Episode 218: The REGAIN trial with Mark Neuman

On this episode: Dr. Jed Wolpaw With Dr. Mark Neuman

In this 218th episode I welcome Dr. Mark Neuman to the show. Dr. Neuman is the PI of the REGAIN trial, published in the NEJM which compared spinal and sedation vs. GA for hip surgery. We discuss the trial and the results.

Questions & Notes

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What are the 2 major options for anesthesia during hip fracture surgery?

What was Dr. Neuman's original hypothesis before the study?

What were some of the main outcomes measured?

What were the main takeaways from the results of the study?

Is there a difference between light or deep sedation and its effect on delirium?

What are Dr. Neuman's thoughts on spinal anesthesia without sedation?

What would Dr. Neuman change about the trial if he could go back?

What is up next after REGAIN? Will there be a REGAIN 2?

Was there anything that limited the trial in terms of funding?

Is it safe to say spinal and general anesthesia have equivalent outcomes for hip fracture surgery?

How did Dr. Neuman pick the study outcomes?

References

What are the 2 major options for anesthesia during hip fracture surgery?

14:30

1. Spinal anesthesia
    a. Single-shot spinal
2. General anesthesia
    a. Endotracheal tube or laryngeal mask airway

- Peripheral nerve blocks can be done before surgery (though uncommon in the U.S.).

What was Dr. Neuman's original hypothesis before the study?

15:10

- Hypothesized that spinal anesthesia during hip fracture surgery would have better main outcomes than general anesthesia.
- Retrospective data had seemed to show better outcomes (Neuman et al. 2012, Neuman et al. 2014), but these may have been confounded by selection bias.

What were some of the main outcomes measured?

17:13

- Primary outcome: composite of death or **inability to walk** approximately 10 ft (3 m) independently or with a walker or cane at 60 days after randomization.
- Secondary outcomes: death within 60 days, new inability to walk at 60 days, new- onset delirium, time from randomization to hospital discharge.
- Exploratory outcomes: medical complications during hospitalization,time to first ambulation, discharge disposition, residential location at 60 days, and functional status at 60 days.

What were the main takeaways from the results of the study?

17:30

- Although there were some slightly higher rates of in-hospital complications (AKI and post-op critical care admission) for general vs. spinal, **by 60 days there were no meaningful differences** by the primary and secondary outcomes measured.
- Surprisingly, there was **no significant difference in delirium, or time to discharge**.

Is there a difference between light or deep sedation and its effect on delirium?

21:37

- Study by Sieber et al. (2010) showed there was **no difference** between light or deep sedation and its effect on delirium during spinal anesthesia for hip fracture surgery.

What are Dr. Neuman's thoughts on spinal anesthesia without sedation?

23:25

- Having some sedation with spinal anesthesia has been the standard of care.
- Patients can be concerned with being completely unsedated in the operating room.
- But this is a theory that can be explored.

What would Dr. Neuman change about the trial if he could go back?

26:22

- 22,000 patients were screened to get to the study's 1600 patients. Many patients were not included due to baseline factors such as anticoagulation contraindicating spinal anesthesia, or some declining due to preference for which anesthesia they want. It would have been nice to have a separate registry study for patients that were eligible but did not enroll, to have information on the selection process into the trial and generalizability of results.
- Look more deeply into **high-risk subgroups**.
    - There was a non-significant difference between outcomes for patients with pulmonary disease and/or cardiac disease, but there was only a small number of these patients.
    - iHOPE study coming out that will pool more data looking into these subgroup analyses.

What is up next after REGAIN? Will there be a REGAIN 2?

28:46

- A follow up study to REGAIN is yet to be determined.
- Dr. Neuman's hope for REGAIN was to encourage anesthesiology to have bigger ambitious studies like this (especially ones that can include outcomes important to patients).
    - For example, Dr. Neuman is involved with an upcoming study, the THRIVE trial, comparing IV vs. inhaled anesthetics.

Was there anything that limited the trial in terms of funding?

30:35

- No, but looking into having the aforementioned separate registry and more subgroup analysis would have been nice.

Is it safe to say spinal and general anesthesia have equivalent outcomes for hip fracture surgery?

32:50

- It depends. If the patient is similar to those in the study, then Dr. Neuman would say they can choose which form of anesthesia they prefer, and will have similar outcomes.
- For someone with serious comorbidities or pathology unlike patients in the study, this trial may not apply to them.

How did Dr. Neuman pick the study outcomes?

34:45

- Before the study, they spoke with patients about what was important to them after hip fracture surgery.
    - **Recovery of walking** was the topic that came up over and over again.
- So not only did they want short-term outcomes, but also outcomes most meaningful for patients themselves.

References

REGAIN Primary Outcome Paper:

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REGAIN Protocol Paper, Methods, Lessons Learned:

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