Nowe metody uśmierzania bólu pooperacyjnego – czy jest dla nich miejsce w polskich szpitalach?

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Ból pooperacyjny - skala problemu

- Pomimo wysiłków naukowców i praktyków na całym świecie, efektywność uśmierzania bólu pooperacyjnego jest nadal niesatysfakcjonująca [1] ,[2]

- Nieskutecznie leczony ból pooperacyjny:

  a) jest źródłem cierpienia chorych

  b) ma niekorzystny wpływ na okołooperacyjną chorobowość i śmiertelność

  c) zwiększa ryzyko powikłań:

  - oddechowych
  - krążeniowych
  - zakrzepowo-zatorowych
  - ze strony przewodu pokarmowego

  d) opóźnia uruchamianie pacjentów oraz ich powrót do zdrowia

  e) podnosi koszty leczenia

  f) zwiększa ryzyko rozwoju przetrwałego bólu pooperacyjnego.

[1] Cullen KA, Hall MJ, Golosinsky A. Ambulatory surgery in the United States. Nati Health Stat Report 2006; 11: 1-25.

[2] Hall MJ, DeFrances CJ, Williams SN et al. National hospital discharge survey: 2007 summary. Nati Health Stat Report 2007; 29: 1-20.

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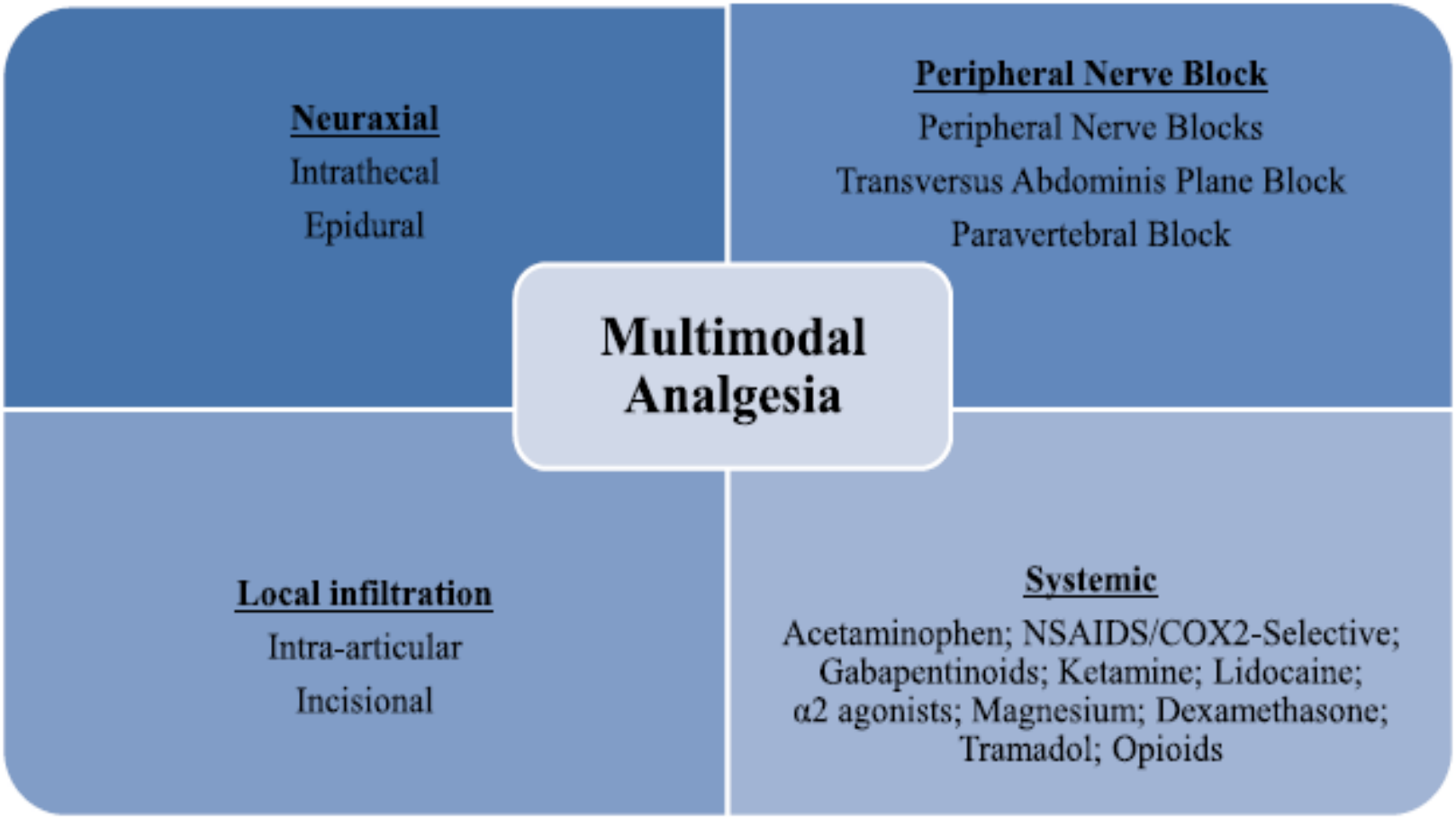
Multimodal therapy in perioperative analgesia

Karina Gritsenko, MD, Co-Director Acute Pain, Chronic Pain,

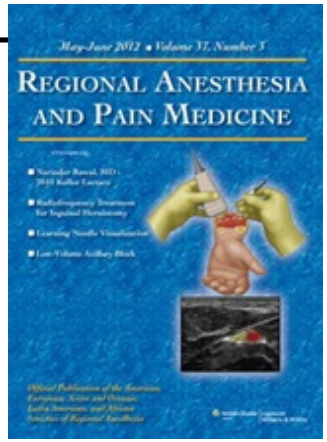
Multimodal analgesic techniques have been useful to target pain along various pathways involving transduction, transmission, modulation, and perception by the central nervous system to assist in acute pain control and also in the attempt to prevent neural sensitization leading to possible persistent postoperative pains.

Multimodal analgesic techniques have been shown to decrease opioid consumption, opioid related adverse effects, postoperative pain, postanesthesia care unit (PACU) and hospital stay, and increase patient satisfaction.

Okołooperacyjna analgezja multimodalna



K. Gritsenko et al. / Best Practice & Research Clinical Anaesthesiology 28 (2014) 59–79



Epidural Technique for Postoperative Pain

Gold Standard No More?

Narinder Rawal, MD, PhD

Abstract: Epidural analgesia is a well-established technique that has commonly been regarded as the gold standard in postoperative pain management. However, newer, evidence-based outcome data show that the benefits of epidural analgesia are not as significant as previously believed. There are some benefits in a decrease in the incidence of cardiovascular and pulmonary complications, but these benefits are probably limited to high-risk patients undergoing major abdominal or thoracic surgery who receive thoracic epidural analgesia with local anaesthetic

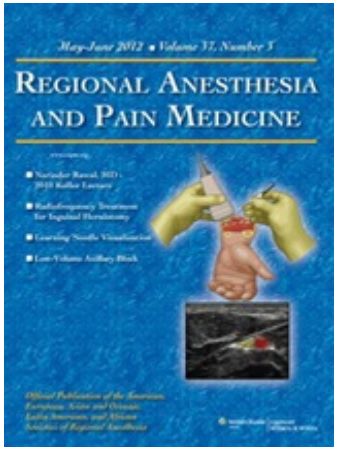
(*Reg Anesth Pain Med* 2012;37: 310–317)

Epidural Technique for Postoperative Pain

Gold Standard No More?

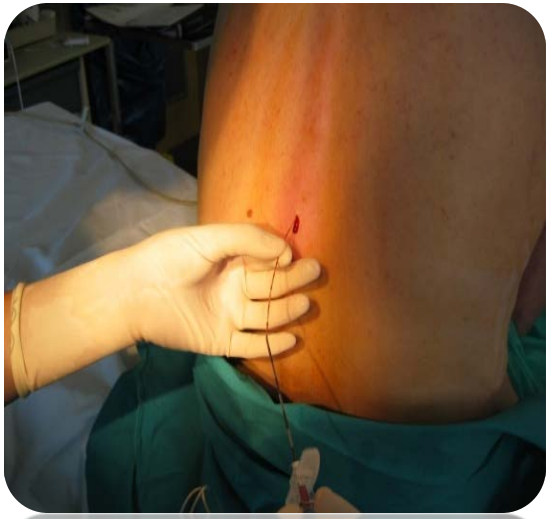
Narinder Rawal, MD, PhD

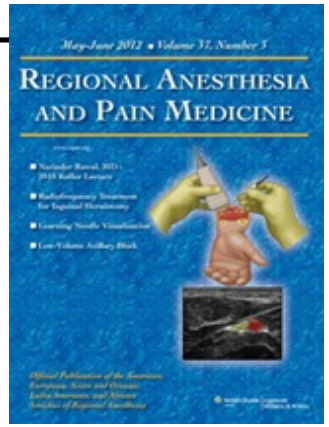
(*Reg Anesth Pain Med* 2012;37: 310–317)



Recently published evidence suggests that the benefits of epidural analgesia are not as significant as previously thought. Although the efficacy of pain relief can be outstanding, and there may be some benefits in decreased cardiovascular and pulmonary morbidity in high-risk patients undergoing major open vascular or cardiac surgery, the use of epidural techniques is generally decreasing. There are several reasons for the decline in the use of this invasive, costly and labour-intensive technique:

- little evidence of a decrease in postoperative mortality associated with the use of epidural analgesia;
- little convincing evidence of decreased morbidity in the low-to-medium-risk surgical population;
- advances in surgical techniques, such that many operations previously performed only on inpatients are now day-case or overnight-stay procedures;
- the use of fast-track, epidural-free, early mobilization, postoperative rehabilitation programmes;
- the widespread implementation of prophylactic anticoagulant regimens;
- increasing evidence that many less invasive, alternative regional analgesia techniques are as good as or even better than epidural analgesia after most major surgical procedures;
- the lack of convincing evidence of cost-effectiveness of epidural techniques despite their use for decades; and
- litigation concerns related to severe neurologic complications.





Epidural Technique for Postoperative Pain

Gold Standard No More?

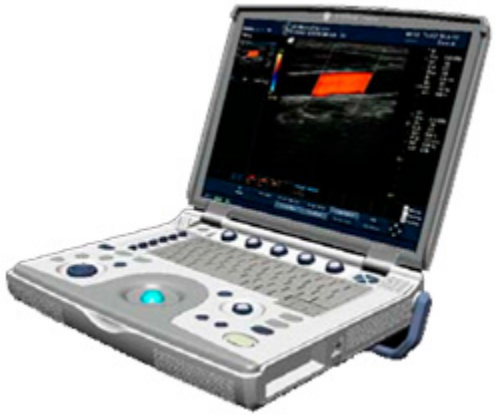
Narinder Rawal, MD, PhD

There is increasing evidence from meta-analyses and systematic reviews that effective and safer alternatives to epidural are now available for thoracic, abdominal, and major orthopedic surgery.[52–59] These analgesic alternatives include paravertebral block for thoracotomy[52,53]; peripheral nerve blocks for hip[54] and knee[55,56] arthroplasty; intravenous lidocaine for colorectal surgery[17–19]; wound catheter infusions for a wide variety of surgical procedures including abdominal, cardiothoracic, vascular, and major abdominal surgery[57]; and transversus abdominis plane (TAP) block for surgery involving the abdominal wall.[58]

(*Reg Anesth Pain Med* 2012;37: 310–317)

Ultrasonografia w anestezjologii

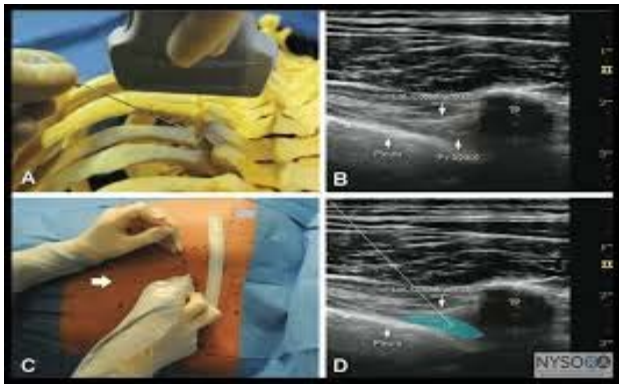
- Zdecydowana poprawa bezpieczeństwa i skuteczności wykonywanych procedur

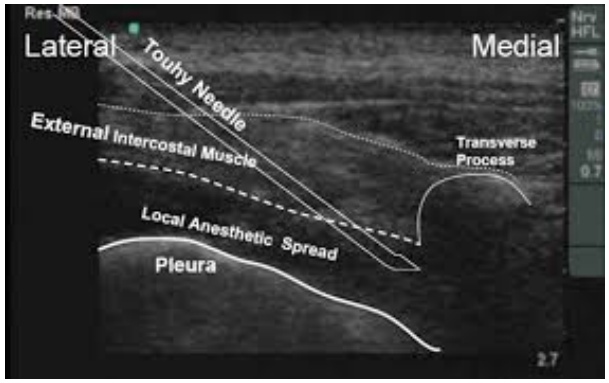


- Dobra identyfikacja struktur nerwowych i tkanek otaczających
- Kontrola położenia igły
- Możliwość obserwacji rozprzestrzeniania się LZM
- Zmniejszenie objętości LZM przy jednoczesnym wzroście odsetka skutecznych blokad.
- Większy komfort znieczulanego pacjenta (krótszy czas wykonywania blokady, celowane wkłucie igły).

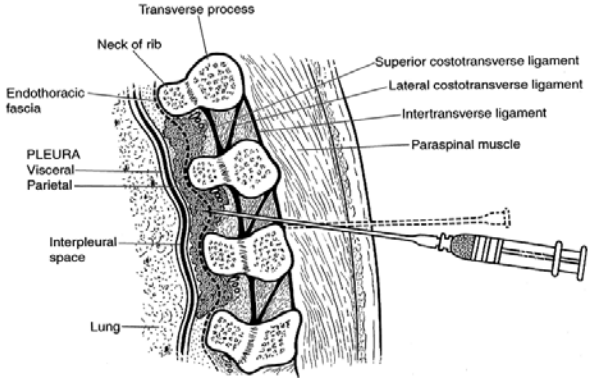
Alternatywa dla ciągłej analgezji zewnątrzoponowej – blokady pod kontrolą USG – klatka piersiowa.

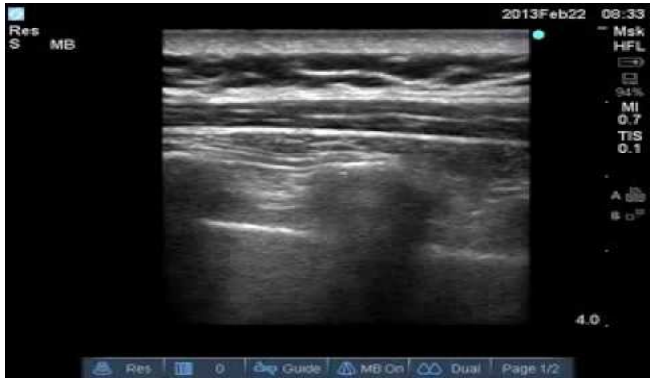
PVB



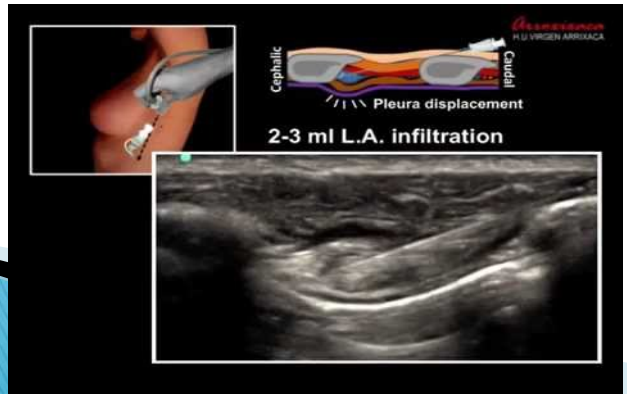


ICNB



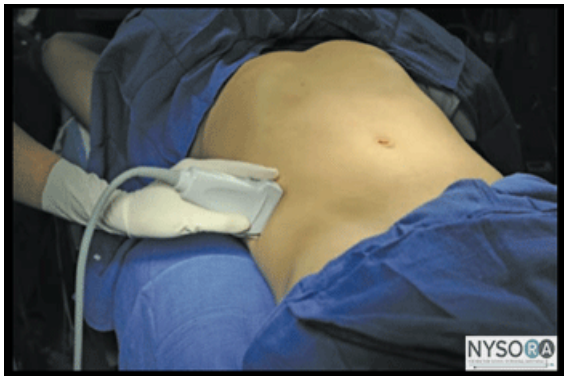


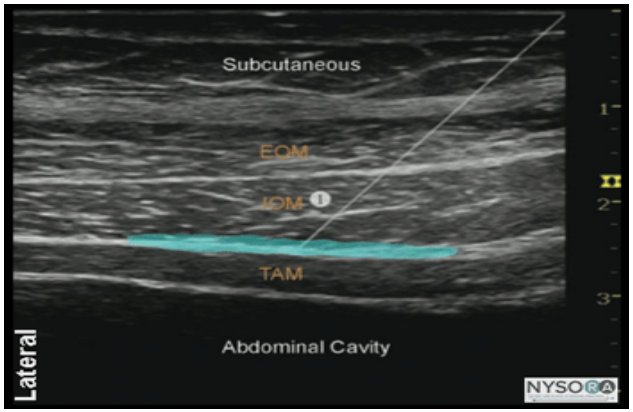
PECS



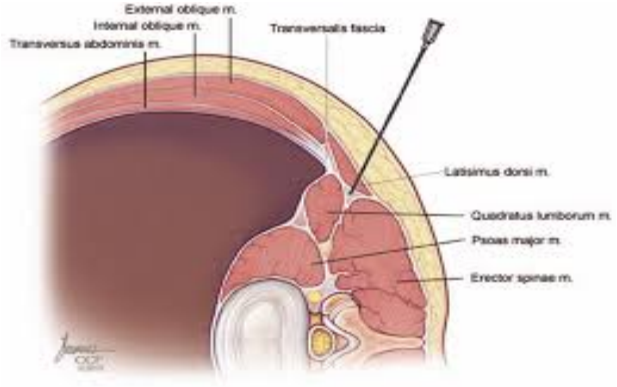
Alternatywa dla ciągłej analgezji zewnątrzoponowej – blokady pod kontrolą USG – jama brzuszna.

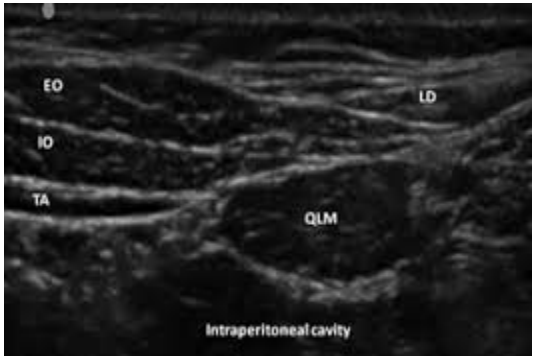
TAP block



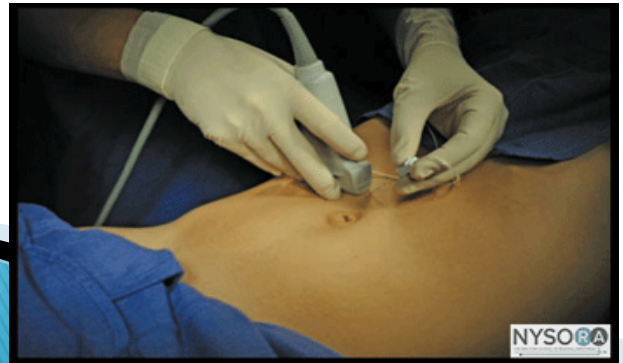


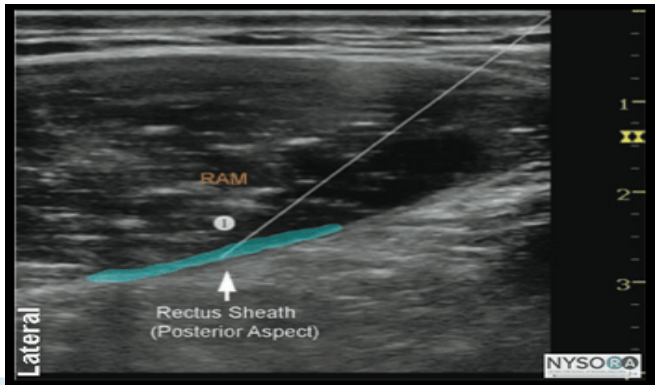
TQL block





RS block





Blokady pod kontrolą USG – jama brzuszna c.d.

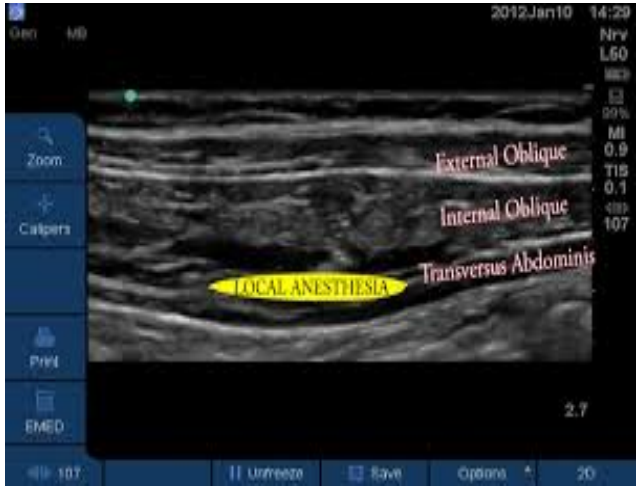
- **TAP block**

  - mniej rozległe zabiegi brzuszne, w tym zabiegi laparoskopowe

  - miejsce podania LZM: pomiędzy mięśniami skośnym wewnętrznym a poprzecznym brzucha

  - krótszy czas działania (do 12 godzin)

  - nie uśmierza bólu trzewnego



- **TQL block**

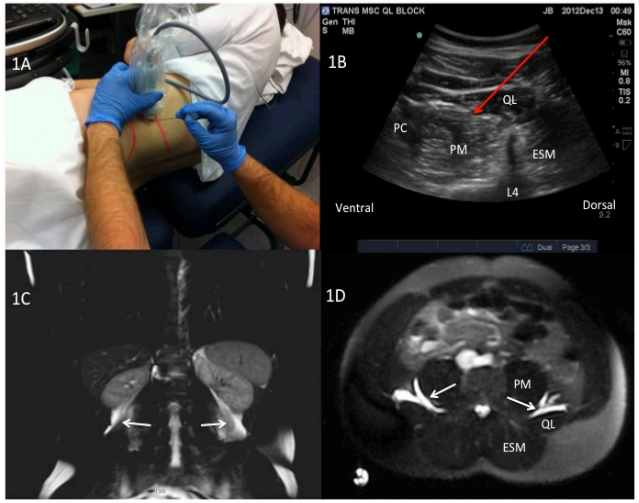
  - wskazania: rozległe zabiegi operacyjne w obrębie brzusznej i przestrzeni zaotrzewnowej (Th6-L1)

  - miejsce podania LZM: pomiędzy mięśniami QL i PM

  - długotrwały efekt: nawet do 24 godzin

  - rozprzestrzenianie LZM do przestrzeni przykręgowej

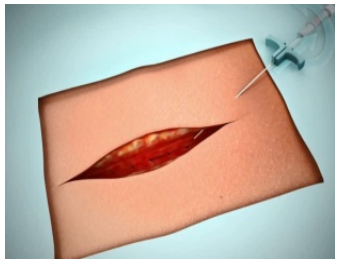
  - skutecznie uśmierza także ból trzewny

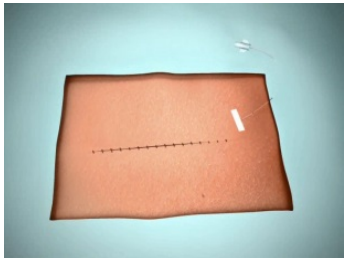


Surgical site catheter analgesia (SSCA)

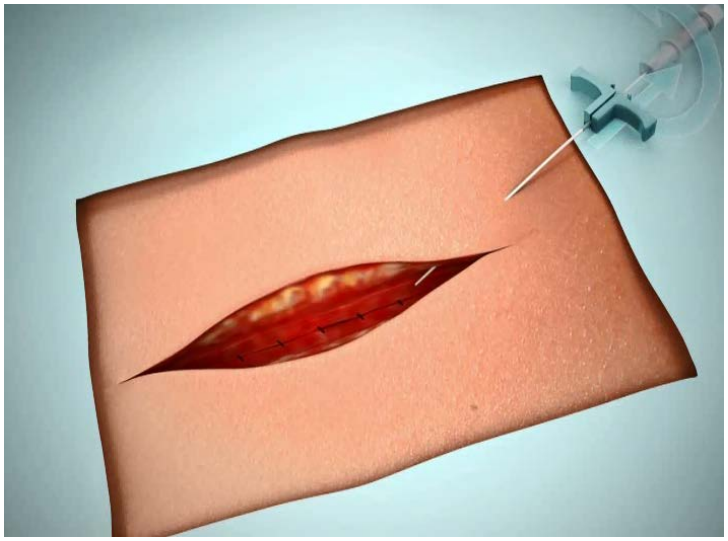
Analgezja pooperacyjna przy użyciu cewników implantowanych do rany:

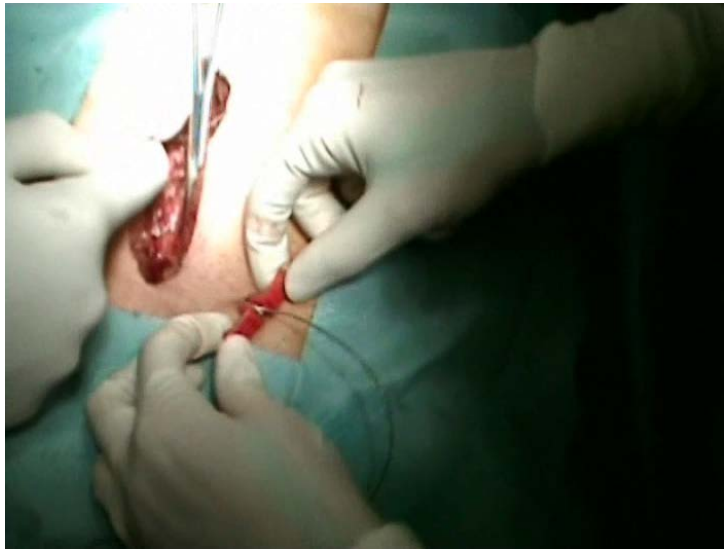
- zapewnia skuteczną analgezję pooperacyjną - optymalnie jako składowa analgezji multimodalnej
- stosowana w wielu specjalnościach zabiegowych (m. in. kardio- i torakochirurgia, ginekologia i położnictwo, chirurgia jamy brzusznej, ortopedia, chirurgia kręgosłupa, urologia)
- ze względu na prostotę metody, jej skuteczność, dobry profil bezpieczeństwa coraz szerzej stosowana zarówno u chorych hospitalizowanych, jak i ambulatoryjnych
- redukcja bólu zarówno w spoczynku, jak i w warunkach dynamicznych
- unikanie lub redukcja koniecznych do zastosowania dawek opioidów i dzięki temu zminimalizowanie związanych ze stosowaniem opioidów działań niepożądanych
- poprawa satysfakcji pacjentów, skrócenie czasu hospitalizacji, redukcja kosztów leczenia.

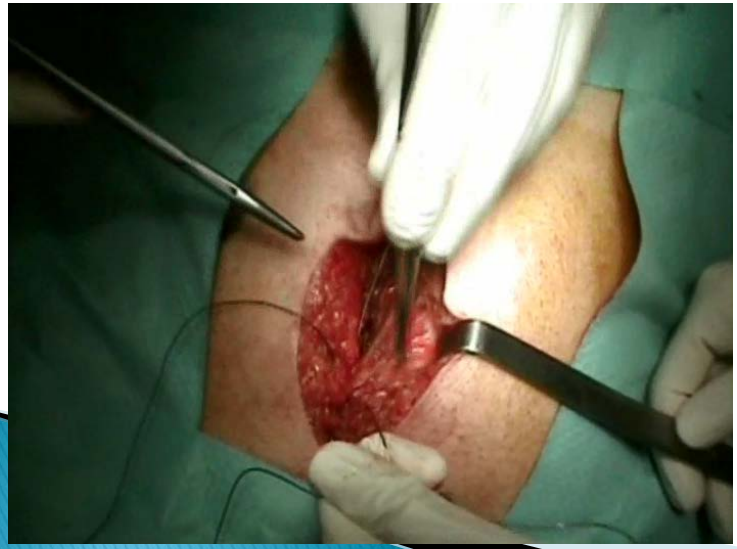


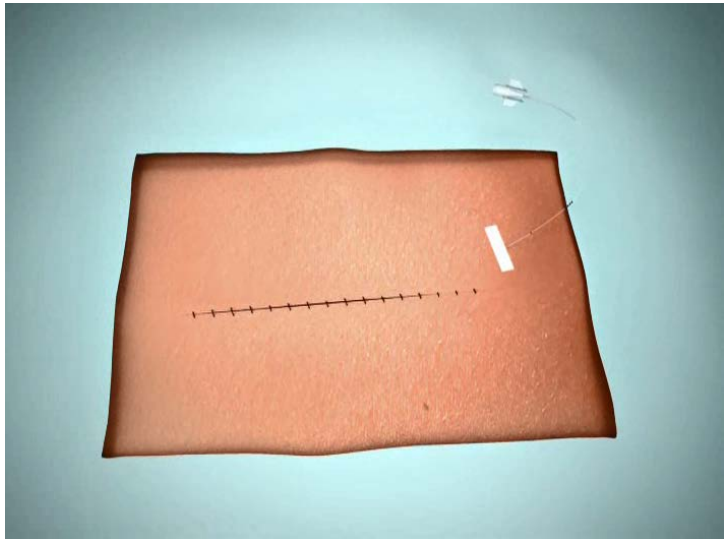


Surgical site catheter analgesia (SSCA)









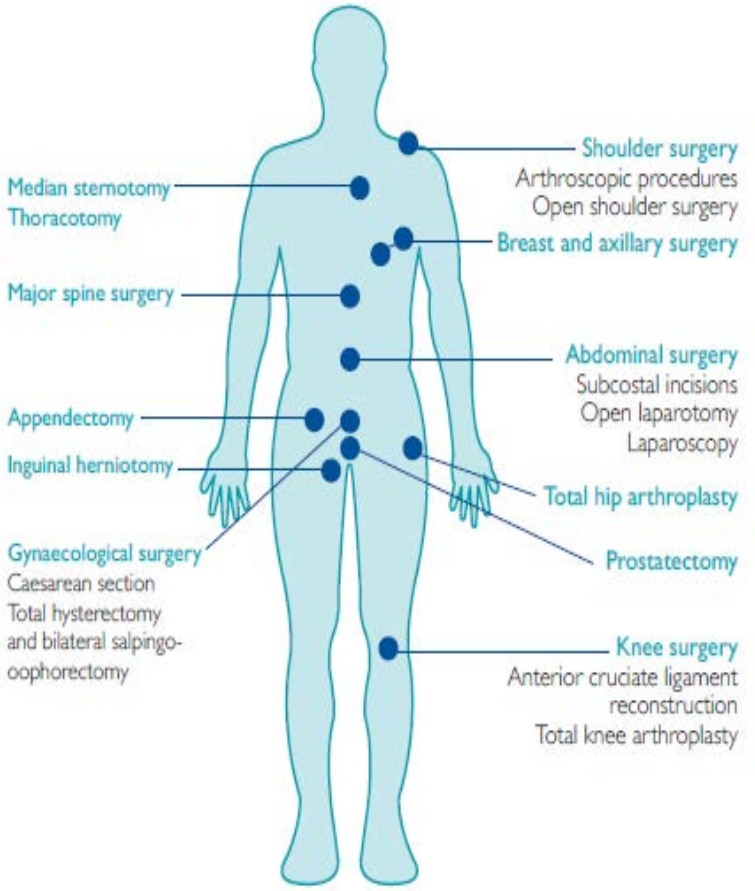
Surgical site catheter analgesia (SSCA)

30 cm	Torakotomia Zabiegi operacyjne kręgosłupa Zabiegi operacyjne wątroby
22.5 cm	Sternotomia Mastektomia Laparotomia Zabiegi operacyjne kręgosłupa
15 cm	Laparotomia Operacje piersi Cięcie cesarskie Zabiegi operacyjne kręgosłupa
7.5 cm	Laparotomia Zabiegi korekcyjne przepuklin brzusznych Operacje laparoskopowe
2.5 cm	Zabiegi na drobnych stawach

Efficacy of Continuous Wound Catheters Delivering Local Anesthetic for Postoperative Analgesia: A Quantitative and Qualitative Systematic Review of Randomized Controlled Trials

Spencer S Liu, Jeffrey M Richman, Richard C Thirlby, Christopher LWu.

J Am Coll Surg 2006; vol 203 (no 6) December: 914-932.



The National Library of Medicine's Medline database and the Cochrane Central Register of Controlled Trials were searched for the time period January 1, 1966 to February 19, 2006. Forty-four RCTs enrolling a total of 2,141 patients were included for final quantitative analysis.

Overall summary of results from quantitative and qualitative review continuous wound catheters consistently demonstrated **analgesic efficacy in terms of reduced pain scores or opioid use for all surgical subgroups**, despite heterogeneity in type of surgical procedure, location of wound catheter, mode of delivery of local anesthetic, dose of local anesthetic, and analgesic mixture.

Opioid-related side effects, patient satisfaction, and length of hospital stay were infrequently assessed for each surgical group, but there was a **global reduction in PONV, increased patient satisfaction, and decreased length of stay**.

Anesthesiology 2007; 107:461–8

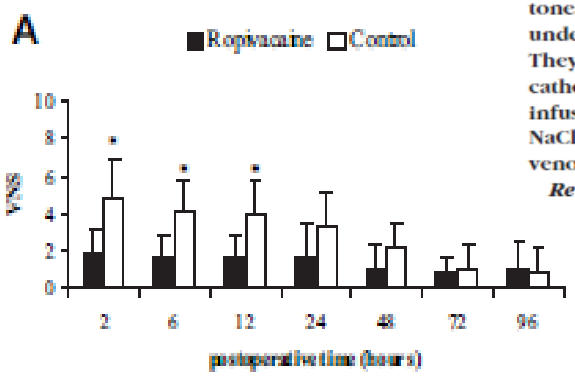
Continuous Preperitoneal Infusion of Ropivacaine Provides Effective Analgesia and Accelerates Recovery after Colorectal Surgery

A Randomized, Double-blind, Placebo-controlled Study

Marc Beaussier, M.D., Ph.D.,* Hanna El'Ayoubi, M.D.,† Eduardo Schiffer, M.D.,‡ Maxime Rollin, M.D.,† Yann Parc, M.D., Ph.D.,§ Jean-Xavier Mazoit, M.D., Ph.D.,‖ Louisa Azizi, M.D.,# Pascal Gervaz, M.D.,** Serge Rohr, M.D., Ph.D.,†† Celine Biermann, M.D.,‡‡ André Lienhart, M.D., Ph.D.,§§ Jean-Jacques Eledjam, M.D., Ph.D.‖‖

Methods: After obtaining written informed consents, a multiholed wound catheter was placed by the surgeon in the preperitoneal space at the end of surgery in patients scheduled to undergo elective open colorectal resection by midline incision. They were thereafter randomly assigned to receive through the catheter either 0.2% ropivacaine (10-ml bolus followed by an infusion of 10 ml/h during 48 h) or the same protocol with 0.9% NaCl. In addition, all patients received patient-controlled intravenous morphine analgesia.

Results: Twenty-one patients were evaluated in each group.



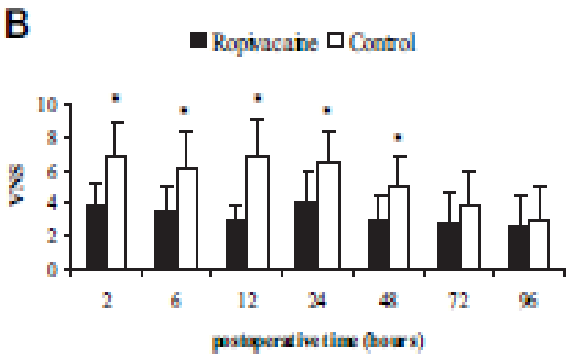


Fig. 4. Pain intensity at rest (*A*) and during coughing (*B*), assessed using a verbal numerical scale (VNS). * $P < 0.05$. Results are mean ± SD.

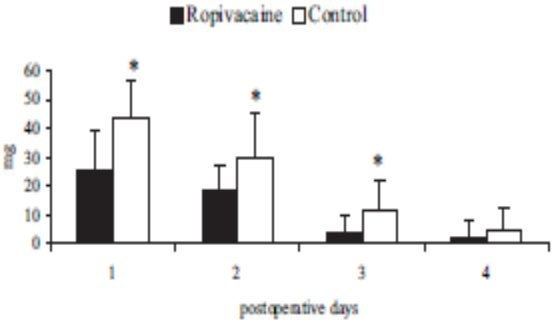


Fig. 3. Daily morphine consumption. * $P < 0.05$. Results are mean ± SD.

Table 2. Side Effects and Recovery Parameters

	Ropivacaine (n = 21)	Control (n = 21)	*P* Value
Sleep quality during first night, cm	7.9 ± 1.6	5.0 ± 3.2	< 0.001
Sleep quality during second night, cm	8.6 ± 1.2	6.9 ± 2.4	< 0.001
Time to recover preoperative DSST, days	3.1 ± 1.1	3.0 ± 1.4	0.8
Time to first flatus, h	54 ± 16	72 ± 41	0.06
Time to first feces, h	74 ± 19	105 ± 54	0.02
Duration of hospital stay, h	115 ± 25	147 ± 53	0.02

Values are mean ± SD.

Conclusions: Continuous preperitoneal administration of 0.2% ropivacaine at 10 ml/h during 48 h after open colorectal resection reduced morphine consumption, improved pain relief, and accelerated postoperative recovery.

Key messages for breast and axillary surgery

- Continuous surgical site infusion with local anaesthetics reduces postoperative pain and opioid medication in breast and/or axillary procedures.
- Continuous surgical site infusion is useful in a large variety of benign and non-benign breast and/or axillary procedures.
- Continuous surgical site infusion is applicable in mastectomy (with or without axillary lymph node dissection), breast augmentation, mammaplasty, or breast reduction.
- A fenestrated catheter is suggested to be placed superior to the surgical site cavity.
- Bupivacaine 0.25% at a flow rate of 2 mL/h per catheter is suggested for immediate postoperative pain management of up to a few days duration.
- Further studies are needed to confirm optimal catheter placement and to assess the effectiveness of a postoperative bolus.

Key messages for open laparotomy catheter analgesia

- For open laparotomy, continuous infusion of a local anaesthetic is an effective technique offering significant reduction of pain and morphine consumption throughout the first 48 h after the operation.
- Preperitoneal (subfascial) catheter placement is most appropriate.
- Some results suggest efficacy of direct intraperitoneal administration.
- Despite a lack of comparative data, infusion in the subcutaneous space appears less effective than in the preperitoneal space.
- Flow rate should be high (~10 mL/h) and set according to the length of the incision.
- Repeated intermittent bolus injection could be used (8–10 mL every 5 to 12 h).
- Surgical site local anaesthetic administration could be beneficial when used in combination with epidural analgesia.

Key messages for major spine surgery

- Surgical site infusion of ropivacaine 0.2% at a rate of 5 mL/h improves postoperative pain relief and reduces opioid requirements after major lower spine surgery.
- No toxicity or wound infection was reported.
- Further large randomized controlled trials are needed to assess the best catheter location (above or below the fascia), the optimal drug concentration, infusion rate and catheter type.
- A double catheter system should be evaluated against a single catheter with a long fenestrated section.

Ropivacaine for Continuous Wound Infusion for Postoperative Pain Management: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Shane Raines[a] Cecilia Hedlund[b] Malin Franzon[b] Stefan Lillieborg[b]
Glen Kelleher[d] Kjell Ahlén[c]

Eur Surg Res 2014;53:43–60

Table 2. Characteristics of included RCTs; wound infusion regimens

First author, year	Ropivacaine, n	Control, n	Procedure	Wound catheter placement	Ropivacaine concentration (bolus; infusion rate)	Duration of wound infusion, h
Bianconi [24], 2003	18	19	Total hip or knee replacement	Between muscle fascia and subcutis	Bolus 40 ml at 5 mg/ml; infusion 2 mg/ml at 5 ml/h	55
Dowling [33], 2003	16	19	Coronary artery bypass	2 catheters anterior to sternum	Bolus 20 ml at 2 mg/ml; infusion 2 mg/ml at 4 ml/h	48
Gottschalk [22], 2003	12	14	Open shoulder surgery	SC	Bolus 20 + 10 ml at 2 mg/ml, infusion 2 mg/ml at 5 ml/h	48
Bianconi [25], 2004	18	19	Spine fusion	Between muscle fascia and subcutis	Bolus 40 ml at 5 mg/ml; infusion 2 mg/ml at 5 ml/h	55
Stewart [20], 2004	23	24	Inguinal hernia repair	On external inguinal ring	No bolus; infusion 7.5 mg/ml at 4 ml/h	24
Blumenthal [34], 2005	18	18	Iliac crest bone graft for shoulder surgery	Over iliac crest harvest site	Bolus 30 ml at 5 mg/ml; infusion 2 mg/ml at 5 ml/h	48
Ansaloni [23], 2007	48	48	Appendectomy	Above parietal peritoneum	Bolus 10 ml at 2 mg/ml; infusion 2 mg/ml at 5 ml/h	48
Beaussier [39], 2007	21	21	Open resection of malignant colorectal tumours	Between parietal peritoneum and transversalis fascia	Bolus 10 ml at 2 mg/mL; infusion 2 mg/ml at 10 ml/h	48
Forastiere [21], 2008	84	84	Open nephrectomy	Two catheters: (1) superior to transverse muscle and below internal and external oblique muscles, (2) SC	Bolus 10 ml at 10 mg/ml; infusion 5 mg/ml at 4 ml/h	48
Dagtekin [35], 2009	8	8	Transverse rectus abdominis musculocutaneous flap reconstruction	Two catheters: (1) SC in abdominal wound in loop over the fascial sheath, (2) loop over m. pectoralis major under the autologous flap extending into the axilla	Bolus 10 ml at 2 mg/ml; infusion 2 mg/ml at 10 ml/h in each catheter (total 20 ml/h)	48
Chan [28], 2010	22	22	Open hepatic surgery	Within the musculofascial layer	Bolus 20 ml at 2.5 mg/ml; infusion 2.5 mg/ml at 4 ml/h	68
Iyer [26], 2010	24	21	Bariatric surgery	Subfascial space and SC	Bolus 30 ml at 5 mg/ml; infusion 2 mg/ml at 2 ml/h in each catheter (total 4 ml/h)	72
Wang [19], 2010	28	27	Laparotomy	Two catheters placed at the level of the musculofascial closure	No bolus; infusion 2 mg/ml at 2 ml/h in each catheter (total 4 ml/h)	67.5
Aguirre [17], 2012	36	36	Minimal invasive hip replacement	Epicapsular	Bolus 20 ml at 3 mg/ml; infusion 3 mg/ml at 8 ml/h	48
Total	376	380				

Control patients received saline. SC = Subcutaneous.

Ropivacaine for Continuous Wound Infusion for Postoperative Pain Management: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Shane Raines[a] Cecilia Hedlund[b] Malin Franzon[b] Stefan Lillieborg[b]
Glen Kelleher[d] Kjell Ahlén[c]

Eur Surg Res 2014;53:43–60

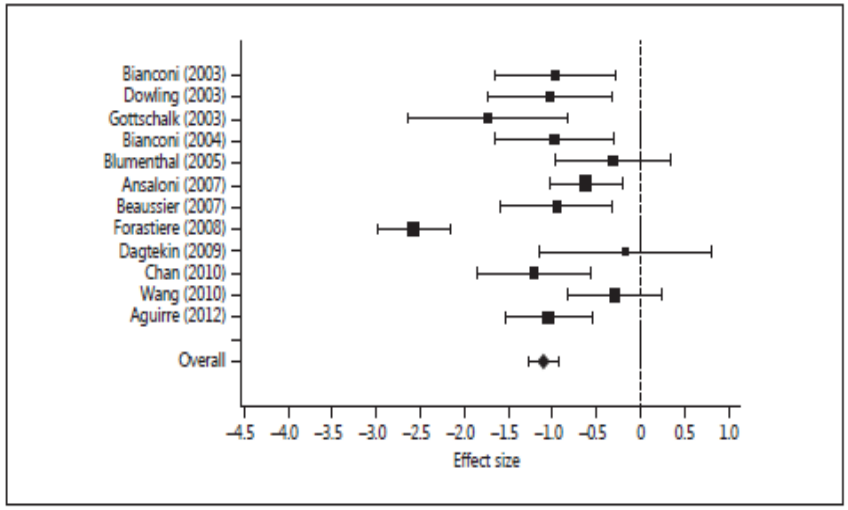


Fig. 2. Forest plot of pain at rest effect size estimates from published CWI studies of ropivacaine versus placebo [17, 19, 21–25, 28, 33–35, 39]. A negative effect size indicates reduced pain in ropivacaine-treated patients as compared to placebo-treated patients. Error bars denote 95% CIs.

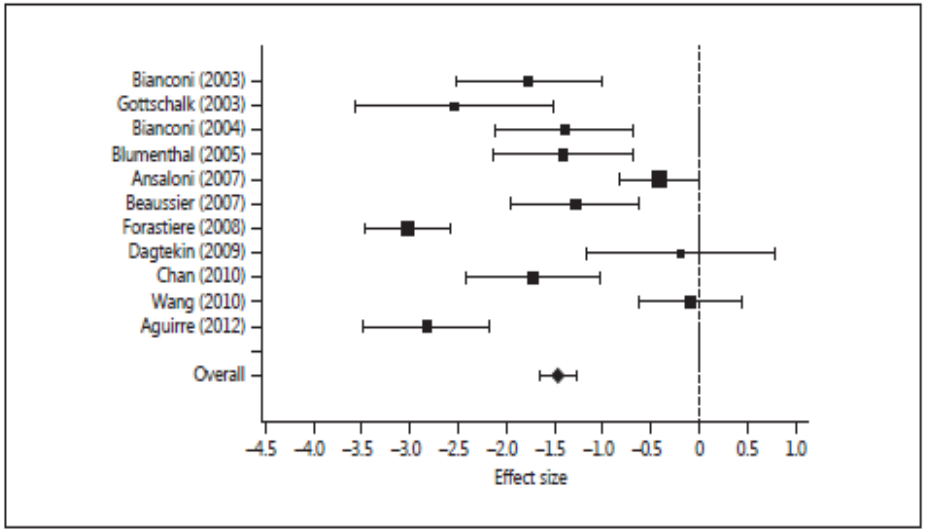


Fig. 3. Forest plot of pain during mobilization effect size estimates from published CWI studies of ropivacaine versus placebo [17, 19, 21–25, 28, 34, 35, 39]. A negative effect size indicates reduced pain in ropivacaine-treated patients as compared to placebo-treated patients. Error bars denote 95% CIs.

Ropivacaine for Continuous Wound Infusion for Postoperative Pain Management: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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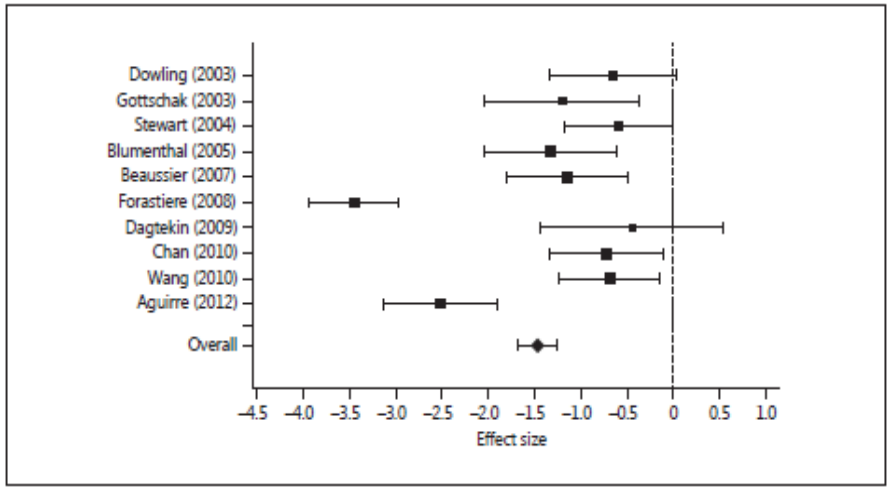

Fig. 4. Forest plot of total opioid rescue medication effect size estimates from published CWI studies of ropivacaine versus placebo [17, 19–22, 28, 33–35, 39]. A negative effect size indicates reduced use of opioids in ropivacaine-treated patients as compared to placebo-treated patients. Error bars denote 95% CIs.

Table 7. Wound infection rate by study versus control groups

First author, year	Ropivacaine, n	Placebo, n	Wound infection ropivacaine, n	Wound infection placebo, n
Bianconi [24], 2003	18	19	0	0
Dowling [33], 2003	16	19	ND	ND
Gottschalk [22], 2003	12	14	0	0
Bianconi [25], 2004	18	19	0	0
Stewart [20], 2004	23	24	0	0
Blumenthal [34], 2005	18	18	NR	NR
Ansaloni [23], 2007	48	48	4	2
Beaussier [39], 2007	21	21	NR	NR
Forastiere [21], 2008	84	84	NR	NR
Dagtekin [35], 2009	8	8	NR	NR
Chan [28], 2010	22	22	NR	NR
Iyer [26], 2010	24	21	NR	NR
Wang [19], 2010	28	27	2	3
Aguirre [17], 2012	36	36	0	0
Total	376	380	6	5

In conclusion, this systematic review and meta-analysis of 14 RCTs provides substantial evidence that CWI of ropivacaine is effective for postoperative pain management for a wide range of surgical procedures. Overall, ropivacaine demonstrated robust and clinically meaningful reductions in opioid use and pain outcomes with no major adverse effects. Infusion rates of 8–20 mg/h for up to 48 h were associated with plasma concentrations of ropivacaine well below the toxicity threshold

The Postoperative Analgesic Efficacy of Preperitoneal Continuous Wound Infusion Compared to Epidural Continuous Infusion with Local Anesthetics After Colorectal Cancer Surgery: A Randomized Controlled Multicenter Study

(Anesth Analg 2012;115:1442–50)

Sergio Bertoglio, MD,*† Fabio Fabiani, MD,† Pasquale De Negri, MD,§ Antonio Corcione, MD,||
Domenico Franco Merlo, PhD,¶ Ferdinando Cafiero, MD,* Clelia Esposito, MD,||
Claudio Belluco, MD,# Davide Pertile, MD,* Riccardo Amodio, MD,§ Matilde Mannucci, BSc,¶
Valeria Fontana, BSc,¶ Marcello De Cicco, MD,† and Lucia Zappi, MD**

Table 1. Baseline Patient Characteristics by Randomization Group, Analgesia Characteristics, and Surgical Intraoperative Data

Covariates	CEI analgesia (n = 53)	CWI analgesia (n = 53)	P value
Age (y)	64.51 ± 6.66	65.70 ± 7.82	0.402
Gender (male/female)	27/26	28/25	0.920
Height (cm)	170.98 ± 6.57	170.42 ± 5.54	0.639
Weight (kg)	70.62 ± 8.54	73.02 ± 10.65	0.207
ASA physical status I/II (n)	14/39	12/41	0.692
Type of surgery (n)			0.295
Right hemicolectomy	13	20	
Left hemicolectomy	10	9	
Sigmoid resection	15	13	
Lower rectal resection	7	4	
Segmentary colonic resection	6	6	
Total colectomy	2	1	
Duration of surgery (min)	158.77 ± 58.74	161.13 ± 50.34	0.825

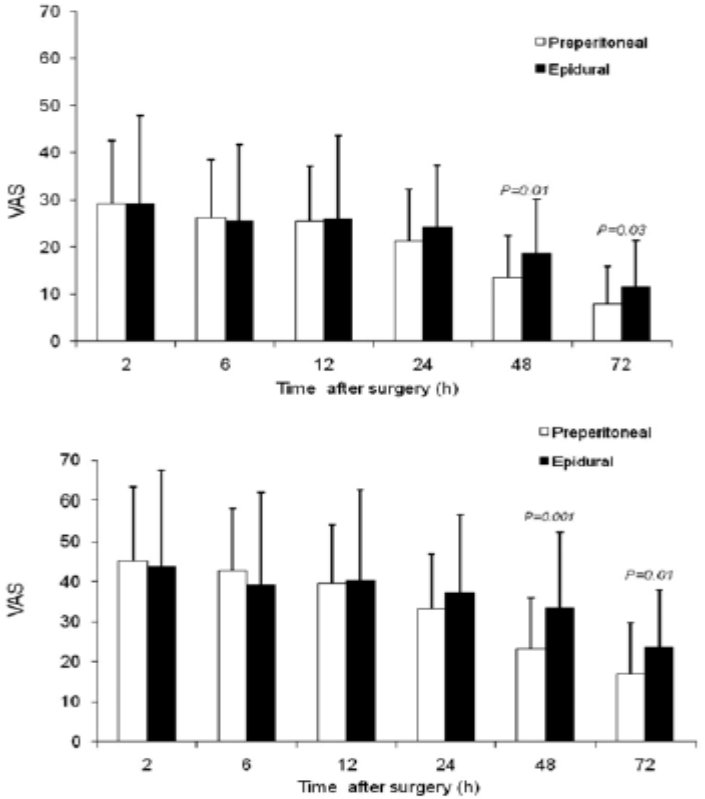

Figure 3. Postoperative visual analog scale (VAS) for pain assessment at rest (A) and after coughing (B) at different times after surgery (scale ranges from 0 = no pain to 100 = very severe pain).

The Postoperative Analgesic Efficacy of Preperitoneal Continuous Wound Infusion Compared to Epidural Continuous Infusion with Local Anesthetics After Colorectal Cancer Surgery: A Randomized Controlled Multicenter Study

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Table 2. Number of Requests for Rescue Analgesia per Time (Hours) After Surgery

	Time after surgery					
Drug	12 h	24 h	48 h	72 h	Total	*P* value
Ketoralac (30 mg)						
CEI analgesia	15	16	7	3	41	NS
CWI analgesia	12	13	7	2	34	NS
Paracetamol (1 g)						
CEI analgesia	28	17	15	7	67	NS
CWI analgesia	32	15	10	4	61	NS

CEI = continuous epidural infusion; CWI = continuous wound infusion; NS = not significant.

Table 3. Comparison of Time to Recovery (Days) of Bowel Function and Discharge from Hospital After Surgery

	CEI analgesia ($n = 53$)		CWI analgesia ($n = 53$)		
	Mean (d)	95% CI	Mean (d)	95% CI	*P* value[a]
Time to first flatus	3.61	3.28–3.97	3.06	2.85–3.26	0.002
Time to first stool	5.29	4.94–5.65	4.49	4.22–4.76	0.001
Discharge from hospital	8.04	7.38–8.69	7.40	6.59–8.20	0.171

CEI = continuous epidural infusion; CWI = continuous wound infusion;

The Postoperative Analgesic Efficacy of Preperitoneal Continuous Wound Infusion Compared to Epidural Continuous Infusion with Local Anesthetics After Colorectal Cancer Surgery: A Randomized Controlled Multicenter Study

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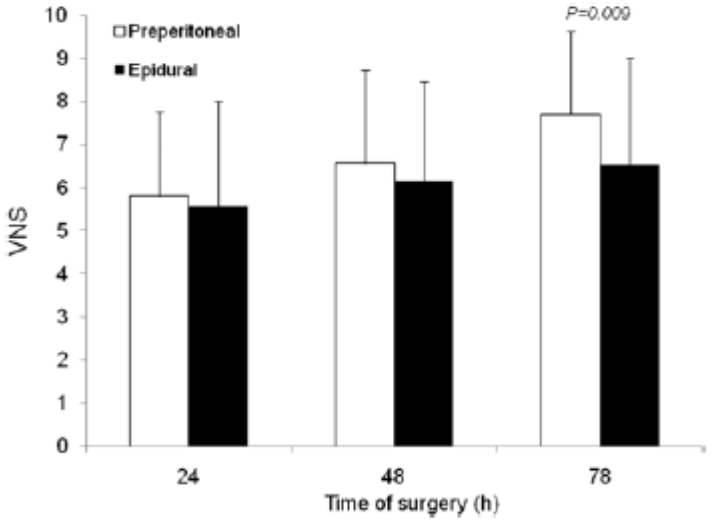


Figure 4. Quality of night sleep at different intervals evaluated with a verbal numerical scale (VNS) ranging from 0 (worst quality) to 10 (best quality) by randomization group. Vertical bars represent standard deviation. *P* values are indicated only for statistically significant differences.

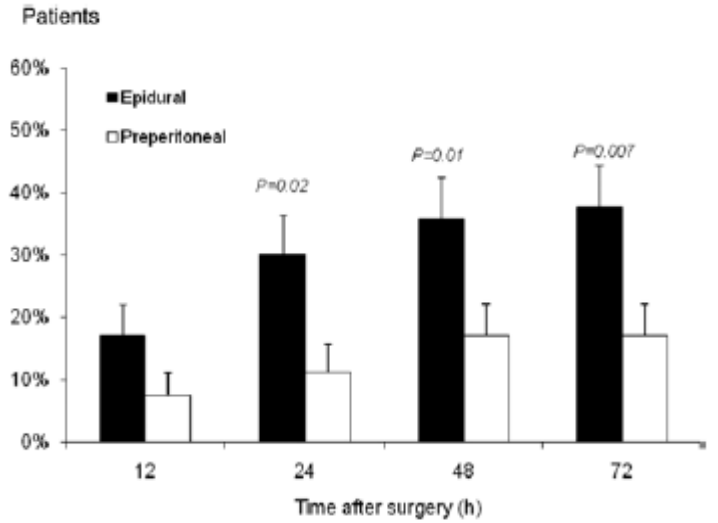


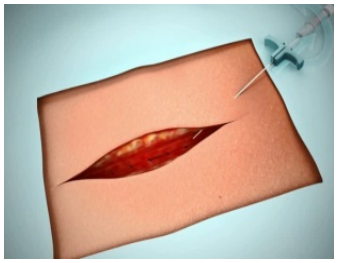
Figure 5. Percentage of patients in each treatment group with postoperative nausea and vomiting requiring pharmacological treatment with metoclopramide or ondansetron at different postoperative intervals by randomization group. Vertical bars represent standard deviation. *P* values are indicated only for statistically significant differences.

CONCLUSIONS: Preperitoneal CWI analgesia with ropivacaine 0.2% continuous infusion at 10 mL/h during 48 hours after open CRC surgery provided effective postoperative pain relief not inferior to CEI analgesia. (Anesth Analg 2012;115:1442–50)

Systematic review and meta-analysis of continuous local anaesthetic wound infiltration *versus* epidural analgesia postoperative pain following abdominal surgery

N. T. Ventham, M. Hughes, S. O'Neill, N. Johns, R. R. Brady and S. J. Wigmore

British Journal of Surgery 2013; **100**: 1280–1289



Methods: A meta-analysis of randomized clinical trials (RCTs) evaluating wound infiltration *versus* epidural analgesia in abdominal surgery was performed. The primary outcome was pain score at rest after 24 h on a numerical rating scale. Secondary outcomes were pain scores at rest at 48 h, and on movement at 24 and 48 h, with subgroup analysis according to incision type and administration regimen (continuous *versus* bolus), opiate requirements, nausea and vomiting, urinary retention, catheter-related complications and treatment failure.

Results: Nine RCTs with a total of 505 patients were included. No differences in pain scores at rest 24 h after surgery were detected between epidural and wound infiltration. There were no significant differences in pain score at rest after 48 h, or on movement at 24 or 48 h after surgery. Epidural analgesia demonstrated a non-significant a trend towards reduced pain scores on movement and reduced opiate requirements. There was a reduced incidence of urinary retention in the wound catheter group.

Conclusion: Within a heterogeneous group of RCTs, use of local anaesthetic wound infiltration was associated with pain scores comparable to those obtained with epidural analgesia. Further procedure-specific RCTs including broader measures of recovery are recommended to compare the overall efficacy of epidural and wound infiltration analgesic techniques.

Reference	Wound infiltration Score*	Total	Epidural Score*	Total	Weight (%)	Mean difference
Bertoglio *et al.*[39]	2·1(1·1)	53	2·4(1·3)	53	15·8	−0·30 (−0·76, 0·16)
Boulind *et al.*[41]	2·6(2·2)	16	2·1(2)	14	8·8	0·20 (−1·30, 1·70)
de Almeida *et al.*[40]	3(3)	19	5(1)	19	9·3	−2·00 (−3·42, −0·58)
Fant *et al.*[36]	2·5(1·7)	25	1·3(1·5)	25	12·9	1·20 (0·31, 2·09)
Niraj *et al.*[35]	1·4(1·5)	27	1·6(1·6)	31	13·6	−0·20 (−1·00, 0·60)
O'Neill *et al.*[38]	1·8(2)	29	2·7(1·4)	29	12·9	−0·90 (−1·79, −0·01)
Renghi *et al.*[33]	1·5(1·7)	30	1(1·7)	29	13·1	0·50 (−0·37, 1·37)
Revie *et al.*[34]	2·4(1·7)	33	1·2(1·5)	31	13·7	1·20 (0·42, 1·98)
Total		232		231	100·0	0·03 (−0·61, 0·66)

Heterogeneity: $\tau^2 = 0{\cdot}61$; $\chi^2 = 30{\cdot}73$, 7 d.f., $P < 0{\cdot}001$; $I^2 = 77\%$
Test for overall effect: $Z = 0{\cdot}08$, $P = 0{\cdot}94$

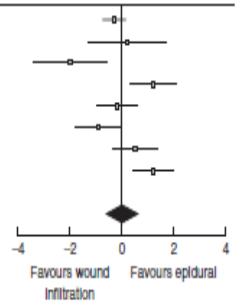


Fig. 2 Forest plot showing pain scores at rest 24 h after surgery on a numerical rating scale from 0 to 10 in wound infiltration and epidural groups. An inverse variance random-effects model was used for meta-analysis. *Values are mean(s.d.). Mean differences are shown with 95 per cent confidence intervals

Reference	Wound infiltration Total (mg)*	Total	Epidural Total (mg)*	Total	Weight (%)	Mean difference (mg)
Bertoglio *et al.*[39]	14·3(10·7)	53	17·2(13)	53	25·5	−2·90 (−7·43, 1·63)
Fant *et al.*[36]	19(17·4)	25	4·6(7·8)	25	23·7	14·40 (6·93, 21·87)
Niraj *et al.*[35]	25·2(16·7)	27	15·2(11·1)	31	23·8	10·00 (2·59, 17·41)
Ranta *et al.*[37]	37(23)	20	37(27)	20	17·5	0·00 (−15·54, 15·54)
Revie *et al.*[34]	73·3(70·5)	33	20·9(45·0)	31	9·5	52·40 (23·61, 81·19)
Total		158		160	100·0	10·04 (−1·03, 21·12)

Heterogeneity: $\tau^2 = 119{\cdot}86$; $\chi^2 = 29{\cdot}96$, 4 d.f., $P < 0{\cdot}001$; $I^2 = 87\%$
Test for overall effect: $Z = 1{\cdot}78$, $P = 0{\cdot}08$

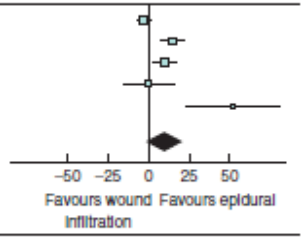
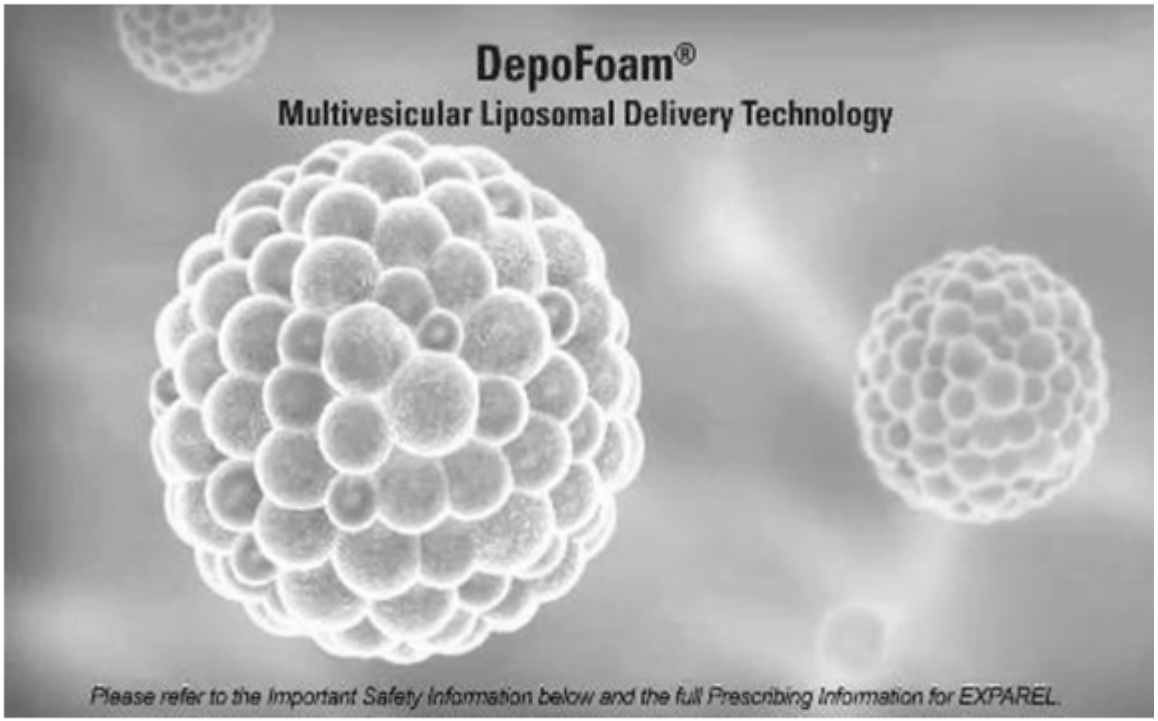


Fig. 3 Forest plot showing total cumulative opiate use in wound infiltration and epidural groups. An inverse variance random-effects model was used for meta-analysis. *Values are mean(s.d.). Mean differences are shown with 95 per cent confidence intervals

Liposomalna bupiwakaina

- Długodziałający lek znieczulenia miejscowego



- Wprowadzona została na rynku amerykańskim i zarejestrowana w 2011 roku w USA przez FDA do znieczulenia miejscowego okolicy operowanej w celu zapewnienia analgezji pooperacyjnej.

Liposomalna bupiwakaina

Technologia DepoFoam: struktura plastra miodu z wieloma niekoncentrycznie ułożonymi strukturami zbudowanymi z dwuwarstwowej, fosfolipidowej otoczki z wodnym (hydrofilnym) środkiem zawierającym bupiwakainę.

Stopniowe, powolne (do 72 h) uwalnianie leku

Produkowana jest w postaci 1,33% roztworu.

DepoFoam(non-concentric)®10–30µm

Cross-sectional diagram of DepoFoam containing bupivacaine.

Image supplied courtesy of Pacira Pharmaceuticals, Inc, 5 Sylvan Way, Parsippany.

Chahar and Cummings 3rd. J Pain Res 2012; 5: 257-264.

Liposomalna bupiwakaina (Exparel)

FDA recommendations:

- EXPAREL is a liposome injection of bupivacaine, an amide-type local anesthetic, indicated for administration into the surgical site to produce postsurgical analgesia.
- EXPAREL is intended for single-dose administration only. The recommended dose of EXPAREL is based on the surgical site and the volume required to cover the area.
- EXPAREL should be injected slowly into soft tissues of the surgical site with frequent aspiration to check for blood and minimize the risk of intravascular injection.
- The maximum dosage of EXPAREL should not exceed 266 mg (20 mL, 1.3% of undiluted drug).
- EXPAREL has not been studied in:
  - patients younger than 18 years of age
  - pregnant patients
  - patients who are nursing
- EXPAREL has not been evaluated for the following uses and, therefore, is not recommended for these types of analgesia or routes of administration:
  - epidural
  - intrathecal
  - regional nerve blocks
  - intravascular or intra-articular use.

www.fda.gov

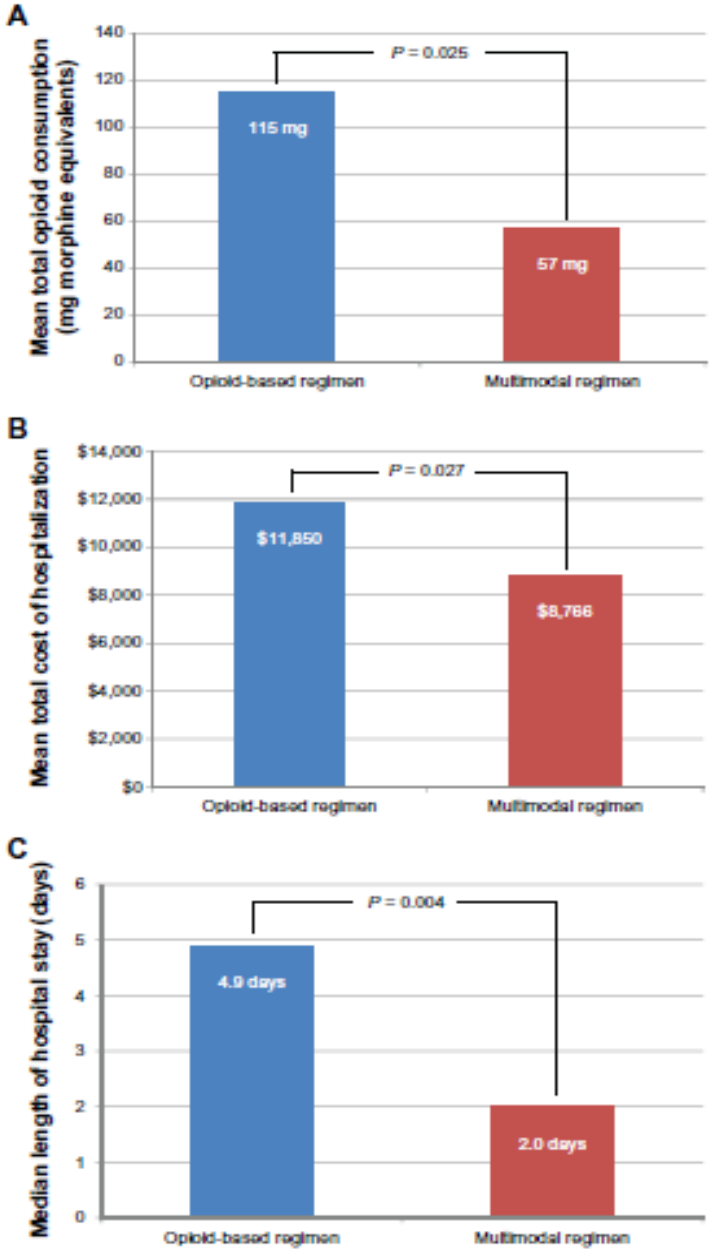


Figure 1 (A) Mean total amount of opioid medications consumed after surgery was 50% less in the group receiving a multimodal analgesic regimen (57 mg) versus the opioid group (115 mg). (B) Total average costs of hospitalization were 26% lower in the multimodal analgesic group ($8766) versus the opioid group ($11,850). (C) Median length of hospital stay after surgery was 59% shorter in the multimodal analgesic group (2.0 days) versus the opioid group (4.9 days).

Journal of Pain Research

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ORIGINAL RESEARCH

Extended pain relief trial utilizing infiltration of Exparel®, a long-acting multivesicular liposome formulation of bupivacaine: a Phase IV health economic trial in adult patients undergoing open colectomy

Stephen M Cohen

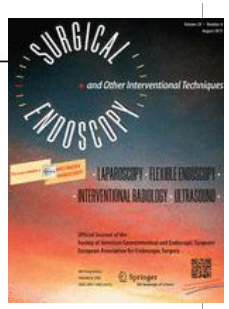
Atlanta Colon and Rectal Surgery, PA, Atlanta, GA, USA

Methods: In this open-label, single-center, sequential-cohort study, adults undergoing open colectomy were assigned to treatment via patient-controlled analgesia with opioids (first cohort) or multimodal analgesia therapy including a single administration of liposomal bupivacaine (second cohort). Both treatment groups were offered rescue analgesia as needed. The main outcome measures were total mg amount of opioids consumed after surgery, total hospital costs, and length of hospital stay. Adverse events, including opioid-related adverse events, were recorded.

Conclusion: This study confirmed that a liposomal bupivacaine–based multimodal analgesic regimen resulted in less opioid consumption, lower hospital costs, and a shorter length of stay than a standard opioid-based analgesic regimen for postsurgical pain in patients undergoing open colectomy.

Journal of Pain Research 2012:5 567–572

Surg Endosc
DOI 10.1007/s00464-015-4459-4



Bupiwakaina liposomalna Obustronny TAP block

Pilot study of a novel pain management strategy: evaluating the impact on patient outcomes

DS Keller[1] · RN Tahilramani[3] · JR Flores-Gonzalez[1] · S. Ibarra[1] · EM Haas[2]

Received: 26 March 2015 / Accepted: 12 July 2015

Methods Consecutive patients undergoing elective laparoscopic colorectal resection were managed with an experimental protocol. The protocol uses a post-induction, pre-incision bilateral TAP block and local peritoneal infiltration at port sites with long-acting liposomal bupivacaine (20 mL long-acting liposomal bupivacaine, 30 mL 0.25 % bupivacaine, 30 mL saline).

Conclusions Our multimodal pain management strategy reduced intraoperative opioid administration. Postoperatively, improvements in PACU time, postoperative pain and narcotic use, and lengths of stay were seen in the experimental cohort. With the favorable finding from the pilot study, further investigation is warranted to fully evaluate the impact of this pain management protocol on patient satisfaction, clinical and financial outcomes.

Values	Experimental	Control	*p* values
Approach (*n*, %)			1.00
Single-incision laparoscopic surgery	25 (100.0 %)	25 (100.0 %)	
Procedure (*n*, %)			0.927
Segmental colectomy	12 (44.0 %)	13 (52.0 %)	
Anterior resection	8 (32.0 %)	8 (32.0 %)	
Low anterior resection	5 (20.0 %)	4 (16.0 %)	
Mean operative time (min, SD)	175.8 (65.5)	163.5 (53.2)	0.406
Mean intraoperative fentanyl (mcg, SD)	158 (66.2)	299 (132.1)	<0.01
Mean blood loss (mL, SD)	53.4 (47.3)	74.2 (76.7)	0.255
Mean final incision length (cm, SD)	3.42 (0.76)	3.38 (0.65)	0.531

Values	Experimental	Control	*p* values
Median initial PACU pain score	0 (0–7)	5.5 (2–10)	<0.01
Medial final PACU pain score	1 (0–5)	3 (2–6)	0.036
Mean time until ready to leave PACU	103.3	118.4	0.471
Mean total PACU time (min)	142.8	165.1	0.342
Mean opioid defined daily dose			
Postoperative day 0	0.7	2.0	<0.01
Postoperative day 1	1.2	1.5	0.064
Postoperative day 2	1.2	1.6	0.055
Postoperative day 3	0.8	1.9	0.083
Median daily pain score			
Postoperative day 1	2 (0–6)	3 (2–7)	0.156
Postoperative day 2	0 (0–5)	2 (2–5)	0.002
Postoperative day 3	2 (0–3)	2 (1–3)	0.170
Mean length of stay (days, SD)	3.0 (1.6)	4.1 (1.8)	0.043
Readmission rate (*n*, %)	1 (4.0 %)	–	
Postoperative complications (*n*, %)	1 (4.0 %)	1 (4.0 %)	1.00
Ileus	1 (4.0 %)	–	
Urinary retention	–	1 (4.0 %)	

Liposomalna bupiwakaina – bezpieczeństwo

Clinical Therapeutics/Volume 35, Number 3, 2013

Impact of Local Administration of Liposome Bupivacaine for Postsurgical Analgesia on Wound Healing: A Review of Data From Ten Prospective, Controlled Clinical Studies

Richard Baxter, MD[1]; Kenneth Bramlett, MD[2]; Erol Onel, MD[3]; and Stephen Daniels, DO[4]

Objective: This retrospective review of 10 clinical trials assessed the potential impact of local anesthetics on wound healing and chondrolysis. Various doses of liposome bupivacaine and bupivacaine hydrochloride (HCl) were evaluated.

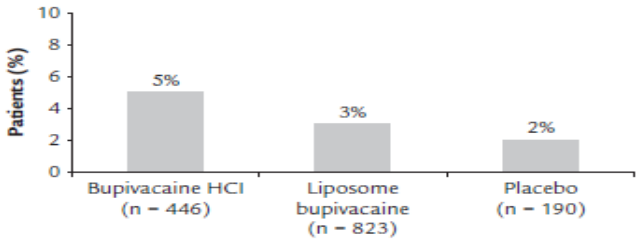


Figure. Proportion of patients in whom an adverse event of infection was reported. System Organ Class = infections and infestations.

Table I. Overview of randomized, double-blind, controlled wound infiltration studies.

Study/Identifier	Phase	Surgical Setting	Study Treatments and Dosages
1 (NCT01203644)[15]	2	Inguinal hernia repair	Liposome bupivacaine 155, 199, 266, and 310 mg vs bupivacaine HCl 100 mg
2 (NCT00485433)[16]	2	Inguinal hernia repair	Liposome bupivacaine 93, 160, and 306 mg vs bupivacaine HCl 105 mg
3 (NCT00485693)[17]	2	Total knee arthroplasty	Liposome bupivacaine 133, 266, 399, and 532 mg vs bupivacaine HCl 150 mg
4 (NCT00529126)[18]	2	Hemorrhoidectomy	Liposome bupivacaine 66, 199, and 266 mg vs bupivacaine HCl 75 mg
5 (NCT01206608)	2	Breast augmentation	Liposome bupivacaine 133 and 266 mg vs bupivacaine HCl 75 mg
6 (NCT00745290)	3	Total knee arthroplasty	Liposome bupivacaine 532 mg vs bupivacaine HCl 200 mg
7 (NCT00744848)	3	Hemorrhoidectomy	Liposome bupivacaine 266 mg vs bupivacaine HCl 100 mg
8 (NCT00813111)[6]	3	Breast augmentation	Liposome bupivacaine 532 mg (266 mg in each breast pocket) vs bupivacaine HCl 200 mg (100 mg in each breast pocket)
9 (NCT00890721)[5]	3	Hemorrhoidectomy	Liposome bupivacaine 266 mg vs placebo (saline)
10 (NCT00890682)[4]	3	Bunionectomy	Liposome bupivacaine 106 mg vs placebo (saline)

CONCLUSIONS

In the studies reviewed here, single administrations of liposome bupivacaine appeared to have had no negative impact on wound or bone healing at doses up to 532 mg when given via local administration during surgery. The overall wound-healing profile of liposome bupivacaine was similar to that of bupivacaine HCl. Additionally, no significant impact on wound healing with liposome bupivacaine was observed for up to 2 years, and no occurrences of chondrolysis were reported in any of the studies. Based on results from this retrospective review, it appears that liposome bupivacaine has no adverse impact on wound healing.

Liposomalna bupiwakaina - miejscowa toksyczność

Research Article

The Safety of EXPAREL ® (Bupivacaine Liposome Injectable Suspension) Administered by Peripheral Nerve Block in Rabbits and Dogs

In conclusion, a single administration of EXPAREL was demonstrated to be safe by peripheral nerve block in rabbits and dogs when tested in comparison with bupivacaine HCl and saline. EXPAREL did not cause overt irritation or local tissue damage even when injected at high dose or concentration around the brachial plexus nerve bundle.

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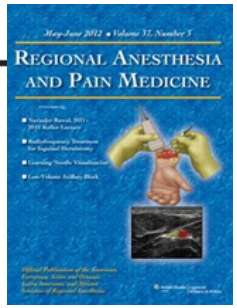

Safety and Side Effect Profile of Liposome Bupivacaine (Exparel) in Peripheral Nerve Blocks

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(*Reg Anesth Pain Med* 2015;40: 572–582)

Methods: Data from 6 controlled (phases I-III) studies were compiled involving single-injection ankle, femoral nerve, and intercostal nerve blocks (2 each). Adverse events (AEs) were monitored for 1 to 30 days after study drug administration.

TABLE 3. Adverse Events

	Liposome Bupivacaine					
Parameter	<266 mg (n = 111)	266 mg (n = 210)	>266 mg (n = 14)	All Doses (n = 335)	Bupivacaine HCl (n = 33)	Placebo (n = 207)
Any AE, n (%)	83 (75)	165 (79)	8 (57)	256 (76)	20 (61)	157 (76)
Maximum severity, n (%)*						
Mild	51 (61)	75 (45)	5 (62)	131 (51)	15 (75)	72 (46)
Moderate	29 (35)	78 (47)	3 (38)	110 (43)	4 (20)	63 (40)
Severe	3 (4)	12 (7)	0	15 (6)	1 (5)	22 (14)
Any serious AE, n (%)	7 (6)	21 (10)	0	28 (8)	0	21 (10)
Deaths,† n (%)	0	2 (1)	0	2 (0.6)	0	4 (2)

*Percentage based on total number of subjects with any AE.

†No serious AEs or deaths were assessed by study investigators as related to study drug.

CONCLUSIONS

The available data from these 6 prospective and controlled clinical studies suggest that liposome bupivacaine may have a similar safety profile to bupivacaine HCl and normal saline. However, further studies are needed to better define the risk of AEs associated with this formulation administered as a peripheral nerve block. The authors emphasize that liposome bupivacaine is not currently indicated for use in peripheral nerve blocks and must be considered experimental at this time.

Dziękuję za uwagę!