Thoracic Epidural Analgesia Versus Rectus Sheath Block Versus Surgeon Infiltration with Liposomal Bupivacaine or Standard Bupivacaine for Post-operative Pain Control after Cystectomy

Dr. Yar Luan Yeap
Indiana University Department of Anesthesia

Dr. Amy McCutchan
Indiana University Department of Anesthesia

Dr. Adam Lemmon
Indiana University Department of Anesthesia

Dr. Timothy A. Masterson
Indiana University Department of Urology

Dr. Hristos Kaimakliotis
Indiana University Department of Urology

Brendon Burke
Medical Student, Indiana University School of Medicine

Version 5.0 10-21-19

1.0 Background

Indiana University Hospital is a large academic health center that performs a large number (~180) of cystectomies per year. Cystectomy is a urologic procedure that involves the radical removal of the bladder, with subsequent need for urinary tract reconstruction. The reconstruction requires harvesting of portions of the small and/or large bowel, and can be in the form of an ileal conduit, orthotopic bladder replacement, or continent urinary reservoir such as an "Indiana Pouch". The postoperative course usually spans on average a 7-day inpatient hospital stay, with the majority of the issues surrounding management of postoperative pain and subsequent ileus. Currently, there is no standard of pain control in cystectomy, though adjunctive mechanisms of analgesia are often utilized to decrease opioid usage. Opioid use has long been associated with postoperative ileus, nausea and vomiting, aspiration, prolonged hospital stay, and several other side effects[1]. Postoperative pain may also decrease patient satisfaction while increasing length of hospital stay and hospital costs[2]. Without a standard practice for postoperative pain control in cystectomy, our study aims to compare thoracic epidural versus rectus sheath block versus surgeon infiltration of local anesthesia for cystectomy. With studies indicating improvements in perioperative outcomes for all three techniques, we believe we should compare these three methods for possible incorporation of the best technique for our enhanced recovery after surgery (ERAS) protocol for cystectomy. This will be done by collection of post-operative pain scores (VAS) at both resting and with movement. The VAS (Visual Analog Scale) pain scores will be measured at 24, 48, 72 and 96 hours under an advanced recovery perioperative care pathway.

Epidural analgesia is well studied in cystectomy patients and with studies indicating improved perioperative outcomes. Ozyuvaci et al found that when combining epidural and general analgesia, radical cystectomy patients had significantly less intraoperative bleeding and pain by visual analogue scale (VAS) at 0, 1, 2, 4, 6, 12, and 24 hours when compared to general analgesia alone[3]. Ladjevic et al saw similar results with combined epidural and general analgesia with decreased intraoperative bleeding and postoperative pain[4]. Epidural analgesia was also associated with decreased incidence of postoperative ileus and blood transfusion requirements in a randomized clinical trial by Mazul-Sunko et al[5]. In a study by Toren et al,

---

[1] H. D. de Boer, O. Detriche, and P. Forget, "Opioid-Related Side Effects: Postoperative Ileus, Urinary Retention, Nausea and Vomiting, and Shivering. A Review of the Literature," *Best Pract Res Clin Anaesthesiol* 31, no. 4 (2017).
[2] J. J. Pozek, M. De Ruyter, and T. W. Khan, "Comprehensive Acute Pain Management in the Perioperative Surgical Home," *Anesthesiol Clin* 36, no. 2 (2018).
[3] E. Ozyuvaci et al., "General Anesthesia Versus Epidural and General Anesthesia in Radical Cystectomy," *Urol Int* 74, no. 1 (2005).
[4] N. Ladjevic et al., "Combined General and Epidural Anaesthesia Versus General Anaesthesia for Radical Cystectomy," *Acta Chir Iugosl* 54, no. 4 (2007).
[5] B. Mazul-Sunko et al., "Thoracic Epidural Analgesia for Radical Cystectomy Improves Bowel Function Even in Traditional Perioperative Care: A Retrospective Study in Eighty-Five Patients," *Acta Clin Croat* 53, no. 3 (2014).

patients receiving patient-controlled epidural analgesia had significantly less pain during activity with a noted trend toward earlier tolerance of solid foods.

Surgeon infiltration has not been studied as much in cystectomy patients specifically, but it is well-studied in a wide variety of other surgeries including large pelvic surgeries. Liposomal bupivacaine injection by surgeon infiltration is associated with decreased opioid usage including rescue IV opioids and PCA use compared to bupivacaine hydrochloride with laparotomies for gynecologic malignancy[6]. In hepatectomy for hepatocellular carcinoma, Wu et al showed improved NRS scores as well as decreased analgesic usage and intestinal function recovery time[7]. Sun et al saw similar decreases in pain and analgesic use in open hepatectomy, but also showed decreases in surgical stress response including hormonal response, heart rate, and mean arterial pressure in the first 48-h postoperatively[8]. In total knee arthroplasty, local wound infiltration analgesia combined with adductor canal block decreased early incisional pain in the postoperative period, decreased operative time, and promoted earlier knee joint mobility[9]. To our knowledge, comparison between epidural analgesia and surgeon infiltration has not been studied for cystectomy.

Exparel®, a liposomal formulation of bupivacaine (LB), has shown significant promise in providing extended analgesic coverage in the postoperative period. Due to its extended release format, LB can provide analgesia coverage for up to 72 hours postoperatively when compared to normal saline and has been suggested to reduce postoperative opioid use as well (9). It has provided effective analgesia in total knee arthroplasty and hip arthroplasty and has shown promise in open and laparoscopic colectomy[10,11,12]. However, there are also studies showing that LB might not be superior to standard bupivacaine (SB) in terms of duration of

---

[6] E. Kalogera et al., "Abdominal Incision Injection of Liposomal Bupivacaine and Opioid Use after Laparotomy for Gynecologic Malignancies," *Obstet Gynecol* 128, no. 5 (2016).

[7] Y. F. Wu et al., "Postoperative Local Incision Analgesia for Acute Pain Treatment in Patients with Hepatocellular Carcinoma," *Rev Assoc Med Bras (1992)* 64, no. 2 (2018).

[8] J. X. Sun et al., "Effect of Local Wound Infiltration with Ropivacaine on Postoperative Pain Relief and Stress Response Reduction after Open Hepatectomy," *World J Gastroenterol* 23, no. 36 (2017).

[9] X. Hou et al., "[Effect of Adductor Canal Block Combined with Local Infiltration Anesthesia on Rehabilitation of Primary Total Knee Arthroplasty]," *Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi* 32, no. 8 (2018).

[10] Yu ZX, Yang ZZ, Yao LL. Effectiveness of liposome bupivacaine for postoperative pain control in total knee arthroplasty: A PRISMA-compliant meta-analysis of randomized controlled trials. Medicine (Baltimore). 2018;97(13):e0171.

[11] Ma TT, Wang YH, Jiang YF, Peng CB, Yan C, Liu ZG, et al. Liposomal bupivacaine versus traditional bupivacaine for pain control after total hip arthroplasty: A meta-analysis. Medicine (Baltimore). 2017;96(25):e7190.

[12] Raman S, Lin M, Krishnan N. Systematic review and meta-analysis of the efficacy of liposomal bupivacaine in colorectal resections. J Drug Assess. 2018;7(1):43-50.

analgesia[13,14,15]. In order to compare the duration of action of both forms of bupivacaine, we'll randomized the surgeon infiltration group to both LB group and SB group.
Our hypothesis is that Thoracic Epidural is superior to rectus sheath block and surgeon infiltration for pain scores, and LB will be superior to SB for duration of action of the block.

2.0 Rational and Specific Aims

All of the pain control modalities in this study have been used as postoperative analgesia in prior studies. The specific aim of this study is to compare the difference between the pain control methods in achieving the following:

1. Decreased opioid requirements
2. Improved postoperative VAS (Visual Analog Scale) pain scores
3. Decreased opioid side effects (Nausea, sedation, ileus, respiratory depression)
4. Decreased hospital length of stay (LOS)

The primary endpoint of this study will be VAS (Visual Analog Scale) pain score at both resting and with movement. The VAS Visual Analog Scale) pain score will be measured at 24, 48, 72 and 96 hours under an advanced recovery perioperative care pathway.

The secondary endpoint includes intravenous opioid consumption, opioid side effects (nausea, sedation, ileus, respiratory depression), and LOS. Hospital length of stay (LOS) will be collected via EMR of the admission and discharge date to calculate the LOS. The IV and PO opioid doses will be quantified at 1, 24, 48, 72, and 96 hours. All the opioid consumption (both PO and IV) will be converted to PO morphine equivalent for analysis. We will also measure postoperative nausea and sedation scores at 1, 24, 48, 72, and 96 hours. Nausea will be measured on a 4-point scale: none, mild, moderate or severe. This is collected as patient reported as well as per nursing documentation. Sedation score is also reported on a 4-point scale: awake/alert, quietly awake, asleep/arousable or deep sleep. This is collected as an observation by nurse coordinator/staff. We will access patient's satisfaction at 24, 48 72 and 96 hours. This will be measured on a 5-point scale; very unsatisfied, unsatisfied, neutral, satisfied and very satisfied. We will also measure time to first flatus, postoperative creatinine, incidence of hypotension (defined as BP decrease of more than 20%), incidence of respiratory depression, and ambulation activity.
Ambulation is defined as anytime out of bed (up in chair, to bathroom and walking in hall with PT/nurse) activity will also be recorded daily. It will be recorded as yes/no.

---

[13] Knudson RA, Dunlavy PW, Franko J, Raman SR, Kraemer SR. Effectiveness of Liposomal Bupivacaine in Colorectal Surgery: A Pragmatic Nonsponsored Prospective Randomized Double Blinded Trial in a Community Hospital. Dis Colon Rectum. 2016;59(9):862-9.
[14] Knight RB, Walker PW, Keegan KA, Overholser SM, Baumgartner TS, Ebertowski JS, 2nd, et al. A Randomized Controlled Trial for Pain Control in Laparoscopic Urologic Surgery: 0.25% Bupivacaine Versus Long-Acting Liposomal Bupivacaine. J Endourol. 2015;29(9):1019-24.
[15] Noviasky J, Pierce DP, Whalen K, Guharoy R, Hildreth K. Bupivacaine liposomal versus bupivacaine: comparative review. Hosp Pharm. 2014;49(6):539-43.

All patients will complete a phone survey approximately 6 months after surgery to assess for pain, quality of life, and satisfaction of hospital stay. Quality of life is measured by how their pain interferes with their general activity, mood, walking ability, normal work, relations with other people, sleep and enjoyment of life. All these data points will be recorded in a post-operative brief pain inventory (BPI) questionnaire. If after four attempts to contact the patient are unsuccessful, the survey will not be completed; this will not be considered a deviation as the survey is not critical to the overall data collection.

3.0 Inclusion/Exclusion

Inclusion criteria:

- Patients undergoing cystectomy surgery
- ASA class 1, 2, 3 or 4
- Age 18 or older, male or female
- Desires Regional anesthesia for postoperative pain control

Exclusion criteria:

- Any contraindication for thoracic epidural, such as coagulopathic states or pre-existing hardware in the thoracic epidural space.
- History of substance abuse in the past 6 months.
- Patients on more than 30mg morphine equivalents of opioids daily.
- Any physical, mental or medical conditions which in the opinion of the investigators, may confound quantifying postoperative pain resulting from surgery.
- Known allergy or other contraindications to the study medications (Acetaminophen, Gabapentin, Bupivacaine, Hydromorphone).
- Postoperative intubation.
- Any patient with history of neuropathic bowel or bladder dysfunction

4.0 Enrollment/Randomization

All cystectomy cases scheduled by the urologists at IU Health University Hospital will be identified. Subjects will be contacted face-to-face prior to surgery by one of the research team members. They will be informed about the study and all questions will be answered. The potential subjects will be given a copy of the informed consent form and authorization form. The subjects will then be contacted face-to-face in POCU on the day of surgery and if participation is agreed, written consent will be taken. All patients will undergo a standardized enhanced recovery perioperative care pathway designed and agreed upon by the perioperative team of anesthesiologists and surgeons.

A total of 160 subjects will be randomized by a computer program into four groups (40 in each group):

1. Thoracic epidural– epidural bupivacaine 0.05%/hydromorphone 0.05mg/ml mix will be given throughout the duration of their epidural analgesia.
2. Rectus Sheath Block - 20 mL of liposomal bupivacaine diluted with 40 mL of 0.125% bupivacaine and 40 ml of injectable saline for a total of 100 mL. The 100 mL will be injected into 4 locations below the rectus abdominis muscle.
3. Surgeon infiltration with Liposomal Bupivacaine (LB) – 20 mL of liposomal bupivacaine diluted with 40 mL of 0.125% bupivacaine and 40 ml of injectable saline for a total of 100 mL. The 100 mL will be injected throughout the incision site by the surgeon at the end of surgery, prior to abdominal wall closure.
4. Surgeon infiltration with Standard Bupivacaine (SB) – 60ml of 0.5% bupivacaine will be diluted with 40ml of saline for a total of 100ml. The 100 mL will be injected throughout the incision site by the surgeon at the end of surgery.

Randomization will be performed using Research Randomizer. The primary investigator will inform the person doing the block as to what group the patients are randomized to

Study procedures:

Thoracic epidural placement will occur in the preoperative period. Both the rectus sheath block and the surgeon infiltration will occur at the end of the case. All procedures will be done using sterile technique with masks, hats, and sterile gloves. Thoracic epidurals and rectus sheath block will be placed under the supervision of the attending anesthesiologist on the acute pain service. Surgeon infiltration will be performed by the surgeon.

Patients will be randomized to one of the four arms by the research randomizer. On the day of surgery, the Principal Investigator will inform the person doing the block as to what group the patients are randomized to.

Thoracic epidural will be performed around T9-T10 interspace since that correlates with surgical incision dermatomes. Utilizing the loss-of-resistance technique, an 18-gauge needle will be inserted in the midline between the lumbar spinous processes and advanced until loss-of-resistance is felt. A small amount of preservative-free saline will be injected to ensure the location in the epidural space. After careful aspiration, a test dose of 2-3 mL local anesthetic containing diluted epinephrine will be injected and the heart rate will be monitored in case of accidental placement in an epidural vein[16].

[16] John F. Butterworth Iv, David C. Mackey, and John D. Wasnick, "Spinal, Epidural, &Amp; Caudal Blocks," in *Morgan &Amp; Mikhail's Clinical Anesthesiology, 6e* (New York, NY: McGraw-Hill Education, 2018).

Rectus sheath block will be performed at 4 locations below the rectus abdominis muscle, using an ultrasound. The locations will be both left and right abdomen, above and below the umbilical region.

Surgical wound infiltration will be performed by the surgeon at the end of the case. It will be performed via a direct technique. In the direct technique, anesthetic is injected after careful aspiration in small boluses into the subfascial tissues until the wound is adequately anesthetized[17].

Opioid usage at 1, 24, 48, 72, and 96 hours after the block will be recorded by a member of the research team. Pain scores at rest and on movement (knee flexion) will be measured by the investigator using Visual Analog Scale (VAS). VAS will measure pain from a scale of 0-10. Nausea will be measured using a categorical scoring system (none=0; mild=1; moderate=2; severe=3). Nausea score will be reported by the patients. Anti-emetic usage will also be recorded. Sedation scores will also be assessed by a member of the study team using a sedation scale. Hospital length of stay (LOS) will be collected via EMR of the admission and discharge date to calculate the LOS. We will also measure time to first flatus, postoperative creatinine, incidence of hypotension (defined as BP decrease of more than 20% from morning of surgery), incidence of respiratory depression (defined by nursing report or naloxone use), and ambulation activity (anytime out of bed (up in chair, to bathroom and walking in hall with PT/nurse) will also be recorded daily. It will be recorded as yes/no.

All these parameters will be measured at 1, 24, 48, 72, and 96 hours after the cystectomy.

All patients will complete a phone survey approximately 6 months after surgery to assess for pain and how it impacts their daily function. This is meant to assess for the incidence of chronic post-op pain after cystectomy with all the different pain interventions. The survey will measure how their pain interfere with their general activity, mood, walking ability, normal work, relations with other people, sleep and enjoyment of life. If after four attempts to contact the patient are unsuccessful, the survey will not be completed; this will not be considered a deviation as the survey is not critical to the overall data collection.

Data management will include quality assurance and quality control measures. All collected data will be monitored by a data and safety monitoring group independent from the research team. Data quality, subject recruitment, accrual,-retention, outcome and adverse event data, assessment of scientific reports or therapeutic development, results of related studies that may impact subject safety and procedures designed to protect the privacy of subjects will be monitored at least annually.

5.0 Reporting of Adverse Events

[17] Q. Guo et al., "Transversus Abdominis Plane Block Versus Local Anaesthetic Wound Infiltration for Postoperative Analgesia: A Systematic Review and Meta-Analysis," *Int J Clin Exp Med* 8, no. 10 (2015).

Patients will be monitored by the primary team during the postoperative period, and any adverse events or unanticipated problems such as local anesthetic toxicity or epidural hematoma formation or nerve damage will be reported to the acute pain service and research team. All adverse events or unanticipated problems that meet the criteria for prompt reporting will be reported to the IRB within 5 business days.

6.0 Study withdrawal/DC

The patient can withdraw from the study at any time by contacting the research team or acute pain anesthesia resident. In such an event, patient may still have access to all the IV and oral pain medications. Anesthesia acute pain team will continue to follow the patient for 24 hours. After 24 hours, the anesthesia acute pain team will sign off and all further pain management will be done by the primary team.

7.0 Statistical consideration

Primary outcome: VAS score with movement at 48 and 72 hours

Primary Research Hypothesis: Thoracic epidural will provide lower postoperative pain scores compared to each of the other three methods used for cystectomy as measured by VAS scores at 24, 48, 72, and 96 hours under an enhanced recovery perioperative care pathway.

Secondary outcomes: Narcotic usage after 1, 24, 48, 72, and 96 hours. Pain scores using VAS at rest and on knee flexion at 1, 24, 48, 72, and 96 hours. Nausea scores at 1, 24, 48, 72, and 96 hours. Sedation scores at 1, 24, 48, 72, and 96 hours. Time to first flatus, postoperative creatinine, hospital length of stay (hospital length of stay (LOS) will be collected via EMR of the admission and discharge date to calculate the LOS), ileus, hypotension (defined as BP decrease of more than 20%), and ambulation/anytime out of bed (up in chair, to bathroom and walking in hall with PT/nurse) activity will also be recorded daily. It will be recorded as yes/no.

If the patient is discharged within 96 hours, every effort will be made to obtain data points, but we will not consider these data point deviations since our 96-hour data point will not change the integrity of the study.

Secondary Research Hypotheses: Thoracic epidural will show improved patient satisfaction scores and decreased nausea and sedation scores compared to each of the other three treatments.

Statistical analysis will be performed using a standard statistical program (SAS or SPSS). All data will be summarized (means, standard deviations, standard errors, and ranges for continuous variables; frequencies and percentages for categorical variables) by group. Demographic data will be compared between the four groups using ANOVA or chi-square tests as appropriate. The primary outcome, VAS (Visual Analog Scale) at 48 and 72 hours, will be compared between the

groups using repeated measures ANOVA; the model will include fixed effects for group, time, and the group by time interaction and random effects to allow correlations between the two times and different variances for the two times.

Pain and satisfaction scores and opioid usage over time will be analyzed using repeated measures ANOVA. Nausea and sedation scores will be compared between groups at each time point using Mantel-Haenszel chi-square tests for ordered categorical data. Time to first flatus, postoperative creatinine, and LOS will be compared between the groups using one-way ANOVA. The binary outcomes of incidence of ileus, hypotension (defined as BP decrease of more than 20%), and incidence of respiratory depression will be analyzed using logistic regression. Distributions of the continuous variables will be examined, and a transformation of the data (e.g. natural logarithm) or nonparametric tests will be used as necessary. A 5% significance level will be used for all comparisons.

Based on prior studies, the coefficient of variation for the VAS (Visual Analog Scale) score at 48 and 72 hours is estimated to be 0.70. With a sample size of 40 per group the study will have 80% power to detect a ratio of means of 1.5 for VAS score between any two of the four treatment groups, assuming two-sided tests each conducted at a 5% significance level.

All patients will receive a phone survey approximately 6 months after surgery to assess for pain, quality of life, and satisfaction of hospital stay. Quality of life is measured by how their pain interferes with their general activity, mood, walking ability, normal work, relations with other people, sleep and enjoyment of life. If after four attempts to contact the patient are unsuccessful, the survey will not be completed; this will not be considered a deviation as the survey is not critical to the overall data collection.

8.0 Privacy

All study papers containing patient identifiers will be kept in each subjects' confidential study file accessible to only the research team. All records will be kept in a locked room in a locked cabinet that only authorized staff enters. Collected data from each enrolled participant will be recorded on Redcap, which is a secure web-based data collection tool. Three years after completion of the study, all electronic information and paperwork containing patient identifiers will be deleted or shredded.

9.0 Follow-up/record retention

The study will start in August of 2019 and will end when a sample size of 160 subjects is achieved. Since Indiana University Hospital performs a large number (~180) of cystectomies per year, the estimated time frame to enroll 160 study subjects is 24 months. After 160 subjects have been enrolled, the study will be stopped and the data collected will be analyzed using statistical methods.

Three years after completion of the study, all study papers with patient identifiers will be shredded and only data without any patient identifiers will be retained by the research team for an indefinite time.

Butterworth Iv, John F., David C. Mackey, and John D. Wasnick. "Spinal, Epidural, &Amp; Caudal Blocks." In *Morgan &Amp; Mikhail's Clinical Anesthesiology, 6e*. New York, NY: McGraw-Hill Education, 2018.

de Boer, H. D., O. Detriche, and P. Forget. "Opioid-Related Side Effects: Postoperative Ileus, Urinary Retention, Nausea and Vomiting, and Shivering. A Review of the Literature." [In eng]. *Best Pract Res Clin Anaesthesiol* 31, no. 4 (Dec 2017): 499-504.

Guo, Q., R. Li, L. Wang, D. Zhang, and Y. Ma. "Transversus Abdominis Plane Block Versus Local Anaesthetic Wound Infiltration for Postoperative Analgesia: A Systematic Review and Meta-Analysis." [In eng]. *Int J Clin Exp Med* 8, no. 10 (2015): 17343-52.

Hou, X., Z. Luo, H. Wang, Y. Zhan, L. Yang, and L. Li. "[Effect of Adductor Canal Block Combined with Local Infiltration Anesthesia on Rehabilitation of Primary Total Knee Arthroplasty]." [In chi]. *Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi* 32, no. 8 (Aug 1 2018): 1006-11.

Kalogera, E., J. N. Bakkum-Gamez, A. L. Weaver, J. P. Moriarty, B. J. Borah, C. L. Langstraat, C. J. Jankowski*, et al.* "Abdominal Incision Injection of Liposomal Bupivacaine and Opioid Use after Laparotomy for Gynecologic Malignancies." [In eng]. *Obstet Gynecol* 128, no. 5 (Nov 2016): 1009-17.

Ladjevic, N., I. Likic-Ladjevic, Z. Dzamic, M. Acimovic, D. Dragicevic, and O. Durutovic. "Combined General and Epidural Anaesthesia Versus General Anaesthesia for Radical Cystectomy." [In eng]. *Acta Chir Iugosl* 54, no. 4 (2007): 89-91.

Mazul-Sunko, B., I. Gilja, M. Jelisavac, I. Kozul, D. Troha, N. Osmancevic, A. El-Saleh*, et al.* "Thoracic Epidural Analgesia for Radical Cystectomy Improves Bowel Function Even in Traditional Perioperative Care: A Retrospective Study in Eighty-Five Patients." [In eng]. *Acta Clin Croat* 53, no. 3 (Sep 2014): 319-25.

Ozyuvaci, E., A. Altan, T. Karadeniz, M. Topsakal, A. Besisik, and M. Yucel. "General Anesthesia Versus Epidural and General Anesthesia in Radical Cystectomy." [In eng]. *Urol Int* 74, no. 1 (2005): 62-7.

Pozek, J. J., M. De Ruyter, and T. W. Khan. "Comprehensive Acute Pain Management in the Perioperative Surgical Home." [In eng]. *Anesthesiol Clin* 36, no. 2 (Jun 2018): 295-307.

Sun, J. X., K. Y. Bai, Y. F. Liu, G. Du, Z. H. Fu, H. Zhang, J. H. Yang*, et al.* "Effect of Local Wound Infiltration with Ropivacaine on Postoperative Pain Relief and Stress Response Reduction after Open Hepatectomy." [In eng]. *World J Gastroenterol* 23, no. 36 (Sep 28 2017): 6733-40.

Wu, Y. F., X. P. Li, Y. B. Yu, L. Chen, C. B. Jiang, D. Y. Li, and M. L. Chen. "Postoperative Local Incision Analgesia for Acute Pain Treatment in Patients with Hepatocellular Carcinoma." [In eng]. *Rev Assoc Med Bras (1992)* 64, no. 2 (Feb 2018): 175-80.