



Real World Experiences with Angiotensin II in Refractory Shock

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BACKGROUND

- Refractory shock is characterized by an inadequate response to conventional catecholamine vasopressors and is associated with increased mortality
- Norepinephrine is considered the first line agent, most notably in distributive shock, followed by vasopressin as the leading second line agent
- A novel agent, Giapreza™ (Angiotensin II, ATII), was FDA approved in 2017 for refractory shock based on findings in the ATHOS-3 trial
- Safety and efficacy data from a pragmatic setting are lacking
- This study describes two institution's real-world experiences with ATII, including prescribing information and patient outcomes

OUTCOMES

Primary

- Characterize when, how, and in what patients ATII was prescribed

Secondary

- Hemodynamic Response
- Incidence of venous thromboembolism (VTE)
- Inpatient mortality
- Drug Expenditure

STUDY DESIGN

- **Design:** IRB-approved, retrospective cohort study
- **Time Frame:** June 2018 to January 2019
- **Setting:** Northeast Georgia (NEGA) Health System
- **Inclusion Criteria:**
 - Adult Patients
 - Admitted to either of two NEGA facilities
 - Received ATII
 - Vasopressors for longer than 3 hours
- **Identification of Patients:** Pharmacy dispensing records
- **Administration Confirmation:** Via chart review

RESULTS

Table 1. Patient Characteristics

Variable	n=34*
Age	68 (57 – 72)
Male Gender	14 (41)
Weight	103 (87 – 113)
Home ACEI/ARB	9 (26)
Distributive Shock	26 (76)
Indication for Vasopressors	
Septic shock	22 (65)
Cardiogenic shock	4 (12)
Combined septic and cardiogenic shock	3 (9)
Vasoplegia	3 (9)
Hypovolemic shock	1 (3)
Vasodilatory shock	1 (3)
Number of Vasopressors	3 (2 – 3)
APACHE IV Score	109

*Values Presented as Median (Interquartile Range) or Number (Percent)
*ACEI – Angiotensin Converting Enzyme Inhibitor; ARB – Angiotensin Receptor Blocker;

Table 2. Angiotensin II Administration

Variable	n=34*
Ordering Location of Angiotensin II	
Critical Care Unit	11 (32)
Cardiovascular Intensive Care Unit	6 (18)
Medical intensive care unit	6 (18)
Surgery/Trauma Intensive Care Unit	6 (18)
Operating Room	3 (9)
Intensive Care Unit	2 (6)
Ordering Service of Angiotensin II	
Critical Care	26 (76)
CT Surgery	3 (9)
Anesthesia	2 (6)
Trauma	2 (6)
Heart Failure	1 (1)
Initial Angiotensin II Dose (ng/kg/min)	10 (10 – 10)
Maximum Angiotensin II Dose (ng/kg/min)	55 (40 – 80)
Appropriate Angiotensin II Dose Titration	21 (62)
Number of Vials of Angiotensin II	2 (1 – 6)
Cost of Angiotensin II (\$)	3000 (1500 – 9000)

*MAP – Mean Arterial Pressure

RESULTS CONTINUED

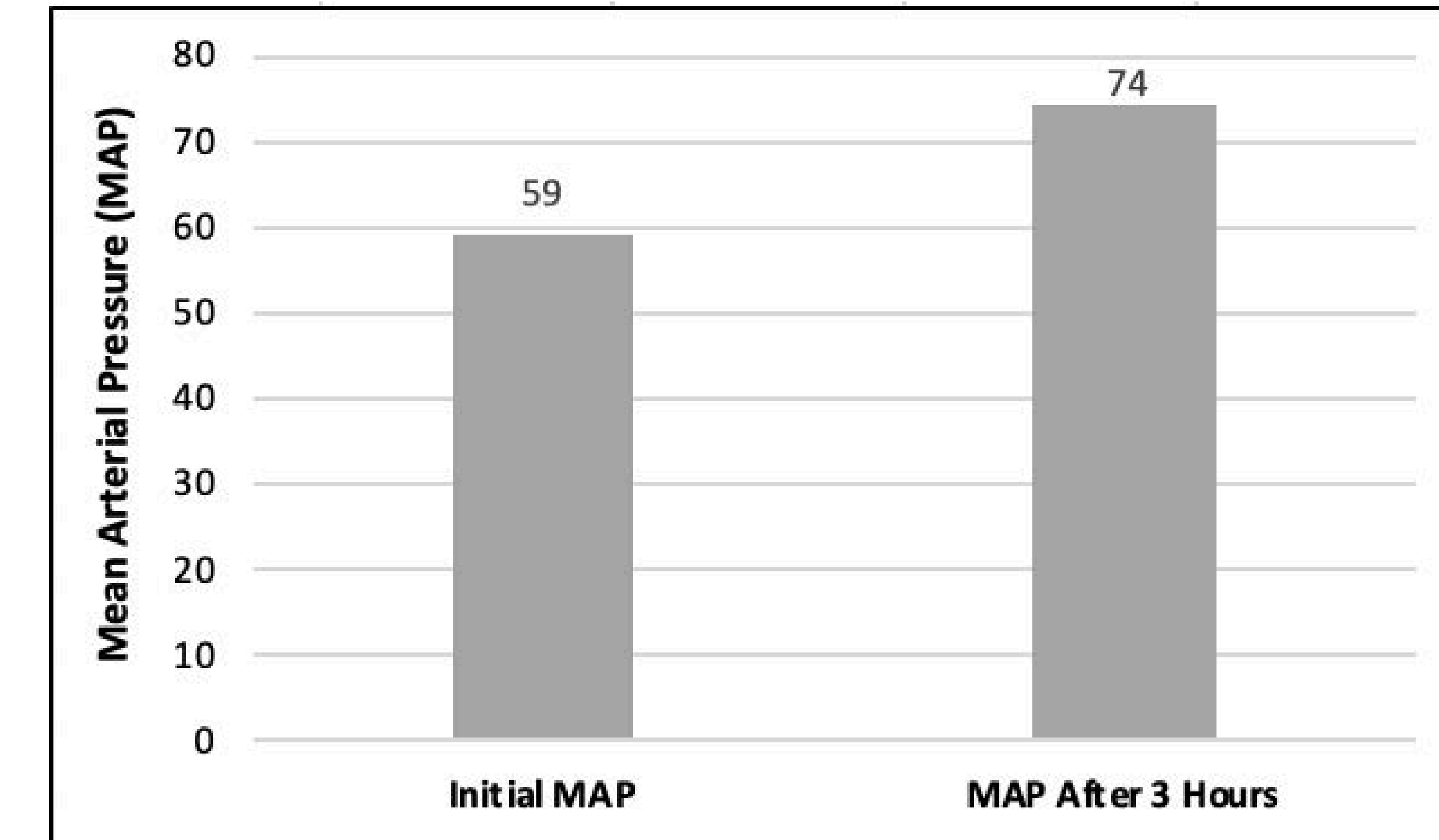


Table 3. Hemodynamic Response and Outcomes

Variable	n=34*
Median Change in MAP (mmHg)	15 (0-51)
Number of Vials of Angiotensin II	2 (1 – 6)
Cost of Angiotensin II (\$)	3000 (1500 – 9000)
Time to Reach MAP ≥ 65 mmHg (min)	16 (7 – 54)
Mortality	15 (44)
Venous Thromboembolism Prophylaxis	27 (79)
Venous Thromboembolism	3 (9)

*MAP – mean arterial pressure

Table 4. Drug Price Comparison

Drug	Average Wholesale Price	
	Amount	Price
Norepinephrine	1mg vial	\$2.63
Vasopressin	20 unit vial	\$215.75
Angiotensin II	2.5mg vial	\$1800

CONCLUSIONS

- The study observed a positive hemodynamic response to ATII and a lower mortality rate in refractory states
- Future research should compare the safety and efficacy of ATII to other second-line vasoactive agents (e.g., Vasopressin)
- Limitations:
 - Small sample size
 - Retrospective design
 - Lack of control group
- Advantages:
 - Largest case series of ATII to date
 - Only one to include mixed shock states

REFERENCES

- Giapreza [package insert]. San Diego, CA: La Jolla Pharmaceuticals; 2017.
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