

“Triple Low” – An Ominous Predictor

Prof Daniel Sessler
Cleveland Clinic
Ohio, USA

Introduction

Hypotension and prolonged periods of low Bispectral Index (BIS) values are independent risk factors for one-year postoperative mortality. Furthermore, end-tidal volatile anesthetic concentrations is lower in non-survivors than survivors.

These observations suggest that the combination of low MAP, low BIS, and low MAC may be especially deleterious. The association between adverse outcomes including mortality and periods of “Triple Low” has been evaluated.

Initial analysis evaluated the association between different combinations of MAP, BIS, and MAC on a full case basis . Subsequently the association between cumulative minutes of Triple Low, length-of-stay (LOS) and mortality was evaluated. And finally, the effects of early versus late vasopressor administration was considered.

Studies

All studies were conducted with Institutional Review Board approval and were based on an electronic medical-record-based registry of non-cardiac surgical patients. Patients younger than 16 years old, undergoing emergency procedures, and those with missing data were excluded.

Only the final procedure for each patient given volatile anesthesia without a concomitant propofol infusion was considered (n=23,999).

BIS, mean arterial pressure (MAP), and end-tidal volatile anesthetic concentrations in MAC-equivalents (MAC) were extracted from the perioperative registry. Pain scores, length of stay, serious complications, and 30-day and 1-year mortality were also extracted.

Values were defined as follows; Low MAC as <0.7 , Low BIS as < 45 and Low MAP as < 75 mmHg; the simultaneous occurrence of each defining a “Triple Low.”

Case-based analysis

A reference cell for BIS, MAP, and MAC values was defined. Cox proportional Hazard regressions were used to create prediction models for postoperative hospital length-of-stay, 30-day mortality, and one-year mortality by identifying significant predictors from MAC, MAP, BIS, demographic predictors (age, gender, race, BMI, ASA Physical Status). To compensate for multiple comparisons, $p < 0.005$ was considered statistically significant.

The average MAC, MAP, and BIS of the High, Reference, and Low groups were, respectively, MAC: 0.72, 0.57, 0.39; MAP: 96, 86, 78 mmHg; and BIS: 52, 45, 38. In-hospital mortality was 0.5%; 30-day mortality was 0.8%, 90-day mortality was 1.8%, and 1-year mortality was 4.8%.

The relative risk of mortality was significantly greater in patients who appear most sensitive to anesthesia as indicated by the combination of low MAC and low MAP; the risk of mortality was further increased in patients who also had low BIS. Patients given low MAC who maintained high MAP and BIS were likely to be discharged soonest

Time-based analysis

Duration of the Triple Low was related to various outcomes, including: complications, post-operative pain, length of stay, readmission, and 30-day and 1-year mortality. Equality of mean outcomes per time block were tested using ANOVA and Kruskal-Wallis as appropriate with $p < 0.05$ as significant.

11,143 (46%) of the 23,999 available non-cardiac procedures had at least one Triple Low episode. Data demonstrates statistically significant differences exist between groups for a wide range of variables including 30 day and 1 year mortality that becomes progressively worse with increasing duration of "triple low". Relative risk for 30 day and 1 year mortality is 0.54% & 4.02% respectively for 0-4 minutes of "triple low" and 1.66% & 6.98% \geq 20 minutes of "triple low".

One-year mortality increased substantially as BIS decreased and as MAP decreased; the increase was especially great when both BIS and MAP were low. Of note, high mortality was associated with values, such as a BIS of 40 and MAP of 65 mmHg, that are common during anesthesia and do not currently provoke much concern.

Vasopressor Administration

Patients were classified into 1 of 5 groups if or when they were given vasopressor (ephedrine or phenylephrine), including "early" (< 5 minutes before vasopressor administered) or "late" (> 5 minutes before vasopressor administered)

Among patients who had a Triple Low episode, the adjusted relative risk of mortality was: +28% in those never given vasopressor, +31% in those given vasopressor after at least 5 minutes in a Triple Low state, +12% in those given vasopressor within 5 minutes of entering a Triple Low state and lowest in patients given a vasopressor who never had a Triple Low.

Discussion

Patients who are sensitive to anesthesia do poorly. The combination of low MAC and low MAP was a strong and highly statistically significant predictor for mortality. When combined with low BIS, mortality was even greater. The combination of low MAC, low MAP, and low BIS is thus an ominous "Triple Low" which is associated with a tripled risk of mortality at 30 days, and doubled risk of mortality at one year. This result is especially concerning since the average low values for each state were well within the range that many anesthesiologists tolerate routinely.

Increasing duration at low MAP, low BIS and low anesthetic concentration worsened postoperative recovery (pain and complications), 30-day readmission, and postoperative mortality (30-day and 1-year).

No causal conclusions should be drawn from observational data, but these results suggest that earlier recognition of Triple Low states may allow adjustments in anesthetic management that could improve outcomes.

Among patients who experienced a Triple Low and were rapidly treated with vasopressor, mortality only slightly (12%) exceeded the reference patients who never experienced an event. Early vasopressor intervention thus appears to largely ameliorate the mortality increase that is otherwise associated with delayed vasopressor treatment or with failure to intervene.

While observational, these results suggest that Triple Low states may not only be a predictor of adverse outcomes, but might be amenable to intervention.

Reference:

Saager L, Greenwald SD, Kelley SD, Schubert A, **Sessler DI**. Duration of a "Triple Low" of Blood Pressure, BIS & Anesthetic Concentration Predicts Poor Outcomes. *Anesthesiology* 2009; 111: A880.

Disclosure Statement:

Some of the co-authors of this paper are employees of Aspect Medical, Inc, which also provided financial support for the work.