight or normal (<25)	9 (45%)	11 (55%)		
Overweight (25–30)	11 (41%)	16 (59%)		
Obese (≥30)	10 (23%)	33 (77%)		
Surgery type			$\chi^2_{[1,N=97]} = 6.60$	.010
Hip	24 (45%)	29 (80%)		
Knee	9 (20%)	35 (80%)		
ASA			$\chi^2_{[1,N=96]} = 5.41$	.020
I–II	5 (17%)	24 (83%)		
III–IV	28 (42%)	39 (58%)		
Blood loss (ml)			$\chi^2_{[1,N=84]} = 0.80$	.372
<200	15 (31%)	34 (69%)		
≥200	14 (40%)	21 (60%)		
Transfusions			Fisher p = .45	1.000
Yes	1 (50%)	1 (50%)		
No	28 (33%)	57 (67%)		
Anesthesia			$\chi^2_{[1,N=84]}$	.008
General	13 (57%)	10 (43%)		
Intrathecal	20 (27%)	55 (73%)		
Pain on day of surgery			$\chi^2 = 1.02$	.312
<5	19 (59%)	30 (48%)		
≥5	13 (41%)	32 (52%)		
Pain on postoperative Day 1			$\chi^2 = 0.28$	.595
<5	6 (19%)	9 (15%)		
≥5	26 (81%)	53 (85%)		
Pain on postoperative Day 2			$\chi^2 = 2.35$	.125
<5	12 (38%)	29 (23%)		
≥5	20 (63%)	35 (77%)		

Note. Sample size not reaching n = 98 is due to data unavailable. χ^2 = Chi-square test statistic with 1 degree of freedom. Fisher p = Fisher's exact total probability.

are more likely related to undertreatment of pain rather than the medications themselves (Sieber et al., 2011). This is also consistent with earlier research that patients receiving low doses of morphine, or having higher levels of pain, were at increased risk of developing delirium (Morrison, Magaziner, Gilbert, et al., 2003).

More research is needed to further explore clinician experience and beliefs related to opioid risk in older adult patients, particularly if clinicians have misconceptions of "anticholinergic risk." A systematic review addressing the cognitive impact on older adults of anticholinergic medications, termed "anticholinergic burden,"

TABLE 3. BIVARIATE ASSOCIATION BETWEEN VARIABLES AND EQUIANALGESIC USE SCORE BY EACH DAY

	Day of Surgery			Postoperative Day 1			Postoperative Day 2		
Variable	Mean ± SD (*n*)	Test Statistic	*p*	Mean ± SD (*n*)	Test Statistic	*p*	Mean ± SD (*n*)	Test Statistic	*p*
Confusion		$t_{95.0} = -0.70$	.486		$t_{92.6} = -2.32$	.023		$t_{95.0} = -1.99$	.049
Yes	1.02 ± 1.90 (33)	$W = 1435.0$	.137	1.91 ± 1.60 (33)	$W = 1288.0$	.011	1.21 ± 1.88 (33)	$W = 1242.0$	.004
No	1.40 ± 3.41 (65)			3.22 ± 3.97 (65)			2.43 ± 4.16 (65)		
Age (years)		$F_{2,95} = 4.16$	.019		$F_{2,95} = 7.44$	.001		$F_{2,95} = 4.16$	.019
50–59	2.42 ± 4.82 (34)	$\chi^2_{KW} = 19.76$	<.0001	4.34 ± 5.21 (34)	$\chi^2_{KW} = 29.32$	<.0001	3.37 ± 5.51 (34)	$\chi^2_{KW} = 21.87$	<.0001
70–79	0.81 ± 0.60 (35)			2.55 ± 1.23 (35)			1.59 ± 1.15 (35)		
≥80	0.49 ± 0.69 (29)			1.24 ± 1.03 (29)			0.96 ± 1.93 (29)		
Body mass index		$F_{2,87} = 1.30$	.277		$F_{2,87} = 2.31$	.105		$F_{2,87} = 2.45$	.093
Underweight or normal	0.65 ± 0.63 (20)	$\chi^2_{KW} = 4.77$	.092	1.68 ± 1.07 (20)	$\chi^2_{KW} = 8.81$	.012	0.78 ± 1.04 (20)	$\chi^2_{KW} = 14.02$	.001
Overweight	1.00 ± 1.02 (27)			2.49 ± 1.52 (27)			1.83 ± 2.05 (27)		
Obese	1.86 ± 4.33 (43)			3.51 ± 4.49 (43)			2.92 ± 4.97 (43)		
Pain on day of surgery		$t_{45.1} = -2.30$	.026		$t_{50.6} = -2.66$	.011		$t_{49.3} = -2.31$	.025
<5	0.59 ± 0.50 (49)	$W = 2581.0$	.001	1.92 ± 1.32 (49)	$W = 2609.0$	.001	1.23 ± 1.27 (49)	$W = 2553.5$	.002
≥5	2.05 ± 4.25 (45)			3.83 ± 2.43 (45)			2.99 ± 4.98 (45)		
Pain on postoperative Day 1		$t_{88.8} = -2.33$	.022		$t_{75.8} = -3.56$	.001		$t_{91.1} = -3.40$	.001
<5	0.53 ± 0.43 (15)	$W = 542.5$	.081	1.33 ± 1.10 (15)	$W = 393.0$	.001	0.73 ± 0.62 (15)	$W = 446.5$	.007
≥5	1.43 ± 3.29 (79)			3.12 ± 3.69 (79)			2.33 ± 3.93 (79)		
Pain on postoperative Day 2		$t_{77.4} = -2.06$	.042		$t_{92.0} = -2.56$	.012		$t_{85.5} = -2.81$	.006
<5	0.62 ± 0.64 (26)	$W = 998.0$	.047	1.80 ± 1.48 (26)	$W = 893.5$	.005	0.95 ± 1.08 (26)	$W = 863.5$	.002
≥5	1.54 ± 3.52 (68)			3.23 ± 3.91 (68)			2.50 ± 4.18 (68)		

Note. W = Wilcoxon nonparametric test statistic. χ^2_{KW} = Kruskal–Wallis nonparametric chi-square test statistic with degrees of freedom of 2. t_{df} = Student's t test under unequal variance. *df* = degrees of freedom. $F_{df1, df2}$ = one-way ANOVA. df_1 = degrees of freedom of numerator, df_2 = degrees of *f*.

found that 25 of 27 studies statistically supported this relationship (Campbell, Boustani, et al., 2009). Similar research has focused on quantification of "cholinergic burden" by agent, along with recommendations for clinicians in the form of the Anticholinergic Risk Scale (Rudolph, Salow, Angelini, & McGlinchy, 2008) and the Anticholinergic Burden (ACB) Scale (Campbell, Boustani, et al., 2009). Consensus has not been reached for the impact of opioid medications and anticholinergic risk. The Anticholinergic Risk Scale as developed does not contain opioids (Rudolph et al., 2008). Morphine and codeine are listed as "mild" on the ACB Scale (Campbell, Boustani, et al., 2009). Additional research has demonstrated that certain medications are associated with increased risk of confusion in older adults, including the analgesics meperidine, butorphanol, dezocine, nalbuphine, and pentazocine (Pasero & McCaffery, 2011). None of those agents were used in the subjects within our sample. A cohort study by Campbell, Perkins, Hui, Khan, and Boustani (2011) found no relationship between delirium development and agents on either the "possible" or "definite" lists of the ACB Scale. Dissemination of findings from our study and others does not support holding recommended opioids in older adults because of confusion (Morrison, Magaziner, Gilbert, et al., 2003; Sieber et al., 2011). Information for point-of-care clinicians would identify "best practice" as promoting adequate pain control using appropriate opioids. Considerable variation in adverse effects of opioids in older adults by specific agent provides limited guidance for clinicians (Solomon et al., 2010).

A positive finding was that postoperative older adults are receiving pain management using appropriate medications recommended in current guidelines. Although tramadol is recommended for use "with caution" in older adults for "mild and some moderate pain" (Herr et al., 2006), many factors determine patient-specific responses to agents used in postoperative pain management. Our study had no information available as to previous patient response or preference for specific agents that could have influenced prescribing practices. Tramadol is widely used and has been shown to be well tolerated and effective in use with older adults (Freye & Levy, 2006; Likar et al., 2006). More research is needed that could help in determining whether previous experiences of both patients and clinicians influence the success of postoperative pain management. Patients often have individual factors and histories that could be incorporated into the postoperative pain management plan, making patients more active participants in care.

Limitations

Because this study was retrospective, we cannot draw conclusions related to the temporal relationship between confusion, opioid medication, and pain scores. In addition, the study only captured confusion that was documented; this is likely to result in "underreporting" rather than overreporting; however, this provides further emphasis on the need for intervention-level studies.

The quality of the EMR documentation determined our information about confusion. Because we used de-identified data, this study was limited on the amount and type of data we had available for analysis, including additional risk factors. Some information was not available with the level of access that was provided.

The decision to report pain as a dichotomous variable appears to have led to "ceiling effects" in that some analysis cells for the <5 group were 6 or lower, making statistical comparisons difficult. As a result, our group plans to reexamine the benchmark of less than 5 (11-point NRS) as an appropriate benchmark for the first 48 hours after arthroplasty. The 11-point NRS is ideal for use in clinical settings because of its simplicity and quick use. Further research could match 11-point NRS scores to more precise measures of pain to determine whether to keep, discard, or adjust the benchmark for optimal surgical outcomes. Likewise, our decision to combine ASA scores to categories I/II or III/IV was done to prevent small cell sizes during analysis from each score being done separately. Given that we did find significance between the dichotomous groups, our further research should focus on determining other differences between ASA groups.

Conclusions

Pain management is a complex process that requires decision making based on factors and current evidence-based recommendations. The finding that lower equianalgesic opioid dosing was associated with higher rates of confusion on POD 1 and POD 2 demonstrates the importance of pain management for the experiences of older surgical patients. Given that increases in arthroplasty surgeries are expected in the future, research is needed to determine the decision-making factors that result in positive patient outcomes.

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