CLOSED LOOP ANESTHESIA SYSTEMS
THE FUTURE OF ANESTHESIOLOGY?

DISCLOSURES

• None!
OBJECTIVES:

• Overview of closed loop anesthesia delivery systems (CLADS)

• Update on current closed loop delivery system applications / research

OPEN LOOP VS CLOSED LOOP

• open loop control
  • user applies an input to the system
  • the system performs
  • output is generated
EXAMPLE: OPEN LOOP CONTROL

ANESTHESIA CLOSED LOOP
COMPLETE CLOSED LOOP DELIVERY

VENTILATION  HYPNOSIS  ANALGESIA

METABOLIC CONTROL  PATIENT  PARALYSIS
TEMPERATURE CONTROL  HEMODYNMIC CONTROL

WHY CLOSED LOOP DELIVERY?

• Ideally...
  • consistent
  • monitor and analyze more frequently
  • act based on live analyzed data +/- models
WHY CLOSED LOOP DELIVERY?

• Most ideally...
  
  • allow anesthesiologist to focus on higher-clinical tasks and decisions

RECAP:

• Anesthesiologists perform closed loop control on a day to day basis

• Closed loop anesthesia delivery systems (CLADS) goal:
  
  • decrease variation in anesthesia practice
  
  • constantly titrate anesthetics
  
  • allow the anesthesiologist to focus on higher clinical tasks
RECAP

- Closed Loop Systems employ a variety of control methods, allowing them to be:
  - reactive
  - predictive
  - adaptive
  - safe

TRANSITION INTO APPLICATIONS

- Timeline:
  - 1950’s (Mayo and Bickford)
    - EEG based automatic delivery of volatile anesthetics
  - 1980’s
    - end-tidal control of volatiles
    - closed loop control of neuromuscular blockers
    - MAP control
TRANSITION INTO APPLICATIONS

• Timeline:
  • 1989
    • Schwilden et al. published closed loop delivery of propofol guided by EEG - 11 healthy volunteers
  • mid 1990’s
    • BIS monitor introduced
    • several guided controlled maintenance of volatile anesthetics
    • one group applied closed loop control for maintenance of isoflurane titrated to BIS & delivered alfentanil to control mean arterial pressure (MAP)

• late 90’s and early 2000’s
  • PID control (proportional-integral-derivative)

\[ u(t) = K \left( e(t) + \frac{1}{T_i} \int_0^t e(s) ds + T_d \frac{de(t)}{dt} \right) \]
TRANSITION INTO APPLICATIONS

- late 90’s early 2000’s
  - Model predictive control
  - control tailored to a specific application, more complex than PID
  - allows for predictive future behaviour of the system
TRANSITION INTO APPLICATIONS

• 2000’s and Present
  • adaptive control
  • intelligent control (Artificial intelligence, fuzzy logic, expert systems, neural networks, genetic algorithms, reinforcement learning)
  • defy accurate mathematical description

APPLICATIONS

http://cdn.bleedingcool.net/wp-content/uploads/2012/04/medpod.jpg?f6a06b
APPLICATIONS

- Present:
  - Pharmacological Anesthesia Robot (Mcgill University)
    - nicknamed “McSleepy”
  - Closed Loop Fluid Administration in Resuscitation
    - In Vivo - application

PHARMACOLOGICAL ANESTHESIA ROBOT - AKA MCSLEEPY

- McSleepy:
  - able to deliver hypnotic (propofol), paralytic (rocuronium), analgesic (remifentany)
  - all three phases of anesthesia (induction, maintenance, emergence)
  - first used in 2008 for partial nephrectomy
  - June 2013 presented an journal submission where they described preliminary results with 15 patients
APPLICATIONS

2010: First robotic surgery via robotic delivered anesthesia.
http://assets.tdca.io/images/McCarry/DrVic_1stroboticsurgery.jpg
MCSLEEPY

- Why was McSleepy different?
  - Developed a new pain score (Analgoscore based on HR and BP)
  - Able to provide anesthesia for all three phases
  - Electronically charts (anesthesia and surgical)
  - GUI & Voice Prompts
  - Telemedical applications

MCSLEEPY - HYPNOSIS

- BIS monitor to titrate hypnosis
  - BIS averages used
    - average of 45 = target
    - average of 20 - 30 = minimal infusion
    - < 20 = stop
    - >60 = automatic bolus
MCSLEEPY - HYPNOSIS

- Safety protocols:
  - artifacts (electrocautery or muscle activity)
  - signal quality index (SQI)
  - BIS measurements valid only if:
    - SQI > 40%, EMG < 40 dB
  - If BIS measurement was lost or contaminated
    - administers propofol based on the mean value over the last 5 minutes
MCSLEEPY - ANALGESIA

• Analgoscore (AS) - was the variable titrated
  
  • ranges from -9 (very profound) to +9 (very superficial) analgesia
  
  • calculated every 2 seconds (HR was measured every 2s and the BP every 2 minutes)
  
  • \( Dose_{remi} = previousDose_{remi} \times K_r \times K_{sr} \)
  
  • \( K_r \) = coefficient proportional to last and present AS score
  
  • \( K_{sr} \) = coeffient based on the stage of surgery

MCSLEEPY - ANALGESIA

• Safety protocols:
  
  • MAP and HR can be affected by other factors
  
  • hypovolemia defined as: increase HR with no increase in MAP
  
  • vagal reactions defined as: decrease in HR with no decrease in MAP
  
  • when encountered: delivered preset minimal remi
**MCSLEEPY - ANALGESIA**

- Acquire MAP and HR
- Calculate Analgescore
- Initial dose
- AS constant for 2 iterations?
- Yes: Keep last infusion dose
- No: Correction factor: K_r depends on the AS slope
- Correction factor: K_r depends on the stage of surgery
- Check if corrected dose is between the minimum and maximum allowed doses
- Final dose
- Pump

**MCSLEEPY - PARALYSIS**

- Based on phonomyography
  - peripheral nerve stimulator, TOF adductor pollicis and corrugator supercili muscles
  - TOF measurement every 15 minutes
  - If TOF > 25 system would give the anesthesiologist the option of no bolus, bolus moderate, bolus profound
  - moderate = 0.15mg/kg, profound = 0.2mg/kg
安全协议：

- 如果 BIS > 60，则不能进行麻醉
- 不能在上一次给药后 5 分钟内进行给药
- 在手术结束前 20 分钟锁定（可以手动设置）
MCSLEEPY RESULTS:

- 15 patients: 3 F and 12 M
- Age: 57 +/- 13 years
- Weight: 79 +/- 16 kg
- Duration of anesthesia: 191 +/- 61 minutes
- Mean doses of drugs:
  - propofol: 129 +/- 23 ug/kg/min
  - remifentanil: 0.16 +/- 0.06 ug/kg/min
  - rocuronium: 1.5 +/- 0.48 mg/kg

MCSLEEPY RESULTS:

- Precision of the system assessed by Varvel’s performance indicies
  - widely used to assess performance of closed loop systems
  - Performance error (difference between real vs target values)
  - Median performance error (bias to describe direction of error)
  - Median absolute performance error (size of the error)
  - Wobble (intra individual variability of PE)
  - Divergence (evolution of the controllers performance through time)
LIMITATIONS:

- did not discuss time to set up or issues with the system
- did not address the application of long acting narcotics
- new pain score although validated in its application via Varvel’s performance indices; has never been used before

MCSLEEPY

- Why was McSleepy different?
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SHIFT TO FUTURE RESEARCH

Closed-Loop Fluid Administration Compared to Anesthesiologist Management for Hemodynamic Optimization and Resuscitation During Surgery: An In Vivo Study

• by Rinehart et al. published in November 2013 issue of Anesthesia and Analgesia

LEARNING INTRAVENOUS RESUSCITATOR (LIR) CLOSED LOOP SYSTEM

• Methods: 16 Yorkshire Pigs underwent 2 phase hemorrhage protocol and were resuscitated by either:
  1) Anesthesiologist
  2) Learning Intravenous Resuscitator (LIR)

• Compared median hemodynamic values and variation of hemodynamics between the two groups
LEARNING INTRAVENOUS RESUSCITATOR (LIR) CLOSED LOOP SYSTEM

- LIR goal: optimize hemodynamics based on goal direct fluid management
- application settings: to be used in the OR or in the ICU
- goal application: to support practitioners

LEARNING INTRAVENOUS RESUSCITATOR (LIR) CLOSED LOOP SYSTEM

- Methods:
  - Pigs were premeditated with ketamine and xylazine (anti-sialagogue)
  - induced with pentobarbital and fentanyl then intubated
  - maintained with isoflurane, fentanyl, rocuronium
  - mechanically ventilated
LEARNING INTRAVENOUS RESUSCITATOR (LIR) CLOSED LOOP SYSTEM

• Methods:
  • Monitored by:
    • HR, BP, SaO2, CVP, CO, SV, PPV, MVSaO2, UO, ABG
    • Right and Left femoral artery catheter (right used to induce hemorrhage)
    • Right IJ central line w/ Swan-Ganz pulmonary artery catheter w/ mixed venous sat
    • Suprapubic urinary catheter, real time UO

LEARNING INTRAVENOUS RESUSCITATOR (LIR) CLOSED LOOP SYSTEM

• How does the LIR algorithm work? 3 components
  • 1) Model Layer: PPV, CO, HR, MAP
  • 2) Model built from previous clinical trials
    • Predicts the increase in SV expected from a fluid bolus
  • 3) Adaptive layer tracks boluses given and patient responses to correct the model layer and any potential errors
• Strengths:

• no presuppositions about the patient undergoing management, no absolute targets for management (Can be applied to any system with a Frank Starling curve human or pig)

• Fluid agnostic (doesn’t matter what fluid you deliver)

LEARNING INTRAVENOUS RESUSCITATOR (LIR) CLOSED LOOP SYSTEM

• LIR Fluid protocol:

• would initial deliver colloid solution until a total of 33ml/kg achieved

• then alternated successive liters of crystalloid and colloid

• i-STAT (ABG) performed every 45 minutes

• whole blood administered for HGB < 70

• fluid administration facilitated by technician (no anesthesia training)

• no access to pressors
LEARNING INTRAVENOUS RESUSCITATOR (LIR) CLOSED LOOP SYSTEM

• Anesthesia providers:
  • told the patient was a healthy 18 year having open abdominal surgery
  • had access to crystalloid, colloid, whole blood
  • also had access to phenylephrine and ephedrine
  • if enquired, they were told whether or not the animal was bleeding
  • had access to i-STAT (ABG) at their discretion

LEARNING INTRAVENOUS RESUSCITATOR (LIR) CLOSED LOOP SYSTEM

• Constants:
  • Fluid administered via pumps (max flow of 2.4L/h)
  • monitors
  • maintenance fluid administration of 3ml/kg/hour of Ringers after induction
LEARNING INTRAVENOUS RESUSCITATOR (LIR) CLOSED LOOP SYSTEM

600CC OVER 30 MIN

1200CC OVER 30 MIN

Table 2. Summary of Baseline Values for Anesthesiologist Practitioner and Closed-Loop Fluid Management Groups

<table>
<thead>
<tr>
<th>Baseline hemodynamic variables</th>
<th>Anesthesiologist practitioner</th>
<th>Closed-loop</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BSA (m²)</td>
<td>1.60 [1.59–1.65]</td>
<td>1.61 [1.59–1.64]</td>
<td>0.94</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>94 [90–104]</td>
<td>86 [83–91]</td>
<td>0.10</td>
</tr>
<tr>
<td>Clₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑᵉ</td>
<td>33 [31–36]</td>
<td>36 [32–39]</td>
<td>0.34</td>
</tr>
<tr>
<td>SVIₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑᵉ</td>
<td>78 [76–100]</td>
<td>84 [78–96]</td>
<td>0.52</td>
</tr>
<tr>
<td>CVP (mm Hg)</td>
<td>15 [14–16]</td>
<td>13 [12–15]</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Data are reported as median [25%-75%].
BSA = body surface area; HR = heart rate; Clₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑᵉ = Swan-Ganz cardiac index; SVIₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑᵉ = Swan-Ganz stroke volume index; MAP = mean arterial pressure; CVP = central venous pressure.
LEARNING INTRAVENOUS RESUSCITATOR (LIR) CLOSED LOOP SYSTEM

**Results:**

- lower HR, better CI, SV, more optimal PPV values, and UO in the closed loop group
- no statistical difference between MAP and CVP
- no statistical difference in fluid administered
- anesthesia delivered a median of 2 boluses of phenylephrine and 0 boluses of ephedrine
LEARNING INTRAVENOUS RESUSCITATOR (LIR) CLOSED LOOP SYSTEM

• Conclusion:

  • under their conditions, the LIR could perform in-vivo resuscitation during mild and severe hemorrhage with reduced hemodynamic variability

  • GDFT has been shown to improve outcomes patients with shock

LEARNING INTRAVENOUS RESUSCITATOR (LIR) CLOSED LOOP SYSTEM

• Limitations:

  • LIR delivered more colloid which may have affected the results

  • there was no follow up of the pigs (ie. one group may have been more fluid overloaded at the end)

  • Anesthesiologist working in artificial environment
RECAP:

- McSleepy is a system that can provide anesthesia for induction, maintenance, emergence
- There exists a “smart” fluid administration closed loop system that bases its fluid on GDFT and real patient vitals

CLOSING STATEMENTS

- These systems are being pursued to act as “anesthesia co-pilots”
- Can have very useful applications in critical care and the OR
- Although we are far from having clinical applications in the next 5 years, the future is indeed exciting (or... extremely frightening if you hate computers)
QUESTIONS?

- Batman & Wonder Woman

REFERENCES:


- Various google images as referenced in order in the presentation
END