Does My Anesthetic Technique Affect Outcomes in Breast Cancer Surgery?
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Stem Case and Key Questions Content
A 53-year-old woman presents for complete mastectomy and axillary lymph node dissection. She weighs 185 lb, and is 62 inches tall. Her past medical history is significant for COPD, hypertension, hyperlipidemia, chronic low back pain, severe post-operative nausea and vomiting (PONV), and history of ovarian cancer.

Her medications include betamethasone inhaler, albuterol inhaler, lisinopril, amlodipine, atorvastatin, meloxicam, pregabalin, and oxygen at 2L per minute as needed.

Her review of systems is positive for bronchitis 3 weeks ago for which she received oral antibiotics for one week. She has residual dry cough now. Her blood pressure is well controlled, and she has low back pain rated as 8/10 in the pre-operative area.

Her physical exam is significant for bilateral scattered wheezes cleared by coughing. Her airway appears normal with full neck range of motion, MP II, positive jaw subluxation and upper lip bite test.

Questions:
1. Is there any evidence that perioperative factors modulate the risk of cancer recurrence after mastectomy?
2. Does the choice of anesthetic impact her risk of cancer recurrence?
3. What is the evidence on the role of opioids in cancer recurrence?

The patient is extremely concerned about post-operative pain but wants to minimize the use of opioids because they cause extreme nausea, vomiting and severe constipation that she experienced after her oophorectomy procedure.
4. What is the prevalence of chronic pain after modified radical mastectomy?

5. What strategies will you use to control her post-operative pain and reduce her risk of chronic pain development?

6. What kind of multimodal analgesic options can be offered?

7. How will you address her concerns of severe PONV?

8. Can a regional anesthetic alone be sufficient to provide surgical anesthesia for this procedure?

9. What type of regional anesthetic techniques can be used for modified radical mastectomy?

10. What is the current evidence on pectoral nerves (PECS) blocks for breast surgery?

11. What are the risks and benefits of offering a thoracic paravertebral versus a thoracic epidural?

12. Are there any difference in outcomes between single level paravertebral block and multilevel block?

13. How will you decide whether to offer a continuous paravertebral catheter?

14. What is your choice of local anesthetic for single shot paravertebral block and continuous infusion?

15. You decide to place a continuous paravertebral catheter at T3 level. What is the current evidence on blind placement versus use of ultrasound?

While placing the catheter through the Touhy needle, the patient coughs and your needle moves in by 5 mm. You immediately get concerned about puncturing the pleura.

16. How will you proceed now? Would you still place the catheter after withdrawing the needle by 5 mm?

17. How will you monitor for evolution of pneumothorax in this setting? How long will you monitor?

18. Would you proceed with surgery? What precautions will you take?

The patient did not have a pneumothorax and has a functioning catheter. She is able to undergo surgery with regional anesthesia and minimal sedation. She is very pleased with the pain control and absence of nausea. She would like to continue the infusion as long as safely possible.
19. How long would you choose to leave the catheter?

20. What are the risks and benefits of discharging the patient home with an elastomeric infusion pump with 0.2% ropivacaine at a low fixed rate?

Model Discussion Content

The perioperative period seems to be a critical window where a number of complex mechanisms modulate how the body handles the release of tumor cells during cancer surgery. There is a growing body of evidence suggesting that perioperative factors such as surgical stress, acute pain, use of opioids, and use of inhalational anesthetics have a negative impact on endogenous immune response to micro-metastases of tumor cells that occur at the time of surgery. If these cancer cells are not handled by cellular and humoral immunity, they can be responsible for cancer recurrence and metastases. Opioids and inhalational anesthetics are shown to suppress the Natural Killer (NK) cells which are cytotoxic to cancer cells. 1-3

A randomized study compared the serum of primary breast cancer patients undergoing surgery under general anesthesia with sevoflurane versus paravertebral block and total IV anesthesia with propofol. Serum from patients given sevoflurane anesthesia and opioids reduced apoptosis in breast cancer cells to a greater extent than serum from patients given paravertebral-TIVA with propofol. 4 In other studies, serum from paravertebral-TIVA group reduced in-vitro proliferation of breast cancer cells more effectively and showed more NK cell cytotoxicity of tumor cells compared to that from sevoflurane-opioid group. 5, 6 This suggests that innate defense mechanisms against circulating tumor cells are more adversely effected by inhalational anesthetics and opioids.

Another study evaluated the effects of anesthetic technique on protective immune cell infiltration in excised breast tissue. The excised tissue was immunohistochemically stained to identify immune cells. They found increased levels of NK cells and Helper T cell infiltration in the breast tissue of patients receiving paravertebral-TIVA with propofol compared to standard GA with inhalational anesthetics and opioids. 7

Opioids may play a twofold role in cancer recurrence. Mu-receptors have been identified on the cellular surface of malignant tissue with high density compared to normal tissue. Chronic mu-receptor agonism results in direct stimulation of cancer cells that promotes tumor growth and metastatic spread. This phenomenon is observed with chronic high doses of opioids. In addition, opioids cause sympathetically suppression of NK cell activity. 8, 9

A retrospective analysis of 129 patients receiving GA versus paravertebral anesthesia showed improved long term survival in the latter group. 1 The mechanism by which regional anesthesia shows
a favorable effect on cancer recurrence and survival is probably due to suppression of surgical stress and pain, and avoidance of potentially immunosuppressant anesthetic and analgesics; thereby preserving the innate immunity against circulating cancer cells. 1, 2, 10

In addition, there is also evidence that addition of a COX-2 inhibitor such as celecoxib may modulate the immunosuppressive effects of certain anesthetics and preserve immunity against cancer cells. 2, 11

The prevalence of chronic pain has been reported to be as high as 51% after axillary lymph node dissection. The overall prevalence at 22 months after breast cancer surgery has been reported to be 32%. 12 Chronic pain after breast surgery has been shown to cause psychosocial distress and negatively influence quality of life. 13 Severe acute post-operative pain is associated with a high risk of development of chronic pain. 14 The common modalities of managing acute post-operative pain include opioids, non-steroidal anti-inflammatory drugs (NSAIDS), acetaminophen and use of local anesthetics as wound infiltration or regional anesthetics. The use of regional anesthesia techniques such as thoracic paravertebral (TPV) blocks may reduce the risk of developing chronic pain after breast cancer surgery. 15, 16 Addition of gabapentinoids such as gabapentin and pregabalin has been shown to reduce post-surgical pain after breast surgery. 17, 18 Antidepressant such as venlafaxine has been shown to significantly reduce the incidence of chronic post-mastectomy pain at 6 months after surgery. 19 Wound infiltration by local anesthetics has shown to modify acute post-operative pain but may not show a long term effect in reducing chronic pain. 20 Intravenous perioperative lidocaine has also shown to decrease the incidence and severity of chronic pain after breast cancer surgery. 21 Based on the available evidence, our patient may benefit from a combination of several strategies described above to avoid opioids and still effectively manage her post-operative pain and reduce the risk of chronic pain.

In a major trial of interventions to prevent post-operative nausea and vomiting (PONV), factors identified to have independent effect on reduction include ondansetron, droperidol, dexamethasone, propofol, avoidance of inhalational anesthetics, and avoidance of nitrous oxide. 22 A recent evidence based review identified duration of anesthesia with volatile anesthetics and use of postoperative opioids as independent predictors of PONV. 23 Addition of transdermal scopolamine further decreases the risk, as shown by a randomized multicenter controlled trial. 24

In our patient we can reduce the risk of PONV by modifying the anesthetic technique to avoid inhalational anesthetics, nitrous oxide, opioids, and using propofol IV anesthesia, along with a combination of prophylactic anti-emetics as suggested above.

Multiple studies have described the use of TPV blocks along with propofol based TIVA (total IV anesthesia) to successfully avoid inhalational anesthetic based GA, reduce post-operative opioid requirement, length of stay, PONV and improve the quality of recovery. 25-29
In addition to TPV blocks, other regional anesthesia techniques for mastectomy include thoracic epidural and pectoral nerves (PECS) blocks. When compared with general anesthesia, thoracic epidural for mastectomy is associated with lower consumption of analgesics, less nausea and vomiting, and decreased hospital length of stay. A minimally invasive fascial plane block between the pectoral muscles (PECS I) and above the serratus anterior muscle at the 3rd rib (PECS II) have been described recently and are being used at some institutions in combination with GA. This technique blocks the pectoral nerves, intercostobrachial, intercostals and the long thoracic nerve. Addition of PECS blocks to GA for mastectomy have shown to reduce overall opioid consumption, PACU sedation scores, nausea and vomiting as well as length of stay. It has not been established whether these blocks can provide sufficient surgical anesthesia for mastectomy. Another newly described technique is called Serratus Plane Block which is an ultrasound guided block performed at the level of fifth rib in the mid-axillary line superficial to the serratus anterior muscle plane. It has been shown to provide anesthesia to the chest wall and breast. Case reports have suggested that this block in conjunction with PECS I block provides good post-operative analgesia and reduces perioperative opioid requirement.

A recent metaanalysis of randomized controlled trials comparing TPV to GA for breast surgery demonstrated a significant reduction of worst post-operative pain scores, post-operative opioid requirement, and PONV in the TPV group. Patients in the TPV group also showed lower incidence of chronic pain. It seems to be a safe block with a low incidence of adverse effects. The complications of TPV include Horner’s syndrome, hypotension (4%), pneumothorax (0.5%), accidental epidural or intrathecal spread (1%), and block failure (6%). There is a case report of a patient with severe hypoalbuminemia having a fatal arrhythmia from ropivacaine systemic toxicity 11 hours after the start of a TPV infusion.

A TPV block may offer advantages over a thoracic epidural. A unilateral TPV block may not cause the same degree of sympathectomy and hemodynamic instability as with a thoracic epidural and avoids the risks of dural puncture and spinal cord injury. A study comparing single injection TPV block to multiple level blocks showed a more reliable spread of radiocontrast and more effective clinical block with multiple level blocks. Single level injection may be appropriate in combination with GA for providing high quality post-operative analgesia, whereas multiple level injections may provide a reliable surgical anesthesia and avoid GA. A retrospective study of single level TPV block showed meaningful postoperative analgesia in the immediate postoperative period after mastectomy but not after the first day of surgery.

Local anesthetic delivery into the paravertebral space can be extended to multiple days by placing a continuous catheter at the T3 or T4 paravertebral space and running a low dose infusion of local anesthetic. This has shown reduce opioid requirements and pain related functional dysfunction for the
duration of infusion in a recent randomized triple blinded controlled study. While these benefits have been demonstrated, there should be a system in place to actively evaluate the ongoing safety of a continuous local anesthetic infusion and active monitoring of potentially critical side effects such as an epidural spread and pneumothorax from initial placement which can take hours to evolve. The most common local anesthetics used for TPV blocks include 0.5% bupivacaine with or without epinephrine or 0.5% ropivacaine. The doses described range from 15-20 ml for single level block or 5 ml per level for multiple injection blocks. For continuous infusion, the commonly used local anesthetics are 0.1 to 0.25% bupivacaine, or 0.2% ropivacaine up to 25 mg per hour. Injecting a high volume at one single space can increase the risk of epidural spread.

The most commonly used technique is landmark based, which involves needle placement at 2-2.5 cm lateral to midline, contacting the transverse process and advancing caudad to it, and piercing the costo-transverse ligament. This is the TPV space and local anesthetic is injected here. Enhancement of this technique includes using a loss-of-resistance technique and/or using a nerve stimulator. However, this is a narrow space and lies immediately posterior to the parietal pleura. The risk of pneumothorax is about 0.5% which can be critical if missed. Further, the number of needle passes to touch the transverse process can be uncomfortable to the patient. Ultrasound can be used as an aid to the landmark-based approach to estimate the depth and location of the transverse process. A live ultrasound guided in-plane or out-of-plane technique can be used to direct the needle to the TPV space immediately posterior to the pleura and to watch the displacement of the pleura anteriorly. This can potentially minimize the risk of pneumothorax. Since no single ultrasound guided technique is universally used, and the reported studies only have a small number of patients, it is too early to establish whether the use of ultrasound reduces the incidence of pneumothorax. The development of pneumothorax may depend on the thickness of the needle used, puncturing both the parietal and visceral pleura, and use of positive pressure ventilation during general anesthesia. Small pneumothorax may not be recognized and may resolve spontaneously without any intervention. Further, it may take several hours for a clinically significant pneumothorax to evolve after TPV block. It would make sense to actively monitor this patient for several hours with serial physical exams and continuous pulse oximetry. Avoiding positive pressure ventilation during GA may prevent the expansion of pneumothorax. The use of continuous ambulatory catheters has been evaluated by two randomized controlled studies with mixed results. One study did not show significant additional pain control benefit of continuous catheter; whereas the other study showed improved pain control for the duration of catheter, and with lower chronic pain scores and better functional recovery at one-year follow-up. As long as there are systems in place for regular follow-up and immediate access to care, an ambulatory TPV catheter can be an option.
References
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