Regional Anesthesia and Cancer Recurrence

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Disclosures

- None
Objectives

- Review various anesthetic techniques applied in oncologic surgery.
- Summarize and critically review current evidence regarding the potential effect of regional anesthesia on the outcome of cancer patients.
- Discuss future directions in regional anesthesia and cancer surgery.
Current Theory

- Surgery ➢ stress response ➢ immunosuppression
- Increased risk of metastasis and tumor recurrence?
- Perioperative factors likely associated with immunosuppression:
  - Surgical stress
  - Blood transfusion
  - Hypothermia
  - Postoperative pain
  - Anesthetics
  - Hypoxia
  - Hyperglycemia
  - Hypotension
Importance of Regional Anesthesia

- Protects CMI
- Anti-inflammatory
- Diminishes the surgical neuroendocrine stress response
- Decreases opioid and VA requirements
- Analgesia
Specific Techniques - Oncologic Surgery

- Opioids ➢ increased risk? Controversial.
- NSAIDs ➢ efficacious? Likley.
- Propofol ➢ efficacious? Promising evidence.
- Volatile anesthetics ➢ carcinogenic? Too premature.
## Current Literature - Retrospective

### Retrospective Analyses – Cancer Recurrence and RA for Cancer Surgery

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>RA</th>
<th>Positive Benefit</th>
<th>Potential Benefit</th>
<th>Negative Benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>Epidural, PVB</td>
<td>1</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Ovarian</td>
<td>Epidural</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Colon</td>
<td>Epidural</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Colorectal</td>
<td>Epidural</td>
<td>2</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Larynx or hypopharynx</td>
<td>Cervical epidural</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Gastric</td>
<td>Epidural</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Gastro-esophageal</td>
<td>Epidural</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Esophageal</td>
<td>Epidural</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Pancreatic</td>
<td>Epidural</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hepatocellular</td>
<td>Epidural</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Prostate</td>
<td>Epidural, Spinal</td>
<td>2</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Bladder</td>
<td>Epidural, Spinal</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>NSC Lung</td>
<td>Epidural</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Abdominal</td>
<td>Epidural</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Melanoma</td>
<td>LA, Spinal</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>
Recent PNB Study

- Retrospective analysis
- Combined spinal & obturator nerve block vs. spinal during TURBT
- Kaohsiung Journal of Medical Sciences (2017)
- N=96
- ONB = significantly >% complete resection (p=0.003)
- Non ONB = significantly higher postop recurrence rate (p=0.025)
# Current Literature – Meta-Analyses

## Meta-Analyses – Cancer Recurrence and RA for Cancer Surgery

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Anesthetic</th>
<th>Author</th>
<th>Number of Studies</th>
<th>Benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human CA</td>
<td>GA/EP vs. GA</td>
<td>Cakmakkaya et al. (2014)</td>
<td>4</td>
<td>Negative</td>
</tr>
<tr>
<td>Human CA</td>
<td>GA/EP vs. GA</td>
<td>Pei et al. (2014)</td>
<td>10</td>
<td>Decreased recurrence or metastasis prostate f/u &lt;= 2 yrs.</td>
</tr>
<tr>
<td>Human CA</td>
<td>GA/RA vs. GA</td>
<td>Sun, Li &amp; Gan (2015)</td>
<td>20</td>
<td>Potential benefit RA and OS. No reduction in recurrence.</td>
</tr>
<tr>
<td>Colorectal</td>
<td>GA/EP vs. GA</td>
<td>Sun, Yang, Li &amp; Ding (2015)</td>
<td>6</td>
<td>Improved OS with EP Decreased all-cause</td>
</tr>
<tr>
<td>Prostate</td>
<td>Neuraxial/GA vs. GA</td>
<td>Lee et al. (2015)</td>
<td>10</td>
<td>Potential benefit RA and OS.</td>
</tr>
<tr>
<td>Human CA</td>
<td>Neuraxial +/- GA vs. GA</td>
<td>Weng et al. (2016)</td>
<td>21</td>
<td>Potential benefit neuraxial, OS and RFS colorectal.</td>
</tr>
</tbody>
</table>
Heterogeneous Results

- Histological grading
- Radiation
- Chemotherapy
- Surgery grade
- Anemia
- Blood transfusion
- Hypothermia
- Anesthetic technique
Interpretation of Results

- Contradictory results of retrospective analyses and meta-analyses
- Unproven survival benefit of supplemental RA on OS and recurrence
- Limited evidence trending toward potential benefits
- Interpret with caution
Future Research

- **Regional Anesthesia/Analgesia**
  - 3 RCTs mainly organized by the Cleveland Clinic, USA
    - Vienna, Beijing, Germany, Dublin, Singapore
    - Buenos Aires, Germany
    - Shanghai
  - 1 RCT designed in Sweden
  - 1 RCT designed in Germany
  - 1 RCT designed in China

- **Propofol vs Volatile Anesthesia**
  - 1 RCT designed in Sweden
  - 1 RCT designed in the Republic of Korea
Breast CA (Cleveland Clinic)

- Can regional analgesia reduce the risk of recurrence after breast cancer?
- Multi-center RCT (n=1100)
- Started in 2007
- Stage I-III breast CA/Mastectomy or lumpectomy with axillary node
- EP or PVB/analgesia, or GA/morphine analgesia
- Up to 10 year follow-up
- Estimated completion date – March 2019
Colorectal CA (Cleveland Clinic)

- Multi-center RCT (n=2500)
- Started December 2007
- Compares recurrence rates
- GA/EP/analgesia or GA/opioid analgesia
- Up to 5 year f/u looking at local recurrence/metastatic cancer after open and laparoscopic resection of colon CA
- Estimated completion date – December 2022
Colorectal CA (Sweden)

- Multi-center RCT (n=300)
- Started March 2011
- Recording cancer-specific as well as all-cause mortality
- Inflammatory and immunological markers measured pre and post surgery
- GA/EP analgesia or GA/PCA
- F/u for up to 5 years
- Estimated completion date – December 2018
Lung CA (Cleveland Clinic)

- Multi-center RCT (n=1532)
- Started August 2010
- GA/EP compared with GA/opioid on cancer recurrence
- Primary outcome – DFS
- Secondary outcome – Immunological markers
- F/U for up to 5 years
- Estimated date of completion – August 2018
Malignant Melanoma (Germany)

- RCT (n=230)
- Patients undergoing radical inguinal lymph node dissection
- Started March 2012
- RA vs. GA – SA/bupivacaine, GA/sufentanil, PPF, roc, sevo
- Primary endpoint – OS up to 5 years
- Secondary endpoint – measurement of changes of the total number of immune cells at different time points perioperatively
- Estimated date of completion – March 2019
Unspecified Cancer Type (China)

- RCT (n=400)
- Examining the effects of regional nerve block on cancer recurrence
- Started July 2017
- Primary outcome – cancer recurrence and survival rates postop
- Secondary outcome – intraop anesthetic dose, nerve block effect on immunocytes and cytokines (0h, 24h, & 48h), VAS, activity, hospital stay
- F/u for up to 5 years
- Estimated completion date – **May 2023**
Breast, Colon or Colorectal CA (Sweden)

- Multicenter RCT (n=8000)
- Study for patients with breast or colorectal cancer after radical surgery
- Started in November 2013
- Comparing GA with or without additional RA PPF for maintenance vs. sevo anesthesia
- OS rates
- F/u up to 5 year (specifically 1- and 5-year survival rates)
- Estimated completion date – December 2022
Breast CA (Korea)

- RCT (n=200)
- Effects of PPF anesthesia and inhalational anesthesia on cancer cell cytotoxicity, micrometastasis, and cancer recurrence
- February 2014
- Primary outcome – number of NK cells 24 h postop
- Postulating that If immunosuppression of TIVA (PPF & remi) is lower than VA (sevo and remi), cancer recurrence may be decreased.
- Estimated completion date – **February 2015**
Recommendations

- Opioids – Insufficient evidence to suggest a change in practice.
- NSAIDs – Promising clinical data, but no formal recommendation.
- TIVA – May evolve as the better option with RA.
- Volatile anesthetics – Too early to say.
- Regional anesthesia...
“Although a definitive proof of cause and effect relationship between regional anesthesia and improved cancer outcomes must await the results of ongoing, long-term follow-up, prospective, randomized trials – the weight of experimental and observational clinical evidence suggests a signal that cannot be dismissed.”


References


