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REPORTS OF ORIGINAL INVESTIGATIONS

Effect of cultural background and healthcare environment on postoperative opioid requirement

Effet du contexte culturel et de l'environnement de soins sur la demande d'opioïdes postopératoires

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Abstract

Purpose *The objective of this prospective observational study was to investigate the interactions between cultural background, healthcare environment, and postoperative pain experience.*

Methods *We enrolled 128 Chinese patients living in rural mainland China and 134 patients in Hong Kong with a higher level of Western cultural influences (defined by educational attainment, place of residence, and ability to understand English). All patients had major abdominal surgery and received patient-controlled analgesia with intravenous morphine for postoperative pain relief. The primary endpoint was total opioid requirement up to 48 hr after surgery. Other measures included pain intensity, opioid-related side effects, and genetic markers for opioid responsiveness.*

Results *The mean (95% confidence interval) cumulative opioid requirement, expressed as morphine equivalent, during the first 48 hr after surgery was significantly less in patients from mainland China (18.8 [15.7 to 22] mg) compared with patients from Hong Kong (42.0 [38.3 to 45.6] mg, $P < 0.0001$). In a multivariable analysis, opioid requirement was influenced by ethnicity, duration of surgery, and severity of pain upon admission to the postanesthetic care unit.*

Conclusions *These results suggest that postoperative pain behaviours and opioid requirement may be influenced by cultural background and healthcare environment in two populations of Chinese descent.*

Trial registration *Australian and New Zealand Clinical Trials Registry (ACTRN12614000601639); registered 6 May, 2014.*

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Résumé

Objectif *L'objectif de cette étude observationnelle prospective était d'étudier les interactions entre le contexte culturel, l'environnement de soins de santé et l'expérience de la douleur postopératoire.*

Méthodes *Nous avons recruté 128 patients chinois vivant en zones rurales en Chine continentale et 134 patients vivant à Hong-Kong avec un haut niveau d'influences culturelles occidentales (définies par le niveau d'éducation atteint, le lieu de résidence et la capacité à comprendre l'anglais). Tous les patients avaient subi une chirurgie abdominale majeure et reçu une analgésie contrôlée par le patient par morphine intraveineuse pour le soulagement de la douleur postopératoire. Le critère d'évaluation principal était la demande totale en opioïdes pendant les 48 premières heures suivant la chirurgie. D'autres mesures ont inclus l'intensité de la douleur, les effets indésirables liés aux opioïdes et des marqueurs génétiques de sensibilité aux opioïdes.*

Résultats *Le besoin cumulé moyen (intervalle de confiance à 95 %) cumulé en opioïdes, exprimé sous forme d'équivalent-morphine, au cours des 48 premières heures suivant la chirurgie était significativement inférieur pour les patients de Chine continentale (18,8 [15,7 à 22] mg) comparativement aux patients de Hong-Kong (42,0 [38,3 à 45,6] mg, $P < 0,0001$). Une analyse multifactorielle a montré que la demande en opioïdes était influencée par l'origine ethnique, la durée de l'intervention chirurgicale et l'intensité de la douleur au moment de l'arrivée dans l'unité de soins postanesthésiques.*

Conclusions *Ces résultats suggèrent que les comportements postopératoires envers la douleur et le besoin d'opioïdes peuvent être influencés par l'arrière-plan culturel et l'environnement des soins de santé dans deux populations différentes d'origine chinoise.*

Enregistrement de l'essai clinique *Registre des essais cliniques d'Australie et de Nouvelle-Zélande (ACTRN12614000601639); enregistré le 6 mai 2014.*

Race is defined as shared common ancestry with distinctive physical attributes, while ethnicity combines race and behaviours brought about through interaction with the environment.[1] Ethnicity may influence the experience of pain but exactly how it does so are challenging to identify. For example, a common perception is that people of Asian ethnicity experience less pain and therefore require lower opioid doses early after surgery.[2-4] This is often attributed to greater tolerance and an unwillingness to challenge the pain management plan. It is also commonly believed that Asians are more reluctant to report pain and have a greater fear of opioids than Caucasians.[5-7] Despite these assertions, few studies have evaluated the influence of ethnicity on postoperative pain.[2-5]

Our group have recently reported findings from a prospective cohort comparing opioid requirement and postoperative pain in a matched group of 136 Chinese patients from Hong Kong and Caucasian patients in Melbourne who received major surgery.[8] Although Chinese patients from Hong Kong required less morphine, they rated their intensity of pain significantly higher than Australian Caucasians. Chinese patients also reported more pruritus and were equally satisfied with pain management. We also showed that Chinese patients expressed a stronger preference for others to control their pain management and had a greater preoperative expectation of severe postoperative pain, but were not more fearful of opioid-related addictive side effects.[8] Our genetic analysis of the opioid receptor μ1 (OPRM1) polymorphism did not explain the higher opioid requirements among Caucasians compared with Asians. In this respect, despite a higher percentage of Caucasian patients carrying the opioid-resistant variant (GG), opioid requirement was similar to those with the wild type (AA). This finding agrees with conflicting data for the opioid receptor polymorphism.[9,10] These observations suggest that the healthcare environment influences how pain is experienced by people of different ethnicities.[11]

In the present study, we aimed to determine the effect of ethnicity on opioid requirement and postoperative pain by comparing a cohort of Chinese patients living in rural mainland China with another cohort living in Hong Kong, who were more influenced by Western culture (defined as urban living, higher education, and ability to understand English). Our hypothesis was that patients from mainland China would self-administer lower opioid doses after surgery compared with patients from Hong Kong. The common Chinese ancestry and biologic similarity allowed the influences of culture and hospital environment on postoperative pain behaviours to be explored in detail in the two populations.

Methods

This prospective observational cohort study was registered in the Australian and New Zealand Clinical Trials Registry (ACTRN12614000601639). Patient recruitment was conducted between November 1, 2014 and August 10, 2015 at the Sir Run Run Shaw Hospital, Hangzhou, China and the Prince of Wales Hospital, Hong Kong Special Administrative Region. The study was approved by the Institutional Review Boards at both sites (Ethics

Committee, College of Medicine, Zhejiang University: 20130910-10 and Joint CUHK-NTEC Clinical Research Ethics Committee: CRE-2013.546). Patients presenting for surgery at each site were approached by the investigators at the pre-admission clinics or the surgical ward, days to weeks before surgery. Both patients and nursing staff managing these patients provided written informed consent.

Eligible patients were between 18 and 80 yr, having major open or laparoscopic-assisted abdominal surgery with an expected wound length $\geq$ 5 cm. All patients also possessed physical features suggestive of Chinese racial background. Patients were excluded if they could not adequately understand the principles of patient-controlled analgesia (PCA), were allergic to morphine or acetaminophen or nonsteroidal anti-inflammatory drugs, had a diagnosis of chronic pain syndrome for at least three months in the six months preceding surgery, or required opioid therapy in the two weeks prior to surgery or planned to receive regional block. All written material and questionnaires relevant to the conduct of the study were prepared in simplified and traditional Chinese for use at the sites in Hangzhou China and Hong Kong.

After patient consent was obtained, research assistants collected demographic data during the preoperative interview. These included age, sex, body mass index, American Society of Anesthesiologists physical status, and type of operation. Special demographic data were also collected to ascertain the level of influence from Western culture, including place of residence (urban or rural), ability to speak and understand English, and highest level of educational attainment (0 = no schooling, 1 = primary level, 2 = secondary level, 3 = tertiary level). Patients then participated in a preoperative survey canvassing their beliefs and attitudes about their pain management. This survey has been utilized in a previous study comparing patients in Hong Kong with Caucasian patients.[8] All questions were statements followed by a five-point scale that reflected the degree of agreement or disagreement, or a range of alternate responses regarding use of analgesics on a four-point scale (Tables 3 and 4). Finally, patients were asked preoperatively to predict the pain intensity level on a scale of 0 to 10, where 0 describes no pain and 10 describes worst possible pain, above which they would feel the need for analgesic intervention.[12]

Nursing staff managing the patients in this study also gave informed consent and participated in a preoperative attitude and belief survey about pain management.[8] After completing the survey, patients and nurses at both sites were provided with standardized education material that explained the principles underlying pain measurement using the 11-point numeric rating scale (where 0 = no pain and 10 = worst possible pain intensity) and the role of PCA in providing analgesia to facilitate deep breathing and coughing after surgery.

Patients at both sites provided blood samples to analyse OPRM1 status. Genomic (DNA) was extracted from 5 mL venous blood samples collected before surgery using QIAamp DNA mini kit 250 (Qiagen, Valencia, CA, USA). Genotyping was performed using Taqman single nucleotide polymorphism assay (Applied Biosystem, Foster City, CA, USA) for OPRM1 [A118G (*rs1799971*)].

Patients recruited for the study received general anesthesia without ketamine and nitrous oxide. Intraoperative analgesia comprised intravenous morphine at a dose considered appropriate by the anesthesiologist. All patients also received 50 mg intravenous flurbiprofen. Regional analgesia, including wound infiltration and neuraxial or transversus abdominis plane block, was not allowed.

In the postanesthetic care unit (PACU), patients were prescribed 1 g intravenous acetaminophen every six hours together with PCA to deliver morphine at an intravenous bolus dose of 1 mg with five minutes lockout for at least 48 hr. Intraoperative and cumulative intravenous doses of morphine over the 24 and 48 hr periods following surgery were recorded.

Patients were educated to use PCA for pain control to enable regular coughing and deep breathing. Opioid-related side effects, such as respiratory rate (breaths·min^{-1}), sedation (0 = no sedation, 1 = mild sedation, 2 = sleepy but easy to arouse, 3 = sleepy but not easy to arouse), presence/absence of nausea, presence/absence of vomiting, and presence/absence of itching were recorded 24 hr and 48 hr after emergence from anesthesia. Throughout the study period, intravenous 4 mg ondansetron was provided to treat nausea or vomiting. Intensity of pain at rest and with coughing were recorded upon discharge from the PACU and at 24 hr and 48 hr after surgery. At the completion of the 48 hr study period, patients were asked to rate their satisfaction with pain management using a 15-point scale where 0 = extremely dissatisfied and 15 = extremely satisfied.[12]

Statistical analysis

Sample size estimation was based on data from our previous study,[8] where at least 128 patients from each of the two cohorts were required to detect a difference in morphine requirement of 7 mg (10% difference or changes in 0.35 standard deviation between groups) with a two-sided P value of 0.05 and type II error of 20%.

Univariable and multivariable statistical analyses were performed with SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA). The primary endpoint was intravenous opioid requirement, expressed as morphine

equivalent, from the end of surgery up to 48 hr after surgery. Comparisons between groups (mainland China *vs* Hong Kong) were tested using Student's *t* test for normally distributed continuous variables, Wilcoxon rank sum test for non-normally distributed continuous variables, and χ^2 or Fisher's exact test as appropriate for categorical variables.

Multivariable linear regression was used to assess the factors that influence cumulative opioid requirement after theatre. In the initial univariable model, we included clinical factors that were likely to influence opioid requirement. The independent variables were ethnicity, sex, urbanization, understanding of English, education, pain intensity when coughing before the commencement of PCA, duration of surgery, history of diabetes, heavy alcohol intake (> six standard drinks per day), type of surgery and the surgical approach (laparoscopic *vs* open surgery), and the OPRM1 polymorphism. Patient responses to the statements "I expect severe pain after my surgery" and "I prefer others to manage my pain", as well as the corresponding nursing responses to "my patient should expect to have severe pain after surgery" and "my patient should control their analgesic therapy" were also included. Variables with a P value ≤ 0.10 in the univariable analysis were included in the multivariable regression model. A two-sided P value of less than 0.05 was considered significant.

Results

A total of 128 patients from mainland China and 134 patients from Hong Kong were included in the study (Fig. 1). Table 1 shows the demographic variables. There were more male patients in mainland China than Hong Kong, 56% *vs* 43%, $P = 0.041$. More patients in mainland China reported having a rural background ($P < 0.001$) and fewer patients understood English ($P < 0.001$). Duration of surgery was longer in mainland China compared with Hong Kong ($P = 0.002$).

Mean (standard deviation) intraoperative opioid doses were greater in mainland China, (18.3 [6.3] mg), compared with Hong Kong (15.3 [7.3] mg; $P < 0.001$). Nevertheless, morphine requirement per unit surgical time was similar in both populations: patients in mainland China, 4.9 (1.7) $mg{\cdot}hr^{-1}$ *vs* Hong Kong, 5.1 (2.4) $mg{\cdot}hr^{-1}$ ($P = 0.44$). The primary endpoint was the cumulative mean (95% confidence intervals) morphine requirement. From the end of surgery up to 48 hr after surgery, this was 42 (38.3 to 45.6) mg among Hong Kong patients and 18.8 (15.7 to 22.0) mg in patients from mainland China ($P <$ 0.001) (Fig. 2A).

After multivariable adjustment, opioid requirement from the end of surgery to 48 hr after surgery was independently associated with ethnicity, duration of surgery, and pain intensity when coughing before PCA (Table 2). We chose to create a linear model because logarithmic transformation of the data did not substantially alter the results (Electronic Supplementary Material [ESM] eTable 1). In addition, a linear model for morphine requirement and duration of surgery produced higher R^2 values compared with various transformed models (ESM eTable 2, ESM eFig. 2). Similar relationships can be observed between morphine requirement and pain intensity upon admission to the PACU before commencement of PCA (ESM eTable 3, ESM eFig. 3). There was no interaction between ethnicity and duration of surgery or ethnicity and pain intensity before commencement of PCA (ESM eTable 4 and eTable 5). Postoperative opioid requirement was similar for both sexes in Hong Kong (female: 38.4 [32.8 to 43.9]

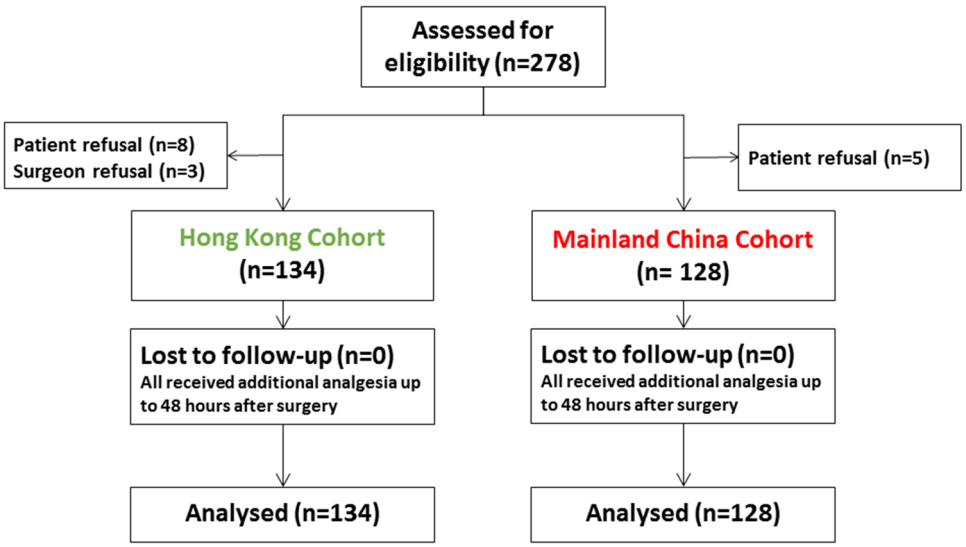

Fig. 1 Flowchart of patients enrolled in mainland China and Hong Kong

Table 1 Demographic characteristics of study participants

Characteristic	Hong Kong	Mainland China	*P* value
No. of patients	134	128	
Male sex	58 (43%)	71 (56%)	0.04
Age (yr)	58 (11)	59 (11)	0.58
Body mass index ($kg \cdot m^{-2}$)	23.8 (4.2)	23 (3.6)	0.11
Rural residence	13 (11%)	70 (55%)	< 0.001
Able to understand English	44 (33%)	0 (0%)	< 0.001
Educational attainment*	1 (1 to 2)	1 (1 to 2)	0.77
ASA physical status	2 (1 to 2)	1 (1 to 2)	0.09
Current smoker	15 (11%)	17 (13%)	0.62
Significant alcohol intake**	3 (2%)	8 (6%)	0.06
Duration of surgery (hr)	3.0 [2.1–4.6]	3.8 [2.9–5.0]	0.002
Opioids in theatre and PACU (mg)	15.3 (7.3)	18.3 (6.3)	< 0.001
Adjusted for duration of surgery ($mg \cdot hr^{-1}$)	5.1 (2.4)	4.9 (1.7)	0.44
Type of surgery			
Laparoscopic surgery	44 (33%)	36 (28%)	0.41
Gynecology/colorectal surgery	66 (49%)	55 (43%)	0.30
Liver/gastric surgery	64 (48%)	65 (51%)	0.81
Urologic surgery	4 (3%)	8 (6%)	0.53

Data are expressed as no. (%), median [interquartile range] or mean (standard deviation). ASA = American Society of Anesthesiologists; PACU = postanesthetic care unit

*Educational attainment 0 = no schooling; 1 = primary; 2 = secondary; 3 = tertiary

**Significant alcohol intake estimated at three or more standard alcoholic drinks daily

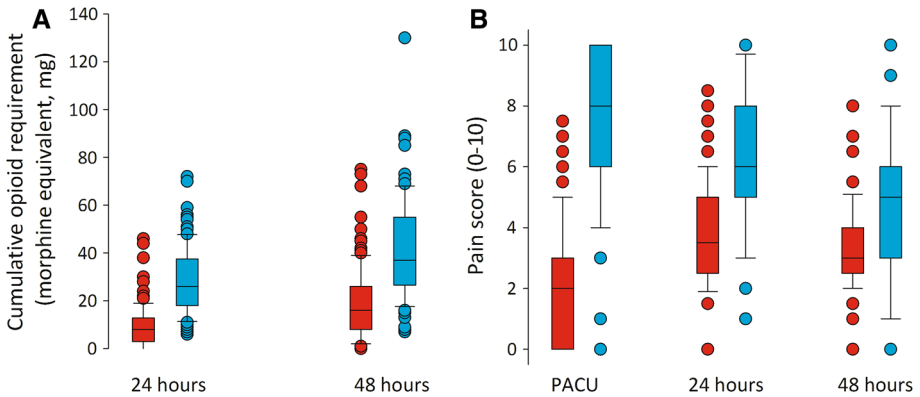

Fig. 2 (A) Cumulative opioid requirement at 24 hr and 48 hr after major surgery in patients recruited from mainland China (red) and Hong Kong (cyan). (B) Pain scores in the postanesthetic care unit (PACU) and at 24 hr and 48 hr after major surgery in patients recruited from mainland China (red) and Hong Kong (cyan). Box and whisker plot: the upper and lower edges of the boxes indicate the interquartile ranges, the line through box is the median value, the whiskers are the 5% and 95% centiles and the closed circles are outliers

mg and male: 44.7 [39.9 to 49.5] mg; $P = 0.09$) and in mainland China (female: 17.3 [12.6 to 222.0] mg and male: 20.1 [15.8 to 24.4] mg; $P = 0.38$).

Beliefs and attitudes to pain management and opioids among patients differed significantly in two statements; patients in mainland China were less likely to agree with the statements "I expect severe pain after my surgery" ($P < 0.001$) and "I prefer others to manage my pain" ($P < 0.001$) (Table 3). Nursing beliefs and attitudes differed significantly in relation to three statements; nursing staff in mainland China were less likely to agree with "My patient should expect to have severe pain after surgery" ($P < 0.001$) and were more likely to agree with "My patient should control their own analgesia therapy" ($P < 0.001$),

Table 2 Multivariable linear regression analysis of risk factors on postoperative morphine requirement up to 48 hr after surgery

Variable	Univariable regression coefficient (95% CI)	*P* value	Multivariable regression coefficient (95% CI)	*P* value
Ethnicity				
Hong Kong	Reference		Reference	
Mainland China	− 23.1 (− 27.9 to − 18.4)	<0.001	− 14.6 (− 23.3 to − 6.0)	0.001
Sex				
Male patients	Reference		Reference	
Female patients	− 4.7 (− 10.3 to 0.9)	0.10	− 4.7 (− 9.7 to 0.3)	0.07
Residence				
Urban patients	Reference		Reference	
Rural patients	− 12.4 (− 18.0 to − 6.8)	<0.001	− 2.9 (− 8.8 to 3.0)	0.34
Understand English				
No	Reference		Reference	
Yes	12.3 (3.4 to 21.1)	0.007	− 4.7 (− 13.3 to 3.9)	0.29
Education				
No schooling	Reference		—	
Primary level	2.0 (− 5.7 to 9.6)	0.62	—	
Secondary level	− 5.5 (− 13.8 to 2.8)	0.20	—	
Tertiary level	− 0.03 (− 11.6 to 11.5)	0.99	—	
Diabetes mellitus				
No	Reference		—	
Yes	6.2 (− 1.4 to 13.9)	0.11	—	
Heavy alcohol intake				
No	Reference		—	
Yes	− 0.5 (− 13.9 to 12.9)	0.94	—	
Duration of surgery (hr)	1.5 (− 0.1 to 3.1)	0.07	2.1 (0.7 to 3.6)	0.004
Type of surgery				
Urologic	Reference		—	
Upper abdominal surgery	4.3 (− 9.3 to 17.8)	0.54	—	
Lower abdominal surgery	− 3.5 (− 17.2 to 10.3)	0.62	—	
Surgical approach				
Laparoscopic	Reference		—	
Open surgery	3.51 (− 1.52 to 8.54)	0.17	—	
Pain intensity upon admission to PACU (for every point increase in pain score)	3.2 (2.5 to 4.0)	<0.001	1.6 (0.4 to 2.8)	0.009
Opioid receptor μ1 gene polymorphism				
AA	Reference		—	
AG	− 4.0 (− 10.0 to 1.9)	0.19	—	
GG	− 1.7 (− 10.9 to 7.5)	0.72	—	
Patient beliefs				
"I expect severe pain after my surgery"				
Disagree or neutral	Reference		Reference	
Agree	7.2 (1.7 to 12.7)	0.01	1.2 (− 4.1 to 6.5)	0.65
"I prefer others to manage my pain"				
Disagree or neutral	Reference		—	
Agree	− 2.8 (− 8.4 to 2.7)	0.32	—	
Nurse beliefs				
"My patient should expect to have severe pain after surgery"				
Disagree or neutral	Reference		Reference	

Table 2 continued

Variable	Univariable regression coefficient (95% CI)	*P* value	Multivariable regression coefficient (95% CI)	*P* value
Agree	8.0 (2.4 to 13.6)	0.005	1.8 (− 3.9 to 7.6)	0.53
"My patient should control their analgesic therapy"				
Disagree or neutral	Reference		Reference	
Agree	8.8 (2.7 to 14.9)	0.005	− 2.9 (− 9.7 to 3.9)	0.40

CI = confidence intervals; PACU = postanesthetic care unit

Table 3 Beliefs and attitudes expressed by patients and the nurses who managed them

Statement	Response	Hong Kong (n = 134)	Mainland China (n = 128)	Percentage difference (95% CI)	*P* value
Patients					
I am frightened of addiction if I use too much opioid after my operation	Agree a little or a lot*	37 (28%)	30 (23%)	4.2 (− 6.4 to 14.7)	0.44
I expect severe pain after my surgery	Agree a little or a lot*	92 (69%)	51 (40%)	28.8 (17.3 to 40.4)	< 0.001
I believe pain after surgery is part of my illness	Agree a little or a lot*	78 (58%)	64 (50%)	8.2 (− 3.8 to 20.2)	0.18
I prefer others to manage my pain after surgery	Agree a little or a lot*	73 (55%)	56 (44%)	10.7 (− 1.3 to 22.8)	0.08
The pain relief I expect after my surgery is:	None or weak analgesics**	34 (25%)	74 (58%)	32.4 (21.1 to 43.7)	< 0.001
Nurses who managed patients involved in the study					
I prefer to give less opioid to my patient because of addiction	Agree a little or a lot*	26 (19%)	21 (16%)	3.0 (− 6.3 to 12.3)	0.53
My patient should expect to have severe pain after surgery	Agree a little or a lot*	90 (67%)	60 (47%)	20.3 (8.5 to 32.0)	0.001
My patient should control their own analgesic therapy	Agree a little or a lot*	123 (92%)	71 (56%)	36.3 (26.5 to 46.1)	< 0.001
The analgesia I expect my patient will need is:	None or weak analgesics**	2 (2%)	42 (33%)	31.3 (22.9 to 39.7)	< 0.001

Data are expressed as number (%)

CI = confidence intervals

*Patient or nurse rated a five-item Likert scale: strongly disagree, disagree, neutral, agree a little, or agree a lot

**Nurse rated either none, weak analgesics, strong analgesics, or weak and strong analgesics

and less likely to describe multimodal analgesia as one of the options in relation to the statement "The pain relief I expect my patient to have following surgery" ($P < 0.001$) (Table 3).

Sedation, nausea, and vomiting were less common among patients in mainland China than Hong Kong throughout the entire study period. Pruritus was less severe in patients from mainland China at 24 hr and 48 hr following surgery (Table 4).

Ratings on pain intensity during coughing were significantly lower throughout the entire postoperative period in patients from mainland China compared with patients from Hong Kong (Fig. 2B). Preoperative predicted pain intensity where patients felt analgesic intervention would be needed varied significantly between the two groups; the mean (standard deviation) predicted pain score in Hong Kong, 6.1 (0.3), was higher than that in mainland China, 4.0 (0.5); $P < 0.0001$. Satisfaction with pain management (where 0 was extremely dissatisfied and 15

Table 4 Opioid-related side effects

Variable	Hong Kong (n = 134)	Mainland China (n = 128)	Percentage difference (95% CI)	P value
Number of patients without sedation on entering PACU	91 (68%)	109 (85%)	17 (7 to 27)	0.001
Number of patients without sedation at 0–24 hr after surgery	90 (67%)	107 (84%)	16 (6 to 27)	0.002
Number of patients without sedation at 24–48 hr after surgery	96 (72%)	112 (88%)	16 (6 to 25)	0.002
Pruritus on entering PACU	9 (7%)	4 (3%)	4 (− 2 to 9)	0.170
Pruritus at 0–24 hr after surgery	15 (11%)	3 (2%)	9 (3 to 15)	0.003
Pruritus at 24–48 hr after surgery	12 (9%)	4 (3%)	6 (2 to 12)	0.047
Nausea on entering PACU	28 (21%)	8 (6%)	15 (8 to 24)	< 0.001
Nausea at 0–24 hr after surgery	63 (47%)	9 (7%)	40 (30 to 49)	< 0.001
Nausea at 24–48 hr after surgery	28 (21%)	8 (6%)	15 (8 to 24)	< 0.001
Vomiting on entering PACU	11 (8%)	1 (1%)	7 (2 to 12)	0.007
Vomiting at 0–24 hr after surgery	25 (19%)	3 (2%)	17 (10 to 24)	< 0.001
Vomiting at 24–48 hr after surgery	11 (8%)	1 (1%)	7 (2 to 12)	< 0.001

*Sedation score: 0 = no sedation, 1 = mild sedation, 2 = sleepy but easy to arouse, 3 = sleepy but not easy to arouse

CI = confidence intervals; PACU = postanesthetic care unit

was extremely satisfied) was significantly higher in Hong Kong patients, 12 (3), compared with patients from mainland China, 11 (3), $P < 0.0001$. The genotypic frequencies for OPRM1 gene polymorphisms in patients from mainland China (AA: 48%; AG/GA: 39%; GG:13%) were similar to those of Hong Kong patients (AA: 51%; AG/GA: 39%; GG:10%) ($P = 0.75$).

Discussion

In this study, we found that opioid requirement was significantly lower in patients from mainland China compared with patients from Hong Kong up to 48 hr after major abdominal surgery. This difference in opioid requirement was influenced by ethnicity, duration of surgery, and pain intensity rating upon arrival at the PACU. This was also accompanied by differences in pain-related behaviours, beliefs, and attitudes between the two populations. Anesthesiologists should consider the influence of ethnicity on postoperative pain and opioid requirement when providing postoperative analgesia to patients with different cultural background or working in different healthcare environments.

The duration of operation was significantly lower among the Hong Kong patients and significantly influenced opioid requirement in our multivariable analysis. Nevertheless, opioid requirement in the theatre and PACU was similar between our two populations after adjustment was made for duration of operation. After discharge from the theatre, the PCA-related morphine requirement was higher among Hong Kong patients. This highlights the differences in patient-related pain behaviours between the two groups regarding the self-administration of opioid analgesia after leaving the PACU.

Opioid-related side effects differed significantly between the two cohorts with rates among the Hong Kong patients similar to early postoperative effects reported in largely Caucasian populations receiving postoperative morphine early after surgery in the United States.[13] Greater use of PCA morphine in Hong Kong patients despite higher rates of opioid-related side effects compared with mainland China likely reflects a stronger drive to eliminate pain.

Our exploration of beliefs and attitudes among patients and the nurses caring for them showed interesting differences and similarities. Patients in Hong Kong were more likely than those in mainland China to expect severe pain after surgery. Similarly, nurses in Hong Kong were more likely to expect severe pain among their patients than nurses in mainland China. This may partly explain the greater opioid requirement among Hong Kong patients, though both groups either slightly disagreed or had neutral feelings about expecting severe pain. Fear of opioid addiction did not appear to play a role in our study since patients and nurses at both sites were not fearful of opioid addiction.

Satisfaction scores were significantly higher among Hong Kong patients, but satisfaction ratings were high in both groups. Essentially, we observed that patients in mainland China reported lower pain intensities and a lower incidence of opioid-related side effects with higher levels of satisfaction with pain management. In contrast, Hong Kong patients had higher pain ratings and more frequent opioid-related side effects, even though they were more satisfied with pain management. In general, satisfaction

with pain management is high when patients perceive that they are given autonomy and have adequate pain management.[14]

Our study has several limitations. It remains difficult to determine the influence of Western culture accurately. In this study, we recorded educational attainment, place of residence, and understanding of English as surrogate measures of the influence of Western culture. Presumably, these are some aspects of cultural characteristics of Europe and North America. Patients attained similar levels of education in the two cohorts, but those in mainland China were less likely to be urban residents and less likely to understand English. We believe these findings suggest a lesser influence of Western culture on patients living in mainland China. It is not possible to fully and accurately measure biologic factors that reflect both responsiveness to opioid treatment and pain-related behaviours. While there are several candidate genes that may reflect pain sensitivity,[15,16] we only measured OPRM1 polymorphisms as a biologic marker because it best suited the context of our study. The influence of the OPRM1 gene polymorphism on opioid therapy has been widely debated. Earlier meta-analyses involving fewer studies attributed a smaller influence of OPRM1 gene polymorphisms on opioid therapy,[9] but recent studies analyzing a larger body of evidence have concluded that OPRM1 gene polymorphisms could account for variable responses to postoperative opioid treatment, particularly among Asians receiving morphine therapy, and after surgery with significant visceral pain.[10] Although the frequency of OPRM1 polymorphisms were similar between the two Chinese patient cohorts, other genetic polymorphisms may also contribute to the differences in opioid requirements. Finally, our study was confined to Chinese patients and the results may not be extrapolated to other populations.

In summary, our study revealed significant differences in opioid requirement between patients in Hong Kong and mainland China after major surgery. These differences were observed in a setting where biologic similarity was expected regarding Chinese descent. These observations highlight the influence of environmental factors in shaping many measurable aspects of pain behaviour and point to a need to study the interaction between ethnicity and pain behaviours.

Conflicts of interest The authors declare that they have no conflicts of interest.

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