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Time to achievement of mean arterial pressure goal in patients with septic shock based on initial norepinephrine dose

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**BACKGROUND**

- Septic shock continues to be associated with high mortality rates, even with early goal-directed therapy.\(^1,2\)
- Norepinephrine is the first-line vasopressor for management of septic shock.\(^3\)
- A mean arterial pressure (MAP) of 60 mmHg is the recommended MAP target.\(^3\)
- Data regarding initial norepinephrine dose and time to achievement of goal MAP is lacking.\(^4\)
- Initial norepinephrine doses at our institution are currently free text entry.
- Recent evidence shows improved shock control rates by 6 hours and improved mortality when norepinephrine is started early (within the first six hours) compared to delayed initiation.\(^5\)

**OBJECTIVE**

- Evaluate whether the initial norepinephrine dose in septic shock patients is associated with the time to achievement of MAP goal.

**METHODS**

- Retrospective chart review of patients aged 18 years or older who were admitted to the Intensive Care Unit (ICU) with septic shock and had an active order for norepinephrine.
- Data collected on patients admitted from 7/2018 through 7/2019.
- **Primary outcome:**
  - Time to achievement of MAP goal of 65 mmHg for at least 4 hours without the need for therapy escalation
  - Therapy escalation defined as:
    - Norepinephrine dose increase
    - Addition of or dose increase of additional vasopressor agent(s)
- **Secondary outcomes:**
  - Norepinephrine dose at achievement of MAP goal
  - ICU mortality
  - ICU length of stay
  - Number of vasopressor agents used
  - Safety endpoints:
    - New onset atrial fibrillation
    - Bowel ischemia

**RESULTS**

- **Baseline Characteristics:**
  - Initial norepinephrine dose, mcg/min, median (IQR)
  - Initial norepinephrine dose, mcg/kg/min, median (IQR)
  - Age, y, median (IQR)
  - Weight, kg, median (IQR)
  - SOFA score, median (IQR)
  - Initial MAP, mmHg, median (IQR)
  - Home antihypertensive use
  - Serum creatinine, mg/dL, median (IQR)
  - Mechanical ventilation
  - Drug dose at start
  - Time from hospital arrival to norepinephrine administration, hours, median (IQR)
  - Fluid volume ordered prior to norepinephrine administration, ml/kg, median (IQR)

- **Primary Outcome:**
  - Time to achievement of MAP goal for at Least 4 Hours Without Escalation of Therapy

- **Secondary Outcomes:**
  - Norepinephrine dose at achievement of MAP goal, mcg/min, median (IQR)
  - ICU mortality
  - Total number of vasopressor used, median (IQR)
  - New onset atrial fibrillation
  - Bowel ischemia

- **DISCUSSION**

  **Discussion and Clinical Impact:**
  - There was no difference in the time to achievement of MAP goal for at least 4 hours without therapy escalation.
  - Previous studies report a time to achievement of MAP goal of 1.5 to 6 hours.\(^6\)
  - Time to achievement of MAP goal was around 10 hours in this study.
  - This difference is likely due to the requirement that MAP goal must be achieved and sustained over 4 hours in our study.
  - The median initial norepinephrine dose was 5 mcg/min (0.063 mcg/kg/min), comparable to doses used in prior studies.\(^7,8\)
  - The low dose group had a greater percentage of male patients and had higher SOFA scores, correlating with a 20-40% mortality rate.
  - This is due to the use of non-weight based dosing at our institution.
  - SOFA scores were comparable between groups, correlating with a 20-40% mortality rate.
  - The observed ICU mortality rates were lower than expected; however, these do not take into account non-ICU mortality.
  - Adverse effects were uncommon which may have been a result of use of diagnosis codes for reporting.

  **Limitations:**
  - Retrospective design limits ability to assess hemodynamic stability.
  - Initial dose at our institution is free text and the majority of patients were started on 5 mcg/min.
  - The dose difference between groups was small.
  - Microbiologic culture reports and antimicrobial coverage were not investigated.
  - Many patients were excluded for having an initial MAP < 65 mmHg.
  - MAP documentation was based on cuff pressures, not arterial line pressures.

**CONCLUSIONS**

- The optimal initial norepinephrine dose remains undefined and practice varies.
- The initial norepinephrine dose may impact the time to achievement of MAP goal, and higher initial doses of norepinephrine may be needed in order to achieve MAP goal sooner.
- Future studies with larger sample sizes are needed to incorporate additional variables, such as appropriate antimicrobial coverage, which may play a role in the time to achievement of MAP goal.
- Implementing standardized initial norepinephrine doses may assist in determining whether higher initial doses impact the time to MAP goal.

**REFERENCES**