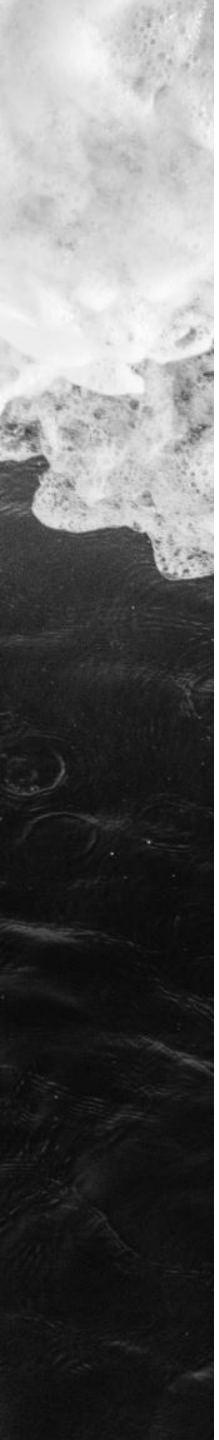


Challenges & updates- perioperative pain management

Engy T. Said, MD
Director, Acute Pain Service
University Of California, San Diego

GOALS OF ACUTE PAIN SERVICE

- Minimize opioids
- Decrease opioid-related adverse events
- Multimodal analgesia
- Improve functional mobility/rehabilitation
- Decrease length of stay

MULTIMODAL ANALGESIA

- NOT GOAL: Total abandonment of intraoperative opioids.
- GOAL: SYNERGY
- GOAL: Decrease total opioid exposure

ACUTE PAIN:

Challenges in acute pain management-

- When poorly controlled --> higher adverse events
- Chronic pain, substance abuse disorder, opioid-tolerance, variable sensitivity profile
- Medical problems: OSA, neurologic disease

ACUTE PAIN:

When poorly controlled → poor physiologic response

- Tachycardia
- Hypertension
- Venous stasis
- Hypercoagulability
- Hyperglycemia
- Decreased alveolar ventilation
- Immunosuppresion
- Cognitive dysfunction

ACUTE PAIN:

When poorly controlled → poor physiologic response

- Persistent Post-Surgical Pain

Opioid Induced Hyperalgesia

Anesthesiology
2000; 93:409–17

Acute Opioid Tolerance

Intraoperative Remifentanil Increases Postoperative Pain and Morphine Requirement

Bruno Guignard, M.D., Anne Elisabeth Bossard, M.D.,† Carole Coste, M.D.,‡ Daniel I. Sessler, M.D.,§ Claude Lebrault, M.D.,* Pascal Alfonsi, M.D.,* Dominique Fletcher, M.D.,* Marcel Chauvin, M.D.‖*

Opioid Induced Hyperalgesia

Perioperative Medicine | February 2013

Intraoperative Infusion of 0.6–0.9 μg · kg^{-1} · min^{-1} Remifentanil Induces Acute Tolerance in Young Children after Laparoscopic Ureteroneocystostomy

Sung-Hoon Kim, M.D.; Min H. Lee, M.D.; Hyungseok Seo, M.D.; In-Gyu Lee, M.D.; Jeong-Yeon Hong, M.D., Ph.D.; Jai-Hyun Hwang, M.D., Ph.D.

+ Author and Article Information

Anesthesiology February 2013, Vol. 118, 337–343.

Opioid Induced Hyperalgesia

AMBULATORY ANESTHESIOLOGY: RESEARCH REPORT

Intraoperative Esmolol Infusion in the Absence of Opioids Spares Postoperative Fentanyl in Patients Undergoing Ambulatory Laparoscopic Cholecystectomy

Section Editor(s): Glass, Peter S. A.Collard, Vincent MD*; Mistraletti, Giovanni MD*; Taqi, Ali MD†; Asenjo, Juan Francisco MD*; Feldman, Liane S. MD†; Fried, Gerald M. MD†; Carli, Franco MD, MPhil*

Author Information

Anesthesia & Analgesia: November 2007 - Volume 105 - Issue 5 - p 1255-1262
doi: 10.1213/01.ane.0000282822.07437.02

Table 3. Analysis of Significant Variables Among the Three Groups

	Control $n = 27$	Esmolol $n = 30$	Remifentanil $n = 28$	*P* 3 groups	*P* Cont versus Esm	*P* Cont versus Remi	*P* Esm versus Remi
Amount of fentanyl used (μg)	168.1 ± 96.8 (155)	91.5 ± 42.7 (100)	237.8 ± 54.7 (238)	**0.0001**	**0.0010**	**0.0036**	**<0.0001**
Nausea in recovery room: n (%)	18 (66.7)	9 (30.0)	19 (67.9)	**0.004**	**0.006**	0.925	**0.004**
Use of ondansetron: n (%)	18 (66.7)	7 (23.3)	20 (71.4)	**0.001**	**0.002**	0.702	**0.001**
No. of patients requiring ondansetron(0/4/8 mg)	9/5/13	23/6/1	8/9/11	**0.0003**	**0.0002**	0.8146	**0.0001**
No. of patients with White-Song score >12 at 1st/30th/60th/90th min or more	16/6/0/5	21/4/3/2	9/8/6/5	0.0409	0.3563	0.0963	**0.0060**
Time from arrival to the PACU to discharge home (min)	180 (130–210)	120 (100–150)	162.5 (110–220)	**0.0033**	**0.0006**	0.3900	**0.0367**

Values are presented as mean ± standard deviation (median), absolute number (percentage), relative number of patients, or median (interquartile range).

P values are calculated with ANOVA one-way analysis of variance with Scheffé test for the parametric normally distributed variables, Pearson χ^2 test for categorical variables, Kruskal–Wallis ranked sum test for comparisons among groups for the parametric not-normally distributed variables and Wilcoxon test between groups for the parametric not-normally distributed variables. Regarding the comparison among the three groups, the Bonferroni correction was used, with the significant value set at $P < 0.017$. Highlighted in bold are the significant differences among or between groups.

PACU = Postanesthesia care unit.

ANESTHESIA & ANALGESIA

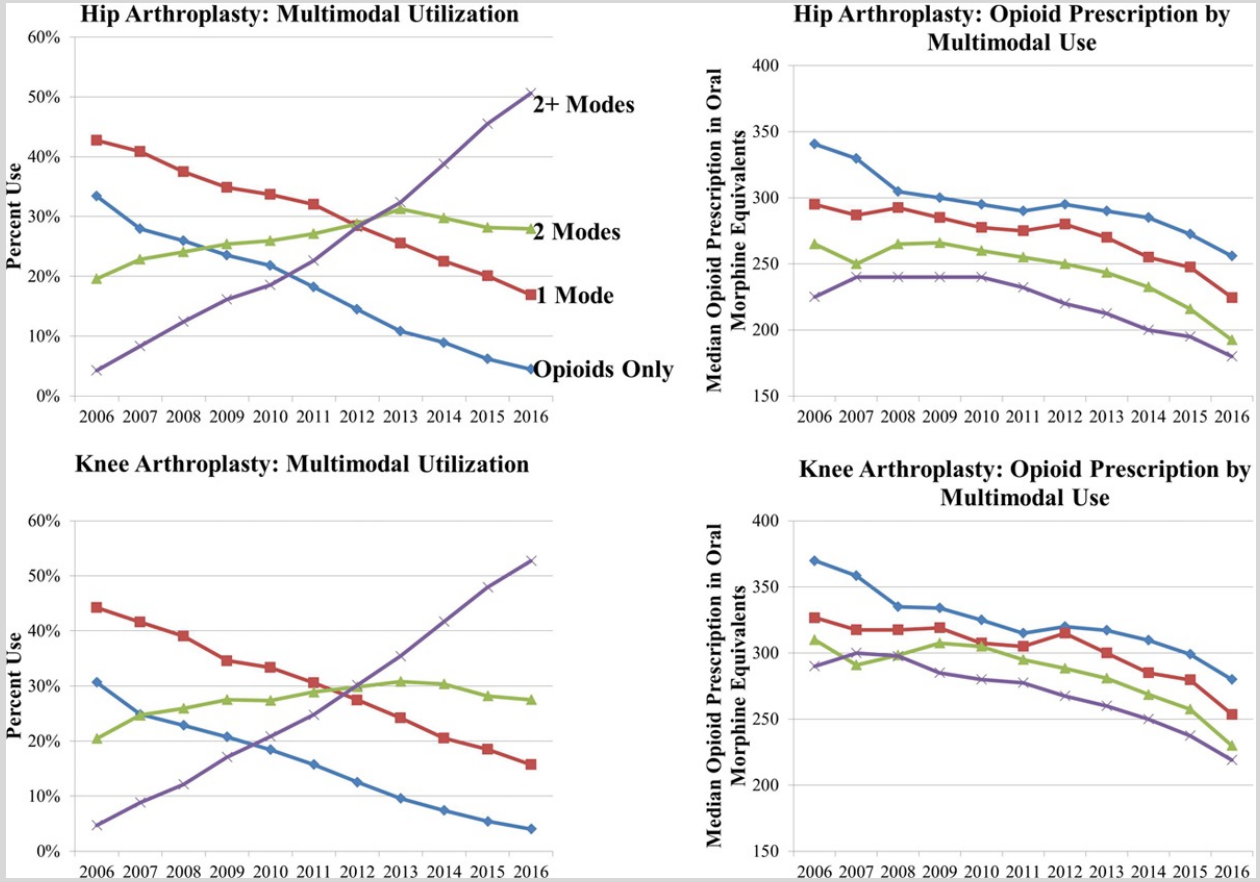
ANESTHESIA & ANALGESIA

Multimodal Analgesia

- Concurrent use of primarily nonopioid analgesics
- Synergistic effects that optimize analgesia while simultaneously preventing adverse effects of opioid medications
- Facilitate enhanced recovery milestones such as early mobilization and return of bowel function
- Key component to ERAS pathways
- Not necessarily Opioid-Free Analgesia

Wick EC, Grant MC, Wu CL. Postoperative multimodal analgesia pain management with nonopioid analgesics and techniques: a review. JAMA Surg. 2017;152:691–697.

ANESTHESIOLOGY
Trusted Evidence: Discovery to Practice



Patterns in multimodal analgesia by number of modes used; utilization (left) and by median opioid prescription (right).

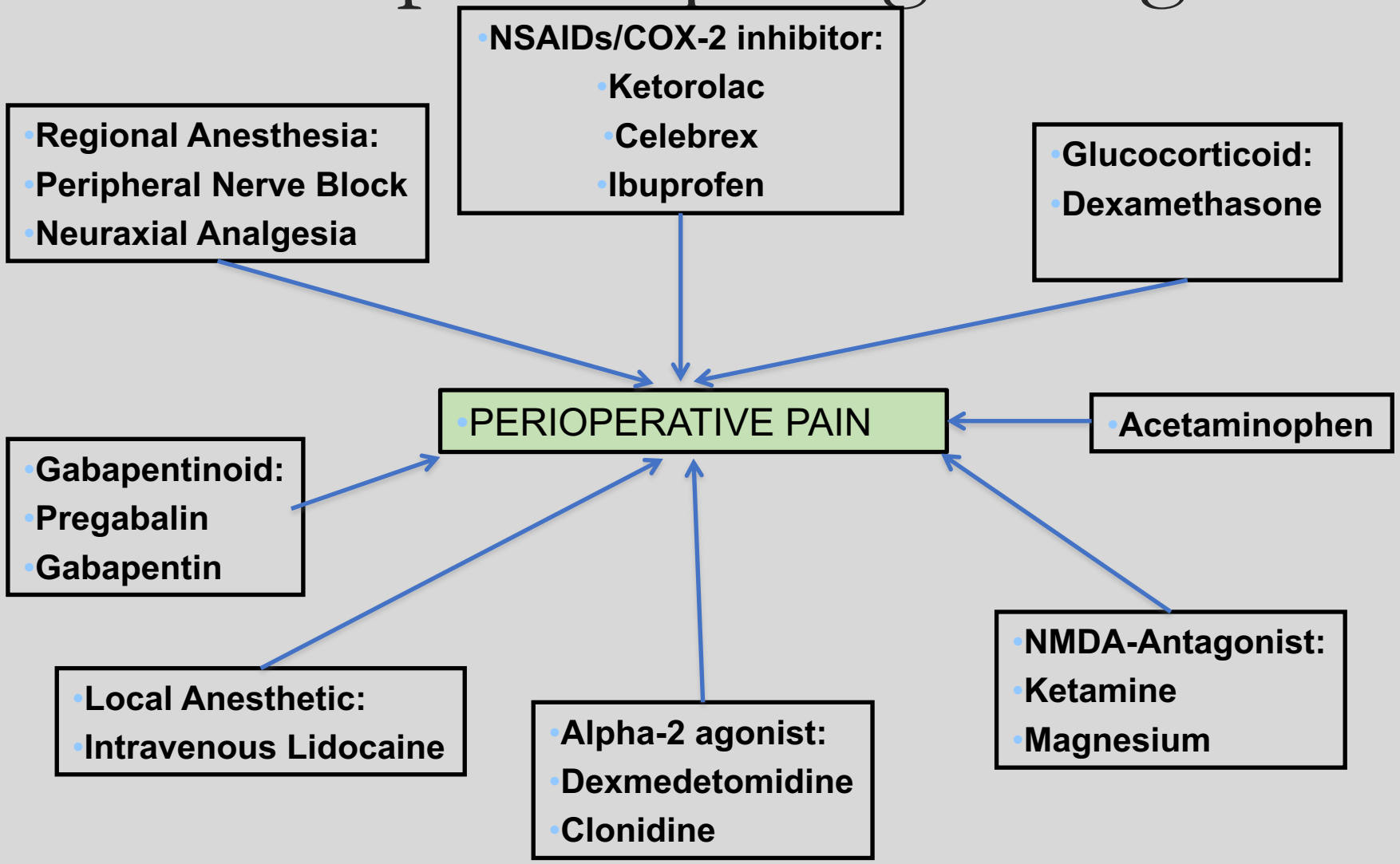
Perioperative Medicine | May 2018

Association of Multimodal Pain Management Strategies with Perioperative Outcomes and Resource Utilization: A Population-based Study

Stavros G. Memtsoudis, M.D., Ph.D., F.C.C.P. ; Jashvant Poeran, M.D., Ph.D.; Nicole Zubizarreta, M.P.H.; Crispiana Cozowicz, M.D.; Eva E. Mörwald, M.D.; Edward R. Mariano, M.D., M.A.S.; Madhu Mazumdar, Ph.D.

2+ mode:
- 19% fewer respiratory events
- 26% fewer GI events

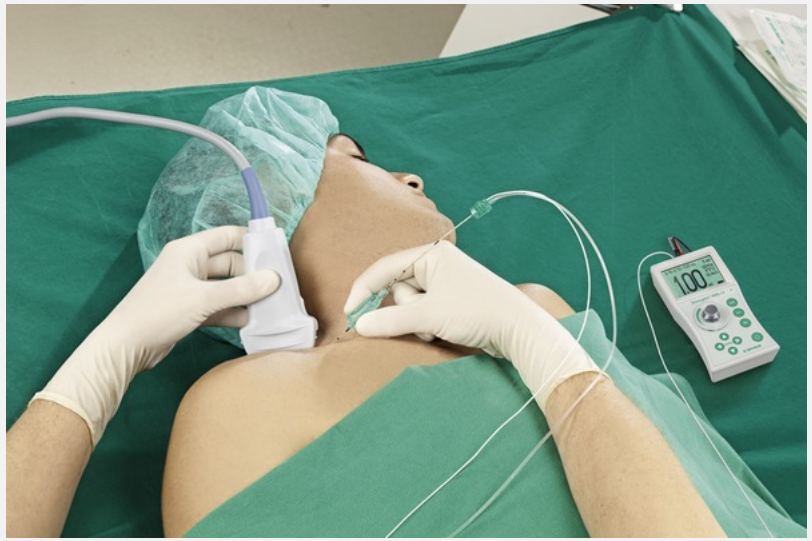
Multimodal Opioid-Sparing Analgesia

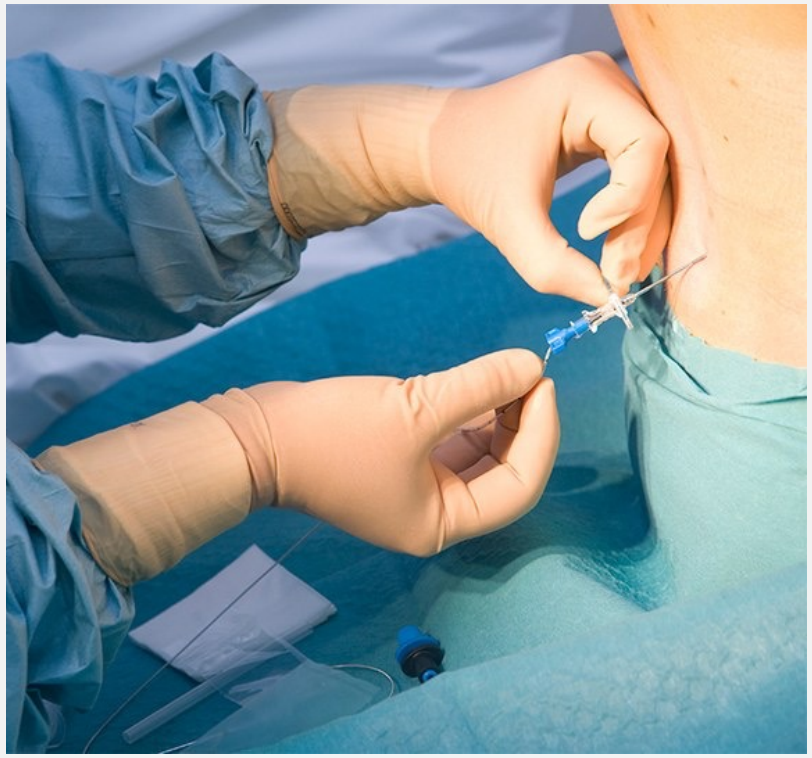


Gabriel et al. State of The Art Drug Treatment Strategies For Post-Operative Pain

Techniques Used

- Peripheral nerve blocks
  - Single-shots (12-24 hours)
  - Catheters
- Neuraxial blocks
  - Thoracic Epidurals
  - Intrathecal Duramorph
- Pharmacologic management
  - NSAIDs
  - Tylenol
  - Gabapentinoids
  - Lidocaine gtt
  - Ketamine gtt
- Peripheral Nerve Stimulation
- Cryoanalgesia
- Mindfulness
- Acupuncture





Thoracic Epidural Analgesia (TEA):

- Superior analgesic choice to intravenous opioids in patients undergoing major open abdominal surgery.
- Reduces postoperative ileus duration after major abdominal surgery by an average of 36 hours.
- The mechanism by which TEA may shorten the duration of ileus may include a decrease in sympathetic tone, stress response and inflammatory processes.
- Has not been shown to decrease hospital length of stay.

T. Werawatganon and S. Charuluxanun, "Patient controlled intravenous opioid analgesia versus continuous epidural analgesia for pain after intra-abdominal surgery," *Cochrane Database Syst. Rev.*, no. 1, p. CD004088, Jan. 2005.
E. Marret, C. Remy, F. Bonnet, and Postoperative Pain Forum Group, "Meta-analysis of epidural analgesia versus parenteral opioid analgesia after colorectal surgery," *Br. J. Surg.*, vol. 94, no. 6, pp. 665–673, Jun. 2007.
H. Jørgensen, J. Wetterslev, S. Møiniche, and J. B. Dahl, "Epidural local anaesthetics versus opioid-based analgesic regimens on postoperative gastrointestinal paralysis, PONV and pain after abdominal surgery," *Cochrane Database Syst. Rev.*, no. 4, p. CD001893, 2000.

TEA- APPROACH

MIDLINE VS. PARAMEDIAN

- Paramedian catheters were observed to cause less epidural tenting, and pass cephalad more reliably than midline catheters.[1]
- Faster catheter insertion times were reported in the paramedian, and higher incidence of paraesthesia in the midline group. [2]
- Adequate local infiltration is a prerequisite for patient comfort during paramedian puncture.[3,4]
- The paramedian approach may be less dependent upon spine flexion.[4]
- No difference in risk of vascular puncture during epidural catheter placement was not associated with lumbar midline or paramedian technique in parturients[3]
  - While another study suggested more paraesthesia and bloody puncture in non-pregnant adults when the midline approach was used.[4]

1. Blomberg RG. Technical advantages of the paramedian ap- proach for lumbar epidural puncture and catheter introduction. A study using epiduroscopy in autopsy subjects. Anaesthesia 1988; 43: 837–43
2. Leeda M, Stienstra R, Arbous MS, et al. Lumbar epidural catheter insertion: the midline vs. the paramedian approach. Eur J Anaesthesiol 2005; 22: 839 – 42
3. Griffin RM, Scott RP. Forum. A comparison between the midline and paramedian approaches to the extradural space. Anaesthesia 1984; 39: 584 – 621
4. Podder S, Kumar N, Yaddanapudi LN, Chari P. Paramedian lumbar epidural catheter insertion with patients in the sitting position is equally successful in the flexed and unflexed spine. Anesth Analg 2004; 99: 1829–32

TEA- APPROACH

- LOR: SALINE VS AIR
  - A meta-analysis in 2009 included five RCTs comparing LOR with saline vs air:
    - 4 in OB population
    - 1 general patient population
    - Total of 4422 patients.
  - No significant difference in any outcome was found, other than a 1.5% reduction in post- dural puncture headache when using saline.

Schier R, Guerra D, Aguilar J, et al. Epidural space identification: a meta-analysis of complications after air versus liquid as the medium for loss of resistance. Anesth Analg 2009; 109: 2012–21

TEA- TECHNIQUE

- **CATHETER INSERTION AND FIXATION**
  - The catheter should be inserted at least 4 cm into the epidural space.[1]
    - Recent study (2009) reported a higher success rate with more than 5 cm[2]
  - Should we tunnel?
    - Cohort of 82 patients with catheters tunneled 5 cm, was associated with less motion of the catheter, but the percentage of catheters maintaining original position was not statistically different.[3]
  - Should we suture?
    - Suturing of the epidural catheter was similarly associated with less migration, but at the cost of increased inflammation at the puncture site.[4]
  - We should DERMABOND!

1. Hamilton CL, Riley ET, Cohen SE. Changes in the position of epidural catheters associated with patient movement. Anesthesiology 1997; 86: 778 – 84; discussion 29A
2. Konigsrainer I, Bredanger S, Drewel-Frohnmeyer R, et al. Audit of motor weakness and premature catheter dislodgement after epidural analgesia in major abdominal surgery. Anaesthesia 2009; 64: 27–31
3. Bougher RJ, Corbett AR, Ramage DT. The effect of tunnelling on epidural catheter migration. Anaesthesia 1996; 51: 191 – 4
4. Chadwick VL, Jones M, Poulton B, Fleming BG. Epidural catheter migration: a comparison of tunnelling against a new technique of catheter fixation. Anaesth Intensive Care 2003; 31: 518 – 22

TEA- HOW WE DO IT

- TECHNIQUE
- TEST DOSE
- SECURING
- INFUSION SETTINGS
  - LOCAL ONLY
  - LOCAL + OPIOID
  - MORPHINE AND PAUSE

TEA- BENEFITS

- Superior pain control in comparison to parental opioids for thoracic and upper abdominal procedures. [1, 2]
- Decrease perioperative cardiac events
  - Better pain relief → decrease stress response
  - sympatholytic effects of TEA could be protective for perioperative myocardial ischemia and infarction. However, the magnitude of this effect is not likely clinically relevant
  - To optimize the reduction in cardiac sympathetic efferent activity, the TEA catheter should be placed at high thoracic levels (T1 or T2).
- GI Benefits
  - Reduced opioid induced GI hypomotility[3,4]
  - Improved intestinal perfusion as long as hemodynamics are maintained.
  - Potentially improve anastomotic perfusion and patency

1. Block BM, Liu SS, Rowlingson AJ, Cowan AR, Cowan JA Jr, Wu CL: Efficacy of postoperative epidural analgesia: A meta-analysis. JAMA 2003; 290:2455–
2. Werawatganon T, Charuluxanun S: Patient controlled intravenous opioid analgesia *versus* continuous epidural analgesia for pain after intra-abdominal surgery. Cochrane Database Syst Rev 2005; CD004088
3. Liu SS, Wu CL: Effect of postoperative analgesia on major postoperative complications: A systematic update of the evidence. Anesth Analg 2007; 104:689–702
4. arli F, Trudel JL, Belliveau P: The effect of intraoperative thoracic epidural anesthesia and postoperative analgesia on bowel function after colorectal surgery: A prospective, randomized trial. Dis Colon Rectum 2001; 44:1083–9

TEA- Benefits

- Reduced Pulmonary Complications
  - Decrease in the incidence of atelectasis, pulmonary infections, hypoxemia, and overall pulmonary complications[1].
- Decreased mortality for patients with multiple rib fractures[2].

Table 3. Benefits of Thoracic Epidural Analgesia

- Superior perioperative analgesia compared with systemic opioids
- Decreased pulmonary complications
- Decreased duration of mechanical ventilation
- Decreased duration of postoperative ileus after abdominal surgery
- Decreased postoperative protein catabolism
- Decreased mortality in patients with multiple rib fractures

Smith C. Manion, M.D., Timothy J. Brennan, Ph.D., M.D.; Thoracic Epidural Analgesia and Acute Pain Management. *Anesthesiology* 2011;115(1):181-188

1. Ballantyne JC, Carr DB, deFerranti S, Suarez T, Lau J, Chalmers TC, Angelillo IF, Mosteller F: The comparative effects of postoperative analgesic therapies on pulmonary outcome: Cumulative meta-analyses of randomized, controlled trials. Anesth Analg 1998; 86:598–612
2. Simon BJ, Cushman J, Barraco R, Lane V, Luchette FA, Miglietta M, Roccaforte DJ, Spector R, EAST Practice Management Guidelines Work Group: Pain management guidelines for blunt thoracic trauma. J Trauma 2005; 59:1256–67

TEA- complications/adverse events

- Increased risk of neurologic injury to spinal cord
- Epidural Hematoma (< 1 in 150,000)
  - Usually in the setting of impaired coagulation
  - Most traumatic events are 1. catheter placement, 2. removal. [1]
- Epidural Abscess
  - Perioperative antibiotics lower the risk
  - No of indwelling catheter days is biggest risk factor
- Dural puncture → Postdural Puncture Headache
- Back Pain
- Catheter migration
  - Intravascular or Intrathecal
- Pleural puncture or Pneumothorax
- Adverse effects to infusing medications
  - Nausea/Vomiting, Hypotension, Urinary Retention, Sedation/Respiratory Depression.

Vandermeulen E: Guidelines on anticoagulants and the use of locoregional anesthesia. Minerva Anestesiol 2003; 69:407–11

SPINAL/EPIDURAL HEMATOMA

- Prominent epidural venous plexus
- Can be spontaneous but primarily in anticoagulated or thrombocytopenic patients
- RARE *but*…

  Recent studies on the incidence of the risk of spinal hematoma in patients without overt risk factors showed an increase to 1:18,000 after epidural and 1:3600, even 1:1000, in elderly patients undergoing lower extremity surgery.

- RISK FACTORS:
  - Increased age (small epidural space?)
  - More frequent in females (osteoperosis → vertebral deformities or fractures)
  - Physiologic or iatrogenic coagulopathy

https://www.nysora.com/foundations-of-regional-anesthesia/complications/diagnosis-management-spinal-peripheral-nerve-hematoma/

SPINAL/EPIDURAL HEMATOMA

- HISTORY AND PHYSICAL EXAM:
  - CLASSIC: back pain radiating to corresponding dermatome
    - Pain- severe, localized and constant. Worse with palpation, anything that increases spinal pressure (cough/straining)
  - Evolving: focal neurologic deficit
    - Progressive lower extremity weakness: most common presenting sign
    - Associated sx: numbness, weakness, urinary or fecal incontinence.
    - Unilateral or bilateral weakness, sensory deficits with unilateral or bilateral radicular paresthesias, various alterations in deep tendon reflexes, and alterations of bladder or anal sphincter tone
    - **RAPID PROGRESSION**

      paraparesis in lumbar or quadriparesis in high thoracic/cervical procedure

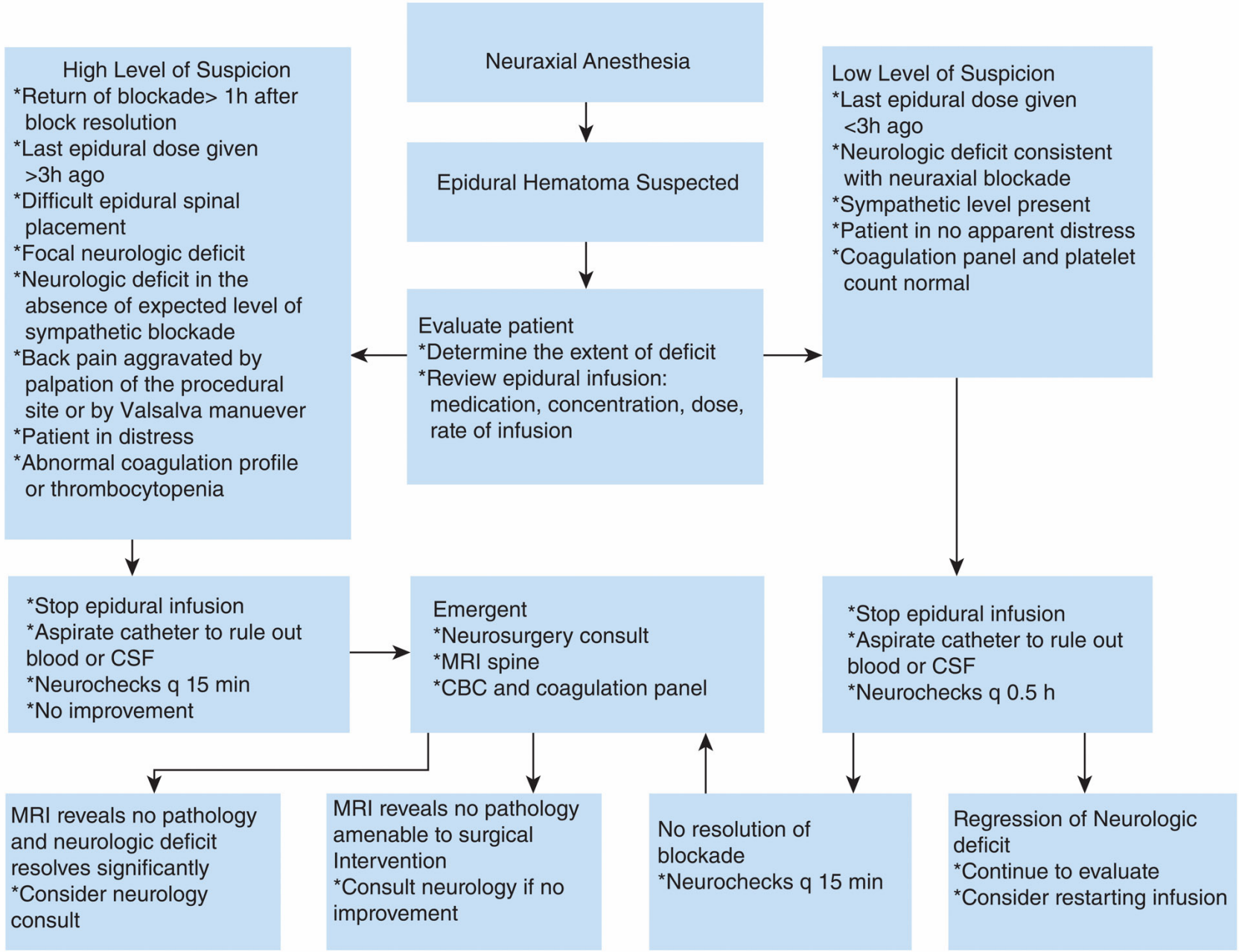
https://www.nysora.com/foundations-of-regional-anesthesia/complications/diagnosis-management-spinal-peripheral-nerve-hematoma/

SPINAL/EPIDURAL HEMATOMA

- DIAGNOSIS
  - Physical exam
  - **Sensory or motor deficit several hours after spinal or epidural block has worn off (with or without back pain) is highly pathognomonic and should be considered and treated as spinal or epidural hematoma until proven otherwise.**
  - MRI is gold standard for diagnostic imaging.
    - Location of epidural hematoma and identify an associated vascular malformation; extent of the hematoma as well as the degree of cord compression

- PROGNOSIS
  - Neurologic recovery after conservative management has been reported in patients with back pain and leg weakness without paralysis.
  - Neurologic recovery can occur if surgery and decompression is performed within 36 hours of a complete motor deficit and within 48 hours of a partial deficit.

https://www.nysora.com/foundations-of-regional-anesthesia/complications/diagnosis-management-spinal-peripheral-nerve-hematoma/


Neuraxial Anesthesia
Epidural Hematoma Suspected
Evaluate patient
*Determine the extent of deficit
*Review epidural infusion: medication, concentration, dose, rate of infusion
High Level of Suspicion
*Return of blockade> 1h after block resolution
*Last epidural dose given >3h ago
*Difficult epidural spinal placement
*Focal neurologic deficit
*Neurologic deficit in the absence of expected level of sympathetic blockade
*Back pain aggravated by palpation of the procedural site or by Valsalva manuever
*Patient in distress
*Abnormal coagulation profile or thrombocytopenia
Low Level of Suspicion
*Last epidural dose given <3h ago
*Neurologic deficit consistent with neuraxial blockade
*Sympathetic level present
*Patient in no apparent distress
*Coagulation panel and platelet count normal
*Stop epidural infusion
*Aspirate catheter to rule out blood or CSF
*Neurochecks q 15 min
*No improvement
Emergent
*Neurosurgery consult
*MRI spine
*CBC and coagulation panel
*Stop epidural infusion
*Aspirate catheter to rule out blood or CSF
*Neurochecks q 0.5 h
MRI reveals no pathology and neurologic deficit resolves significantly
*Consider neurology consult
MRI reveals no pathology amenable to surgical Intervention
*Consult neurology if no improvement
No resolution of blockade
*Neurochecks q 15 min
Regression of Neurologic deficit
*Continue to evaluate
*Consider restarting infusion

NYSORA©

IT Duramorph- Benefits

- What is IT Duramorph-
  - A very small dose of preservative free morphine into the CSF via spinal procedure.
  - 100-400mcg

- BENEFITS-
  - Excellent postoperative analgesia with very small dosage.
  - No motor, sensory or autonomic side effects
  - = less BP changes in the OR
  - = less intraop opioids
  - Decreased pain at rest and with movement for 24hours after major surgery

Patient Monitoring

- Should not have any motor/sensory changes
- Monitor for respiratory changes
- Reverse with Narcan

IT Duramorph- delayed respiratory depression

- Hydrophillic property- stays in CSF longer
- Peak time for respiratory depression is 6-10hours
- CSF concentration significantly declines after 12hours

Practice Guidelines for the Prevention, Detection, and Management of Respiratory Depression Associated with Neuraxial Opioid Administration

*An Updated Report by the American Society of Anesthesiologists Task Force on Neuraxial Opioids and the American Society of Regional Anesthesia and Pain Medicine**

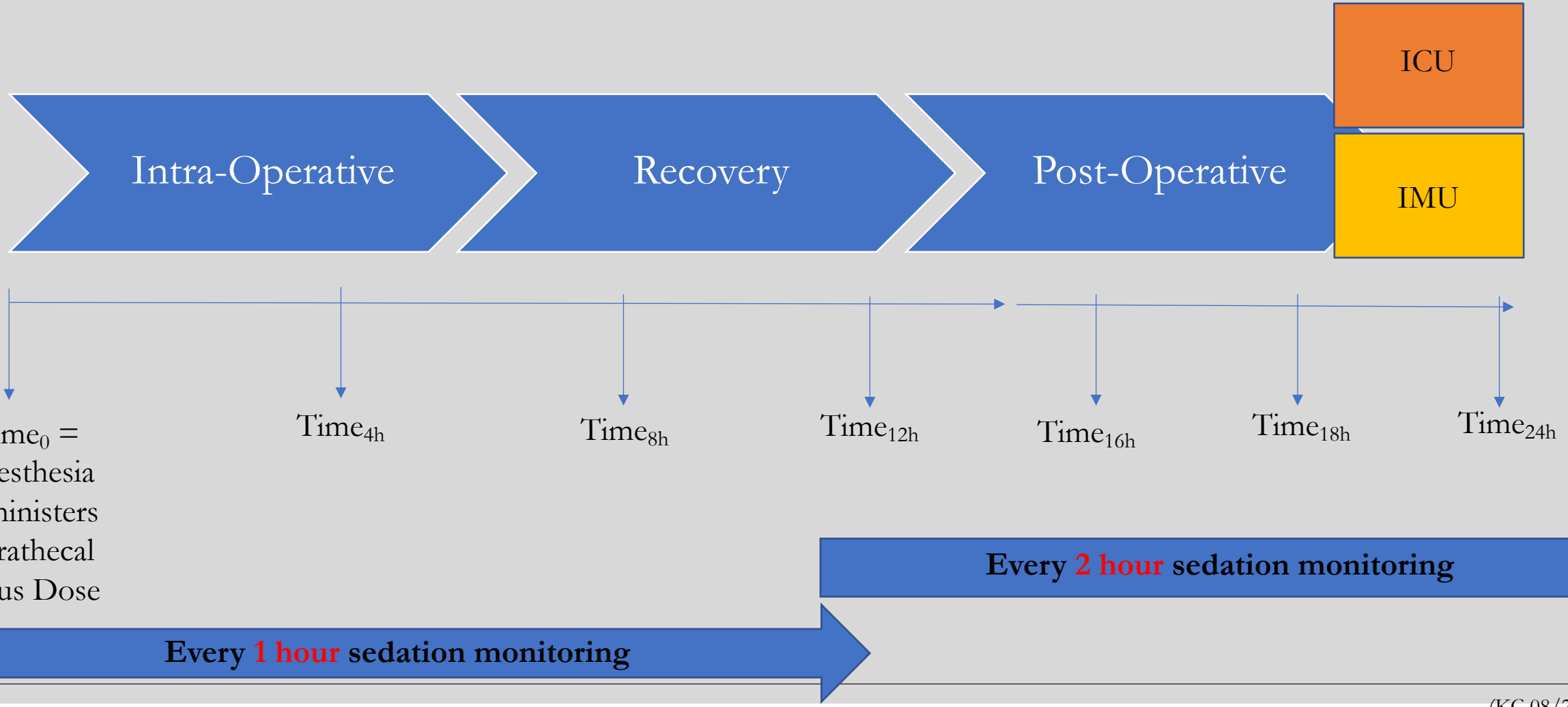
Recommendations for Detection and Monitoring for Respiratory Depression

- Monitor all patients receiving neuraxial opioids for adequacy of ventilation (*e.g.*, respiratory rate, depth of respiration [assessed without disturbing a sleeping patient]), oxygenation (*e.g.*, pulse oximetry when appropriate), and level of consciousness.**
- Increased monitoring (*e.g.*, intensity, duration, or additional methods of monitoring) may be warranted for patients at increased risk of respiratory depression (*e.g.*, unstable medical condition, obesity, obstructive sleep apnea,†† concomitant administration of opioid analgesics or hypnotics by other routes, extremes of age).

Single-injection Neuraxial Hydrophilic Opioids (*e.g.*, Morphine, not Including Sustained or Extended-release Epidural Morphine).

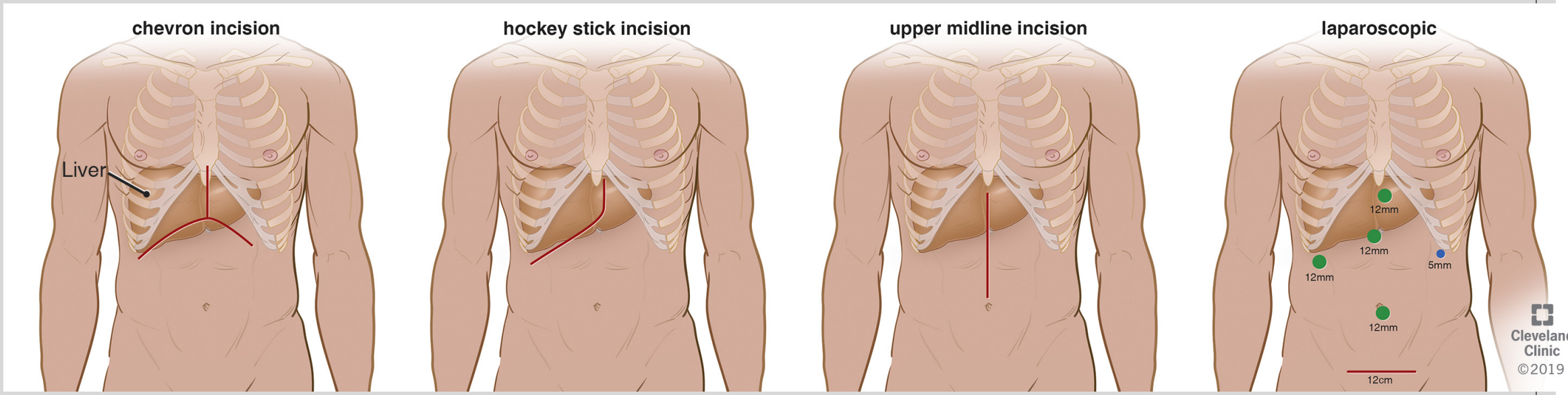
- Monitor for a *minimum* of 24 h after administration.
- Monitor *at least* once per hour for the first 12 h after administration, followed by monitoring *at least* once every 2 h for the next 12 h (*i.e.*, from 12 to 24 h).
- After 24 h, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.

Timeline of Phases of Care



(KC 08/2019)

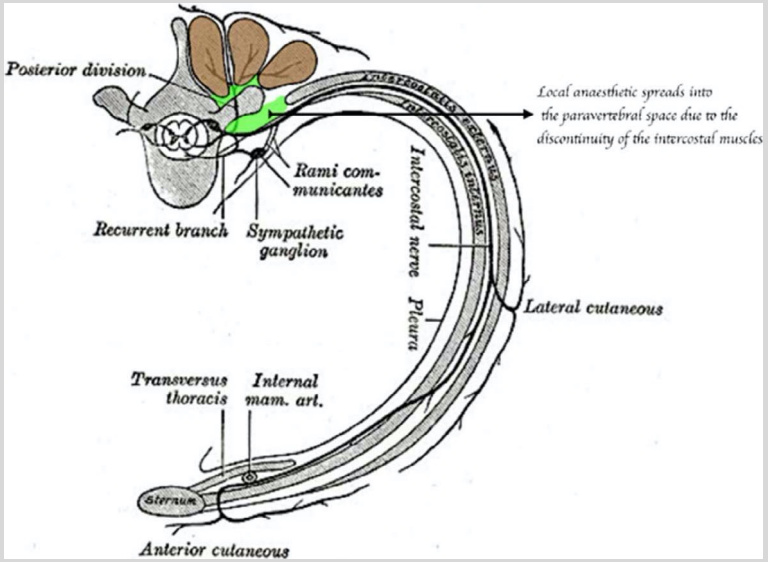
Liver Resections- Incisions

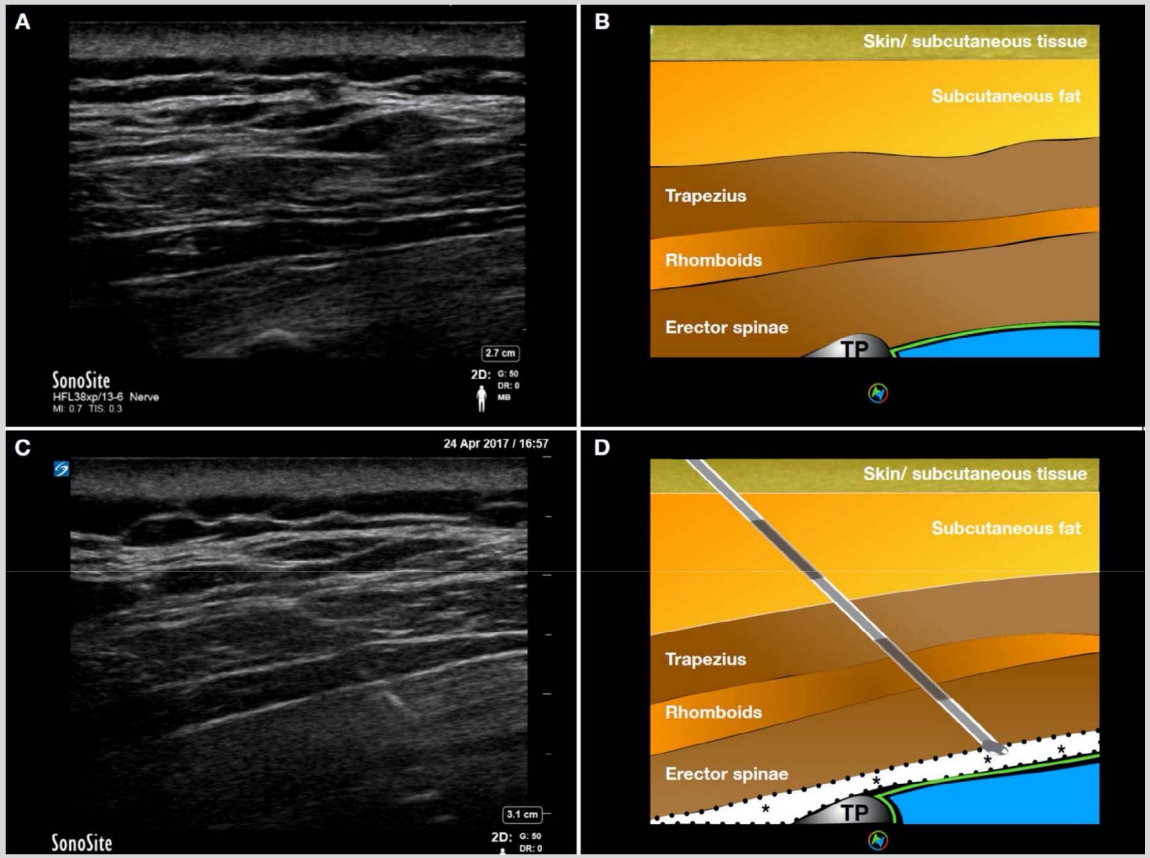


https://newsroom.clevelandclinic.org/wp-content/uploads/sites/4/2019/10/19-DDSI-1702729-LDLT_EvolutionFormat.jpg

Erector Spinae Block Catheter?

- Interfascial plane blocks = VOLUME, low concentration for efficacy
- LA spread to PVB space



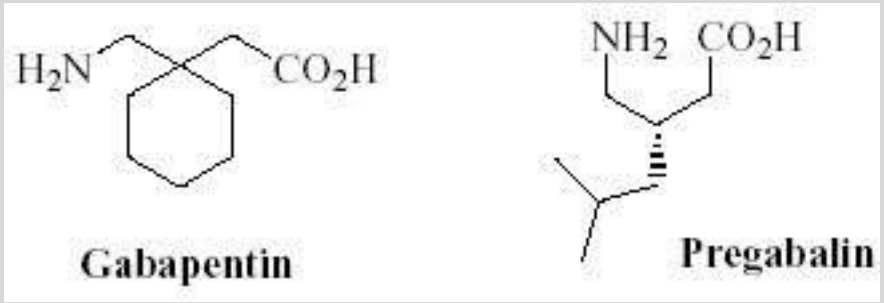


https://www.wfsahq.org/components/com_virtual_library/media/435d726bce0438186341fc2e8bd688ec-atow-414-00.pdf

PHARMACOLOGIC OPIOID-SPARING ANALGESICS

Gabapentinoids

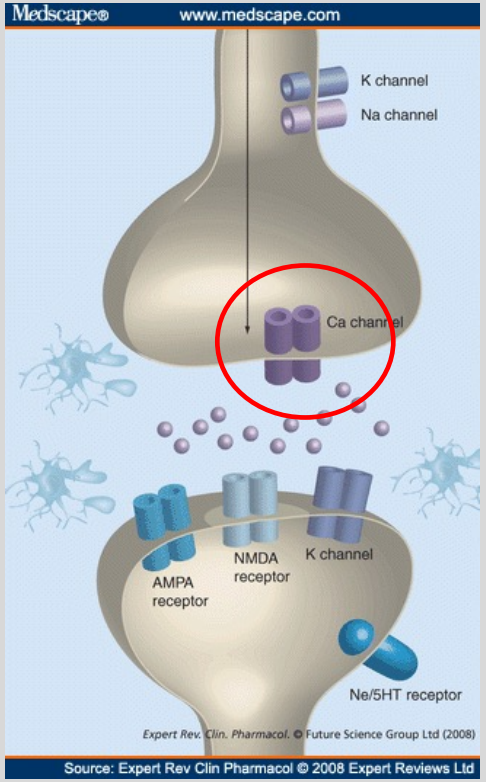
- Gabapentin
- Pregabalin/Lyrica



PHARMACOLOGIC OPIOID-SPARING ANALGESICS

Mechanism of Gabapentinoids

- Derivatives of GABA neurotransmitter, which blocks voltage-dependent calcium channels



PHARMACOLOGIC OPIOID-SPARING ANALGESICS

Gabapentin/Pregabalin - Literature

- Controversy in its benefit as well
- A meta-analysis demonstrated it **decreased postoperative opioid consumption but increase sedation**[1]
- In hysterectomy and myomectomy, there is a **decrease in postoperative opioid use**, but no change in analgesia during acute and chronic stage[2]
- A meta-analysis demonstrated **no benefit in acute pain for total knee arthroplasties**[3]
- A perioperative course had **no benefit in cesarean delivery**[4]
- A meta-analysis demonstrated that gabapentin and pregabalin **decreased chronic pain** following various surgeries[5]

[1]Arumugam et al. Use of preoperative gabapentin significantly reduces postoperative opioid consumption: a meta-analysis. 2016 J Pain Res
[2]Fassoulaki et al. Perioperative pregabalin for acute and chronic pain after abdominal hysterectomy or myomectomy: a randomised controlled trial. 2012 Eur J Anaesthesiol
[3]Hamilton et al. A Meta-Analysis on the Use of Gabapentinoids for the Treatment of Acute Postoperative Pain Following Total Knee Arthroplasty. 2016 J Bone Joint Surg Am
[4]Monks et al. A Perioperative Course of Gabapentin Does Not Produce a Clinically Meaningful Improvement in Analgesia after Cesarean Delivery: A Randomized Controlled Trial. 2015 Anesthesiology
[5]Clarke et al. The prevention of chronic postsurgical pain using gabapentin and pregabalin: a combined systematic review and meta-analysis. 2012 Anesth Analg

PHARMACOLOGIC OPIOID-SPARING ANALGESICS

- Pregabalin:
  - Anticonvulsant agent
  - 25% opioid sparing rate at 24 hrs
  - optimal dose or frequency in this setting remains unclear, varying from 75mg-300mp po preoperatively.
  - no difference in acute pain outcomes between single and multiple dosing
  - side effects include increased sedation and visual disturbances.

Mishriky BM, Waldron NH, Habib AS. Impact of pregabalin on acute and persistent postoperative pain: a systematic review and meta-analysis. Br J Anaesth. 2015;114:10–31.

ANESTHESIOLOGY

Perioperative Use of Gabapentinoids for the Management of Postoperative Acute Pain

A Systematic Review and Meta-analysis

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What We Already Know about This Topic

- Gabapentinoids such as gabapentin and pregabalin are often included in perioperative multimodal analgesia regimens in an attempt to reduce acute, subacute, and chronic pain after surgery
- Current American Pain Society and European Society of Regional Anaesthesia and Pain Therapy guidelines offer conflicting recommendations for the use of gabapentinoids in the perioperative period

OPIOID-FREE ANESTHESIA

Systematic review and meta-analysis of 281 randomized controlled trials in adult surgical patients

- Trials of pregabalin or gabapentin initiated between 1 week before and 12 h after surgery
- Included 24,682 participants
- **Primary outcome**: intensity of postoperative acute pain. Clinical significance was based on the minimally important difference (10 points out of 100)

From: Perioperative Use of Gabapentinoids for the Management of Postoperative Acute Pain: A Systematic Review and Meta-analysis. *Anesthesiology*. 2020;133(2):265-279. doi:10.1097/ALN.0000000000003428

Co-primary Outcomes:

- Postoperative acute pain at 6, 12, 24, 48, and 72h after surgery. Measured by any quantitative pain scale

Secondary Outcomes:

- Intensity of postoperative subacute pain (weeks 4 to 12)
- Incidence of postoperative chronic pain (3+ months)
- Cumulative opioid use 24, 48, and 72h after surgery.
- Persistent opioid use- 60+ days
- Length of stay
- Incidence of adverse events: dizziness, fall or ataxia, delirium, drug addiction or abuse, visual disturbance, respiratory failure, opioid-related adverse events (Opioid-Related Symptom Distress Scale), and postoperative nausea or vomiting

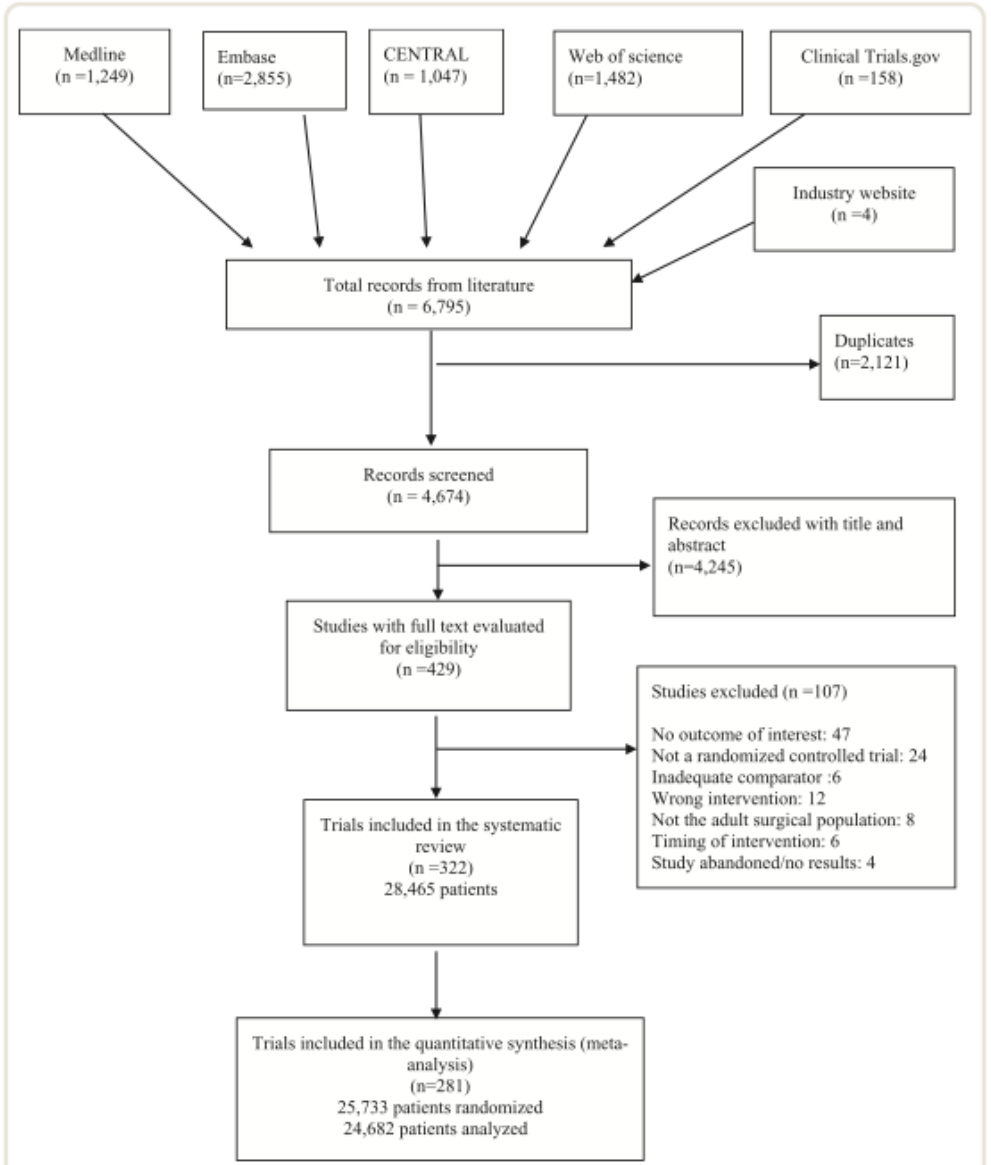

Fig. 1. Flow diagram of trials

27% orthopedic or spine surgery
23% open abdominal surgery
15% endoscopic abdominal surgery
10% ENT, ophtho
7% plastics, breast
1% neurosurgery
10% miscellaneous

52% gabapentin, 43%pregabalin
5% both drugs

71% given pre-op
4% postop
25% both time periods

9% regional analgesia
84% no regional
7% did not mention

Primary/Co-primary Outcomes:

Gabapentinoids were associated with statistically lower postoperative pain intensity

Postoperative time period	Gabapentinoids *vs.* Controls Pain Score Mean Difference (100-point scale), [95% CI]
6 h	-10, [-12 to -9]
12 h	-9, [-10 to -7]
24 h	-7, [-8 to -6]
48 h	-3, [-5 to -1]

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- A slightly lower postoperative pain intensity was observed at 6, 12, 24, and 48 h with gabapentinoids administration but *not at 72h*.
- *Not clinically significant* ranging below the minimally important difference (10 points out of 100) for each time point.

Secondary Outcomes:

- **Intensity of postoperative subacute pain (weeks 4 to 12)**
  Slightly lower postoperative subacute pain intensity. Not clinically significant.

- **Incidence of postoperative chronic pain (3+ months)**
  Not associated with the risk of development of postoperative chronic pain

- **Cumulative opioid use 24, 48, and 72h after surgery.**
  Slightly lower at 24h & 48hrs

- **Persistent opioid use- 60+ days**
  One trial evaluated the risk of persistent opioid use associated with ganapentin versus placebo and found no effect

Secondary Outcomes:

- **Length of stay**

  Longer hospital length of stay, no difference for the length of stay in ICU or PACU

- **Incidence of adverse events**

  -Less nausea & vomiting
  -Greater dizziness & visual disturbances
  -Not significantly associated with respiratory failure, ataxia/falls, or delirium.
  -Risk of respiratory failure was not different when gabapentinoids were used with opioids.
  -Two trials showed no effect of gabapentinoids use on opioid-related adverse events.

- Gabapentinoids were not associated with clinically meaningfully different postoperative pain intensity

Results do not support the routine use of gabapentinoids for the management of postoperative pain in adults.

Verret M, *et al*. ANESTHESIOLOGY. August 2020.

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What This Article Tells Us That Is New

- In a meta-analysis of 281 randomized controlled trials comparing gabapentinoids with controls, no clinically meaningful difference in acute, subacute, or chronic pain was observed
- Although the risk of postoperative nausea and vomiting was slightly lower, adverse events of dizziness and visual disturbance were greater with gabapentinoids use

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NEUROLOGY

FDA Issues Warning About Breathing Difficulties With Gabapetinoid Use

A Dedicated Acute Pain Service Is Associated With Reduced Postoperative Opioid Requirements in Patients Undergoing Cytoreductive Surgery With Hyperthermic Intraperitoneal Chemotherapy

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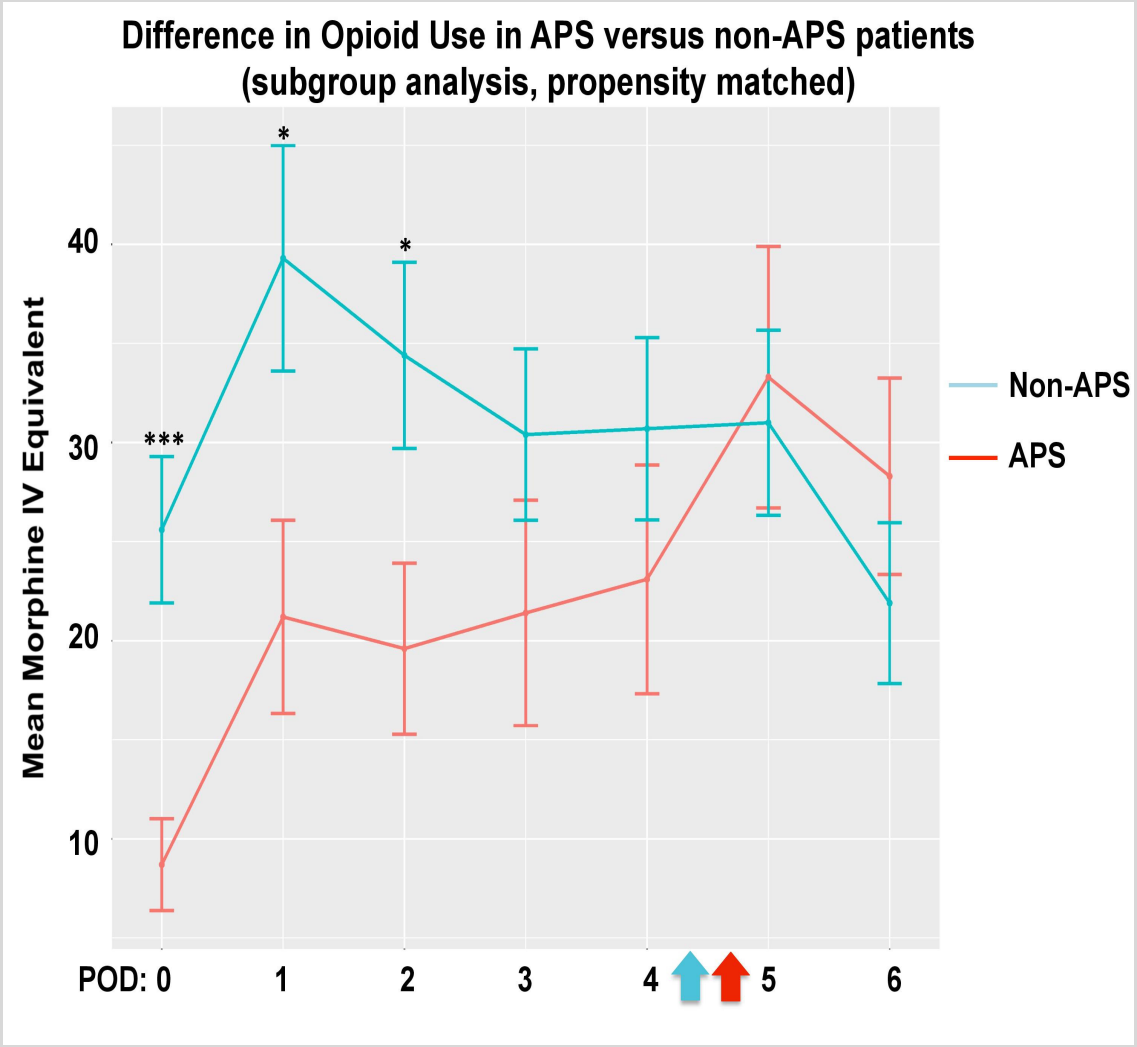
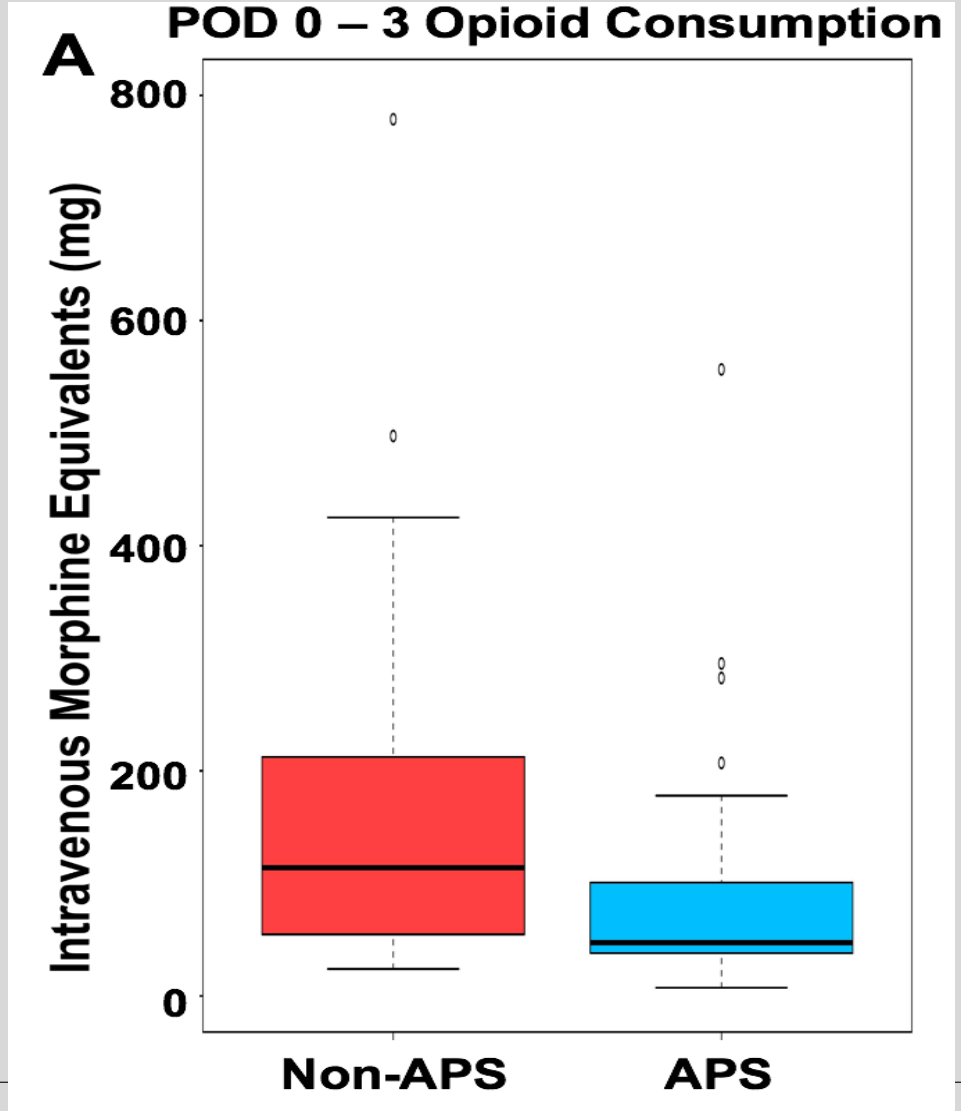
APS OUTCOME- HIPEC

- Mean MEQs POD 1
  - 21.2 vs 39.3
- Mean MEQs POD 0-3
  - 55.9 vs 102.7



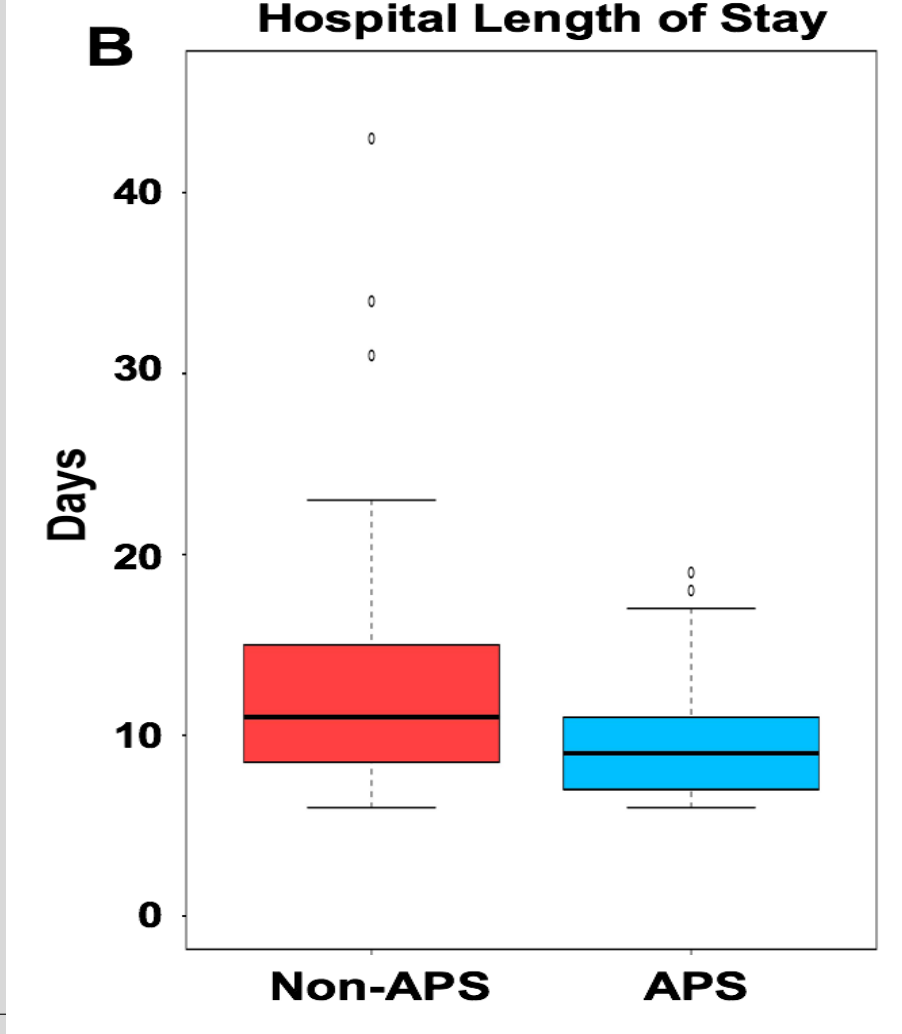
APS OUTCOME- WHIPPLE PROCEDURE

- Non-APS:
  - 114mg MEQs [54.7, 212.4mg MEQs]
- APS:
  - 47.4mg MEQs [38.1, 100.8mg MEQs]
- **Median difference was 44.8mg MEQs (95% CI 14.2 - 90.2mg MEQs, p = 0.002)**



APS OUTCOME- WHIPPLE PROCEDURE

- Median hospital length of stay
- Non-APS:
  - 11 days [9, 15 days]
- APS:
  - 9 days [7, 11 days]
- **Median difference was 2.0 days (95% CI 0.8 – 4.0, p = 0.01)**



APS OUTCOME- WHIPPLE PROCEDURE

Table 2. Outcomes

	Unmatched			Propensity-Score Matched		
	non-APS	APS	p-value	non-APS	APS	p-value
Intensive Care Unit Admission [%]	27 [77.1]	25 [59.5]	0.16	27 [77.1]	19 [54.3]	0.08
Time to ambulation (days), median [quartiles]	3 [2,4]	2 [2,3]	***0.01***	3 [2,4]	2 [1,2]	***0.007***
Time to oral diet (days), median [quartiles]	6 [4,7]	4 [3,5]	***0.0006***	6 [4,7]	4 [3,5]	***0.001***
Time to bladder catheter removal (days), median [quartiles]	2 [2,3]	4 [2,5]	***0.007***	2 [2,3]	3 [2,5]	***0.01***

quartiles = [25%, 75% quartiles]

p-value calculated by Wilcoxon Rank Sum Test or Pearson Chi-Square test for continuous and binary variables, respectively

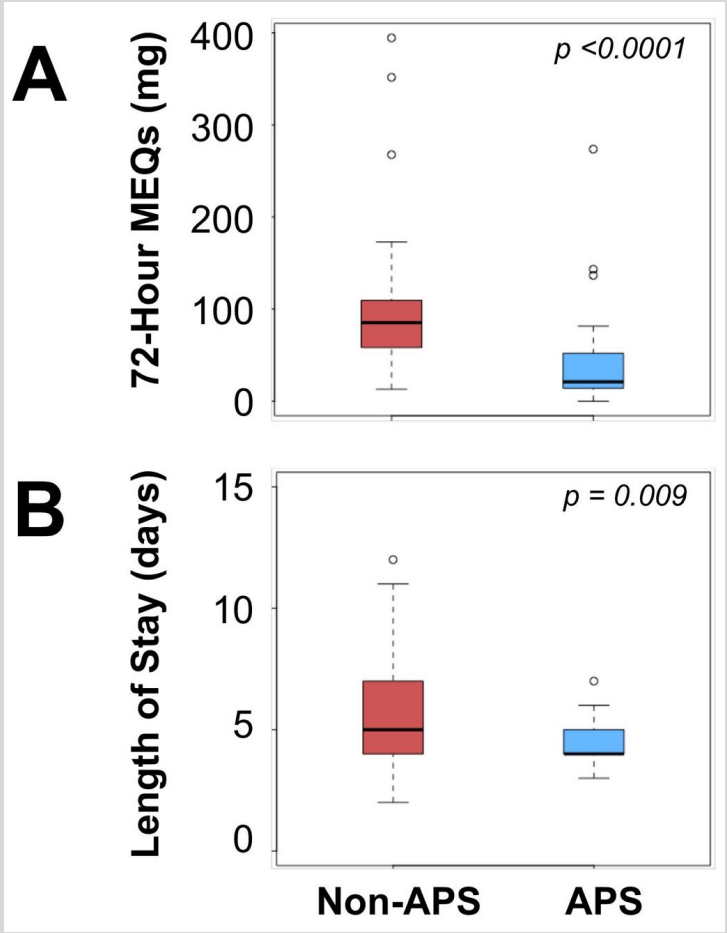
- **APS was associated with a decrease in time to ambulation and tolerance of oral diet**

APS OUTCOME- WHIPPLE PROCEDURE

	Non-APS (%)	APS (%)	p-value
Any Complication	23 (63.9)	18 (43.9)	0.079
In-hospital mortality	0 (0)	0 (0)	N/A
Neurologic Event	1 (2.8)	2 (3.9)	0.635
Cardiac Event	4 (11.1)	3 (7.3)	0.563
Pulmonary Event	2 (5.6)	3 (7.3)	0.754
Ileus	10 (27.8)	4 (9.8)	0.041
Intra-abdominal infection, leak	11 (30.6)	7 (17.1)	0.163
Wound infection	3 (8.3)	3 (7.3)	0.868
Clostridium difficile infection	2 (5.6)	0 (0)	0.126
Urinary tract infection	1 (2.8)	2 (4.9)	0.635
Other infection	1 (2.8)	1 (2.4)	0.926
Deep vein thrombosis/Pulmonary Embolism	1 (2.8)	1 (2.4)	0.926
Significant bleeding	1 (2.8)	2 (4.9)	0.635
Acute kidney injury	2 (5.6)	0 (0)	0.126
Return to the operating room	1 (2.8)	1 (2.4)	0.926
Other complication	3 (8.3)	0 (0)	0.059

- Ileus occurred in 27.8% of Non-APS patient cohort vs 9.8% of APS cohort group. APS group had 60% less incidence of ileus.

APS OUTCOME- VENTRAL HERNIA REPAIR W/ MESH

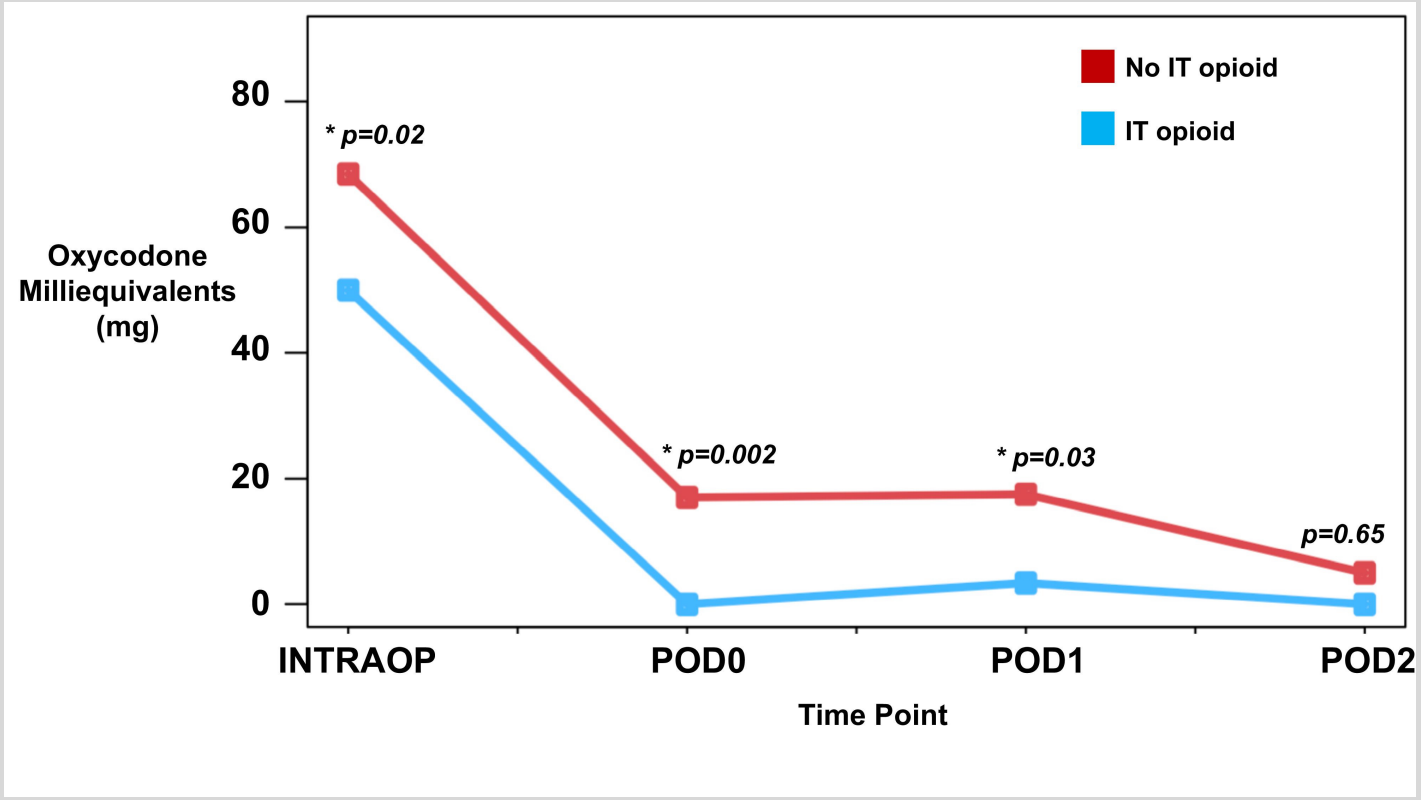


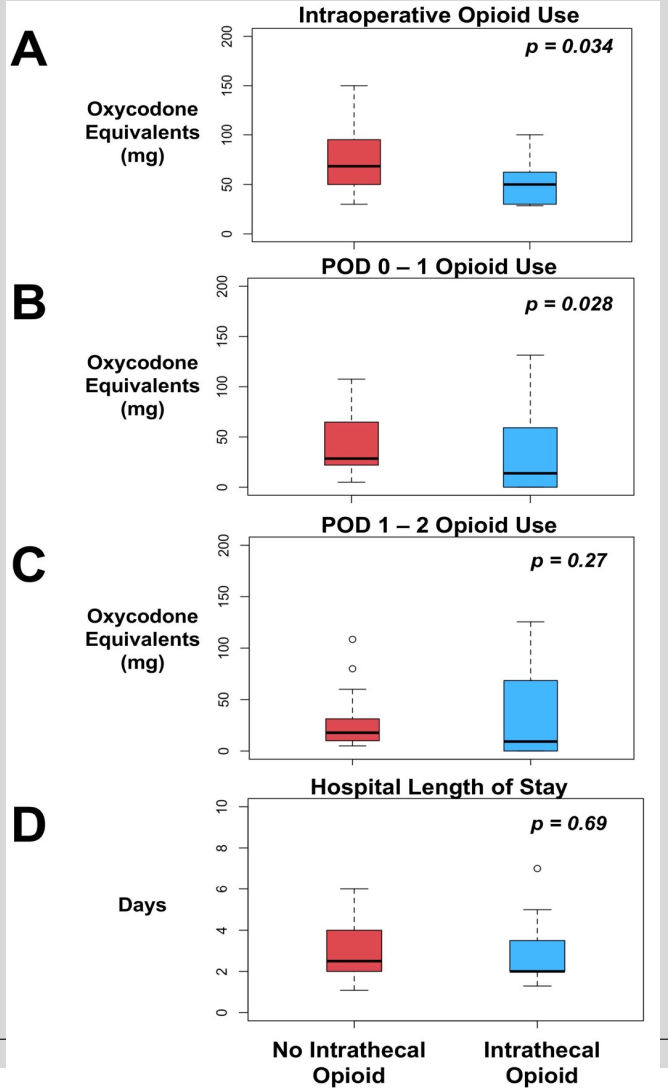
- **Median total opioid consumption-**
  - Non-APS: 85.6mg MEQs [58.9mg, 112.8mg MEQs]
  - APS: 31.7mg MEQs [16.0mg, 55.3mg MEQs]

  Decreased by 75%
- **Median Hospital Length of Stay-**
  - Non-APS: 5 days [4, 7 days]
  - APS: 4 days [4, 5 days]

  Median difference was **1.0 day**

APS OUTCOMES- DURAMORPH & ROBOTIC NEPHRECTOMY





CONCLUSION

- No one size fits all
- Work with your resources
- Sometimes, less is more.

THANK YOU!

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