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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 65 mmHg is the recommended MAP target.[3]
- Data regarding initial norepinephrine dose and time to achievement of goal MAP are lacking.
- 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.[4,5]

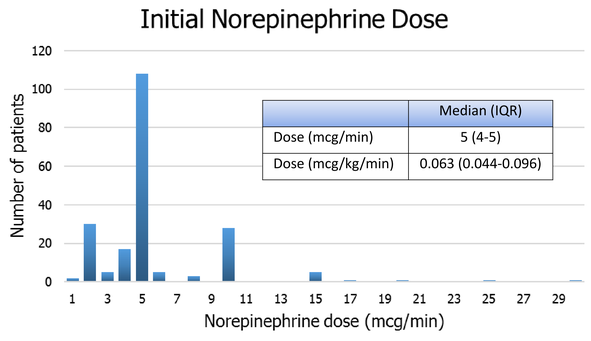
OBJECTIVE

- 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
  - Total number of vasopressor agents used
  - Safety endpoints
    - New onset atrial fibrillation
    - Bowel ischemia

RESULTS



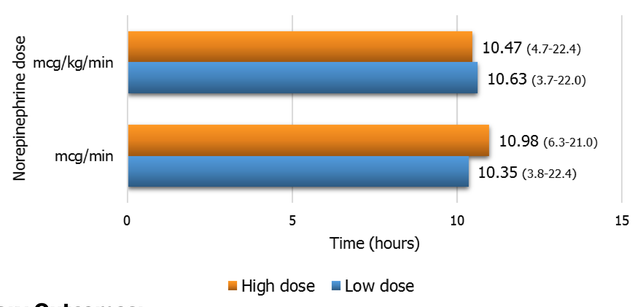
RESULTS

Baseline Characteristics:

	Low dose (≤0.063 mcg/kg/min) n=105	High dose (>0.063 mcg/kg/min) n=102
Initial norepinephrine dose, mcg/min, median (IQR)	5 (2-5)	5 (5-10)
Initial norepinephrine dose, mcg/kg/min, median (IQR)	0.044 (0.026-0.054)	0.097 (0.074-0.128)
Age, yrs, median (IQR)	63 (52.0-72.0)	66 (53.3-75.8)
Sex (male)	64.8%	49.0%
Weight, kg, median (IRQ)	95.0 (83.6-112.3)	67.3 (55.5-74.8)
SOFA score, median (IQR)	9 (8-11)	9 (8-12)
Initial MAP, mmHg, median (IQR)	56 (51-61)	54 (49-59)
Home antihypertensive use	43.8%	40.2%
Serum creatinine, mg/dL, median (IQR)	1.6 (1.1-2.9)	1.3 (0.9-2.7)
Mechanically ventilated	8.6%	9.8%
Stress dose steroid use	22.9%	24.5%
Time from hospital arrival to norepinephrine administration, hours, median (IQR)	11.3 (4.3-26.0)	8.5 (3.8-30.2)
Fluid volume ordered prior to norepinephrine administration, mL/kg, median (IQR)	32.0 (18.0-57.4)	46.0 (28.4-79.4)

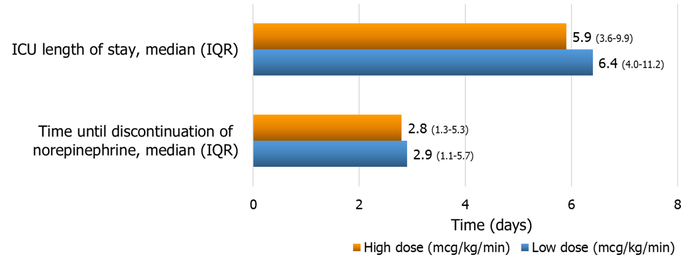
Primary Outcome:

Time to Achievement of MAP Goal for at Least 4 Hours Without Escalation of Therapy



Secondary Outcomes:

	Low dose (≤0.063 mcg/kg/min) n=105	High dose (>0.063 mcg/kg/min) n=102
Norepinephrine dose at achievement of MAP goal, mcg/min, median (IQR)	5 (3-7)	7 (5-10)
ICU mortality	12.4%	17.6%
Total number of vasopressors used, median (IQR)	1 (1-2)	1 (1-2)
New onset atrial fibrillation	4.8%	2.9%
Bowel ischemia	0%	0%



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.[4,5]
  - 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.[4,6,7]
- The low dose group had a greater percentage of male patients and had higher body weights.
  - 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.

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Disclosure

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