Recurrence of breast cancer after regional or general anaesthesia

Authors: Sessler DI et al., on behalf of the Breast Cancer Recurrence Collaboration

Summary: Women undergoing potentially curative primary breast cancer resection were randomised to receive regional anaesthesia-analgesia (n=1043) or general anaesthesia (n=1065) and were followed for a median of 36 months in this trial. There was no significant difference between the regional anaesthesia-analgesia and general anaesthesia arms for: i) local or metastatic breast cancer recurrence rate (primary outcome; 10% vs. 10% [p=0.84]); ii) the proportion who experienced incisional pain at 6 months (52% vs. 52%) or at 12 months (28% vs. 27%); or iii) the proportion who experienced neuropathic breast pain at 6 months (10% vs. 10%) or at 12 months (7% vs. 7%). A preplanned futility boundary was crossed and the study was terminated.

Comment (JB): “Three perioperative factors impair host defence against recurrence during cancer surgery: the surgical stress response, use of volatile anaesthetic, and opioids for analgesia” – is the opening sentence of the paper’s abstract, yet this ambitious RCT was stopped just past the halfway point of recruitment because the futility boundary was crossed at the second interim analysis. Eleven years of toil across 13 countries and a negative result. A huge well-powered study that was powered to identify a 30% difference in recurrence rates. Somehow I doubt that this is the end of the story. The animal data that made this trial a reasonable investment remain quite compelling. Are there other factors confounding the results further to the three factors considered? As the editor points out, did the cancer model need to involve a greater surgical insult, more pain and more opioids? Does the surgical stress control with regional anaesthesia need to extend further into the postoperative period? Why did the authors use morphine in both groups for postoperative pain control when this is thought to be the most immunosuppressant opioid? As is often the case, there are more questions generated than answers, but it must be fair to assume the difference between general and regional anaesthesia is not massive.


Abstract

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Association of preoperative serum chloride levels with mortality and morbidity after noncardiac surgery

Authors: Oh TK et al.

Summary: Relationships between preoperative hyperchloraemia or hypochloraemia and 90-day mortality and morbidity following noncardiac surgery were explored in a retrospective cohort of 106,505 patients aged >20 years stratified as normochloraemic, hyperchloraemic (n=617) or hypochloraemic (n=2147) according to respective serum chloride levels of 97–110, >110 or <97 mmol/L within 1 month of surgery. Compared with normochloraemic patients, hypochloraemic and hyperchloraemic patients had greater risks of death within 90 days of surgery (primary endpoint; respective hazard ratios 1.46 [95% CI 1.16, 1.84] and 1.76 [1.13, 2.73]), and hypochloraemia patients had a greater likelihood of acute kidney injury (odds ratio 1.83 [1.53, 2.19]).

Comment (JB): Perhaps we should be paying closer attention to chloride levels – maybe you already do. This retrospective case series demonstrated a strong association between preoperative hyper- or hypochloraemia and 90-day mortality. While hypochloraemia was almost 4 times less common (617/106,505) than hyperchloraemia, it was associated with both a greater risk of death and in additional risk of acute kidney injury. Concern about hyperchloraemic acidosis has led to balanced salt solutions becoming the default crystalloid fluid used in theatre. Possibly there is more that anaesthetists should be doing in response to disordered chloride handling. On the basis of the results of this study, hypochloraemia should be on that list of things that make anaesthetists increase their vigilance, use invasive monitoring, tighten up control of physiological parameters and increase the frequency of electrolyte level testing.


Abstract

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The intraoperative use of non-opioid adjuvant analgesic agents

Authors: Thiruvenkatarajan V et al.

Summary: These researchers sent surveys on nonopioid analgesic use as part of opioid-sparing practice to 985 NZ and Australian anaesthetists, of whom 33.4% responded. The most frequently used nonopioid analgesic was paracetamol (acetaminophen) with 72% of respondents describing >70% usage, followed by parecoxib (42%) and dexamethasone (35%). Most respondents reported they would never consider using dexmedetomidine, magnesium, esmolol, pregabalin or gabapentin, mainly due to concerns regarding side effects, lack of evidence for benefit and anaesthetists’ experience.

Comment (JB): Presumably you have the same love-hate relationship with anaesthesia-related surveys that I do – love the chance to see what my colleagues get up to (presuming that they are answering truthfully), and hate filling them in myself. A response rate of only 33.4% certainly supports the ‘hate filling them in’ presumption. Perhaps the college CPD committee could do more to encourage fellows to fill in any survey that has been supported by the ANZCA trials group. The act of filling in the survey represents a responder’s self-reflection on their practice, and given that a responder was keen enough to complete the survey, it seems likely that they will take a personal interest in, and reflect on, the results. The authors of this trial are unashamedly pro-adjuvant analgesia and they apparently work in a department of largely likeminded individuals. The article is dotted with statements like “the uptake of tramadol, lidocaine, and magnesium amongst respondents… was poor”. The inference being that greater uptake would be good; i.e. would result in better outcomes. In writing for a scientific journal, the authors have avoided diving into personality-based decision making, yet in my view whether an anaesthetist chooses to use mixtures of adjuvant analgesics is just as much personality-based as evidence-based. Are you the kind of anaesthetist who is an early adopter of novel techniques, comfortable to use multiple infusions of medications during general anaesthesia, and really worried about your personal contribution to any local opioid epidemic? Alternatively, are you more of an ‘if it ain’t broke don’t try to fix it, keep it simple stupid’ kind of anaesthetist who has used opioids in their practice for years, and they seem to have been effective and reasonably safe? Imagine the consent conversation that would be necessary to adequately inform a patient about the options for adjuvant analgesic infusions so that they could make their own choices. Fortunately, most patients prefer to take comfort in the statement ‘you are the expert’, rather than in a detailed discussion of the medication options open to them. Ultimately our profession moves forward through a mixture of science and collective wisdom. The simpler the question, the more likely that a clinical trial will add clarity; the more complex, the more important collective wisdom becomes. The use of adjuvant analgesia seems complex to me.

Reference: BMC Anesthesiol 2019;19:188

Abstract

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A pilot randomized controlled trial comparing mindfulness meditation, cognitive therapy, and mindfulness-based cognitive therapy for chronic low back pain

Authors: Day MA et al.

Summary: Adults with chronic LBP (low back pain; n=69) were randomised to group-delivered mindfulness meditation, cognitive therapy or mindfulness-based cognitive therapy in this Australian trial. Mindfulness-based cognitive therapy was reported to be acceptable, feasible and well tolerated with favourable ratios of dropout and attendance. An intent-to-treat analysis revealed significant improvements in post-treatment scores for pain interference, pain intensity, physical function and depression, with no significant between-group differences. Follow-up data from 43 participants indicated that mindfulness-based cognitive therapy was associated with significantly better results for pain interference, physical function and depression compared with mindfulness meditation, and cognitive therapy was superior to mindfulness meditation for physical function. None of the measures evaluated differed significantly between the mindfulness-based cognitive therapy and cognitive therapy groups.

Comment (GL): This was another study testing a modified psychological intervention for chronic pain, this time focusing on chronic LBP. This intervention had a more standard timeframe and was essentially designed to see if a combined mindfulness and cognitive therapy intervention is better than its individual components. As an aside, given the first author developed the combined intervention, I was surprised to see that she also delivered all three interventions. While it may seem to account for therapist effects, I would have preferred each intervention to be delivered by separate therapists who were proponents of the individual approaches. There was not much separating the approaches in terms of outcomes and acceptability, although it was acknowledged the study was underpowered for detecting differences between the interventions. These findings appear similar to exercise approaches for chronic LBP – doing some sort of exercise/activity is better than doing nothing, but it doesn’t seem to matter what type of exercise you do. Perhaps it is the commitment to do something – whether that is exercise or psychological management – that makes the difference, rather than the specific content of what you are doing. Of note, the gains following therapy increased over time for most outcome measures, which is in contrast with previous study, perhaps indicating the benefit of full duration psychological programmes.


Abstract

Say what? Patients have poor immediate memory of major risks of interscalene block disclosed during the informed consent discussion

Authors: Bai JW et al.

Summary: Patients’ immediate memory of risks related to ISB (interscalene block) disclosed by an anaesthesiologist during preoperative informed consent discussions was explored in a prospective cohort of 125 patients scheduled for arthroscopic shoulder surgery. Only 21% of participants were able to remember all four major risks of ISB when queried immediately after their preoperative informed consent discussion; the mean number of major risks remembered was 2. All nine true risks were remembered by 12% of the participants, with a mean number of true risks remembered of 6. No significant association was detected between the participants’ self-rated assessment of their memory and their actual recall.

Comment (JB): During the preoperative assessment, the patients lining up for shoulder surgery were read a carefully crafted and standardised script describing four major complications and five minor complications of ISB. After the assessment, they were then invited to take part in a study examining what knowledge of complications of ISB they had retained (125 of 187 patients agreed to take part). The authors had expected 50% of patients to be able to identify all four of the major complications when asked to identify them from a list of 18 complications (the nine ISB-related complications noted during the preoperative assessment and nine ‘distractor’ unrelated complications). The actual recall rate was much worse with only 21% correctly identifying the four major complications. Rates of recall were unrelated to patients’ education level or their perceived understanding of the ISB discussion. There was a weak association with the patients’ English language skills. Perhaps the authors could have delved a little deeper into why the results were poor. For instance, they could have asked the patients ‘Do you normally have a good memory for facts?’ or ‘Do you remember things better when you hear them or when you read them?’. Regardless, the take-home message is that we can’t rely on patients remembering information given to them as a single conversation during a preoperative visit. If we believe the information is vital for them to remember at a later date then we will need to reinforce the memories.


Abstract

Brief cognitive behavioral therapy for chronic pain

Authors: Beehler GP et al.

Summary: Preliminary effectiveness data were reported for 118 patients with chronic pain who received the Brief CBT-CP (Brief Cognitive Behavioral Therapy for Chronic Pain), an abbreviated, modular treatment designed for use in primary care. The patients had experienced significant improvements for a composite of pain intensity and functional limitations by their third appointment, with an improvement also seen for pain-related self-report measures evaluated differed significantly between the mindfulness-based cognitive therapy and cognitive therapy groups.

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Abstract
Individualization of migraine prevention: a randomized controlled trial of psychophysiological-based prediction of duloxetine efficacy

Authors: Kisler LB et al.

Summary: Patients who experience migraines were randomised to receive duloxetine (n=27) or placebo (n=26), and psychophysiological pain measures were used to predict efficacy for migraine prevention. Compared with placebo, duloxetine was associated with greater participant estimation of migraine improvement (52.3% vs. 26.0% [p=0.001]) with higher pretreatment pain ratings for tonic heat pain (p=0.012). Greater pain sensitivity at baseline was a significant predictor of greater migraine improvement among duloxetine recipients (r=0.47 [p=0.013]) but not among placebo recipients (r=–0.36 [p=0.060]).

Comment (GL): This one is right out of our lab’s manual. It involved a lovely neurophysiological probe of the nociceptive system coupled with a hypothesis-driven test of efficacy of a specific type of medication. There was a simple prediction that those with impaired central modulation of nociception would benefit the most from a drug that facilitates central inhibition of nociception. Prescribing duloxetine as a preventative medication when there are known side effects (and they were common in this study) is problematic, so it would obviously be advantageous if we could predict who is most likely to benefit. The participants almost ruined the carefully planned study with actual data. While one of the psychophysical measures did pan out to relate to treatment efficacy, it wasn’t what was predicted, and the authors well-grounded hypotheses weren’t really supported. Thus, the findings are a little more difficult to explain, and may be why such an elegantly designed study didn’t end up in a higher ranked journal.


Abstract

Relationships between opioid dosing, pain severity, and disability in a community-based chronic pain population

Authors: DiBenedetto DJ et al.

Summary: Relationships between opioid dose change, pain severity and function were explored for a retrospective cohort of 778 patients with chronic pain in this exploratory analysis. Opioid dose decreases occurred for 31.2% of the patients, 28.7% had a dose increase and 40.1% had no significant dose change (i.e. <20% change). A weak negative correlation was identified between opioid dose change and pain severity change (r=–0.08 [p=0.04]), but no significant association was seen between dose change and disability score change (p=0.13). A weak positive correlation was also detected between pain severity rating change and disability score change (r=0.16 [p=0.001]).

Comment (GL): The authors start out indicating the lack of high-quality studies investigating chronic opioid use, then go to conduct a low-level evidence study themselves. I feel like they missed their own point. Despite this, they did do quite a complex analysis of how changes in opioid dose relate to changes in pain severity and disability. I think the point they are trying to make from their findings is that changing dose for those on long-term opioid use, whether that is an increase or decrease in dose, does not necessarily alter pain or physical function. While the retrospective nature of the study design makes it impossible to attribute cause, there are some neurophysiological links that may account for the relationships among these, so some potentially important clinical messages — increasing opioid dose won’t necessarily make someone better, while decreasing opioid dose won’t necessarily make them worse.


Abstract

Risk factors for new-onset depression or anxiety following total joint arthroplasty: the role of chronic opioid use

Authors: Wilson LE et al.

Summary: The incidence of and risk factors for new-onset depression/anxiety following total joint arthroplasty were assessed in patients who had undergone a total of 106,260 such procedures (34.3% and 65.7% hip and knee, respectively), with specific focus on the role of opioid use. The respective proportions of hip and knee replacement recipients for new-onset depression/anxiety were 3.6% and 4.8%. Factors predictive of new-onset depression were preoperative chronic opioid use (odds ratio 1.88 [95% CI 1.47, 2.40]), isolated postoperative opioid use (2.61 [2.08, 3.28]), continued postoperative opioid use (2.08 [1.74, 2.49]), female gender, younger age, comorbid psychological conditions and hospital readmission within 6 months of surgery; predictors of new-onset anxiety were similar.

Comment (GL): Regular readers will know that outcomes from joint arthroplasty are an interest of mine, but I tend to focus on pain outcomes. This study takes a different focus and looks at psychological distress following joint replacement. The cyclic association between pain and negative affect provides a legitimate reason to change the focus of outcome, even if the prevalence of (new-onset) postoperative anxiety and depression is fairly low compared with the prevalence of persistent pain. It is a retrospective study, so the conclusions that can be made are limited by nature, but it makes up for some of that with a decent (over 100,000) sample size. I’m not entirely sure why they chose to focus so much on opioid use, other than to gather more ammunition in the war against opioid prescription, but they did find evidence of some association between opioid use and new-onset depression or anxiety. There are some neurophysiological links that may account for the relationships among these, so this study may provide some impetus to look at this further.


Abstract

Independent commentary by Gwyn Lewis

Associate Professor Gwyn Lewis is a neurophysiologist based at AUT University’s North Shore Campus in Auckland. She obtained a PhD in motor control from the University of Auckland in 2003. Gwyn had an extended post-doctoral experience undertaking research in motor control, rehabilitation and neurophysiology at the Rehabilitation Institute of Chicago. She currently spends half her time teaching in AUT’s physiotherapy programme and the other half undertaking pain research in the Health and Rehabilitation Research Institute. Most of her research is in pain neurophysiology and how it relates to persistent pain development, efficacy of pain modulation pathways, and cognitive factors and psychosocial influences.


Abstract

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