Updates in Hospital Medicine: 2022

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Updates in Hospital Medicine 2022

No Conflicts of Interest

Updates in Hospital Medicine 2022

Objectives

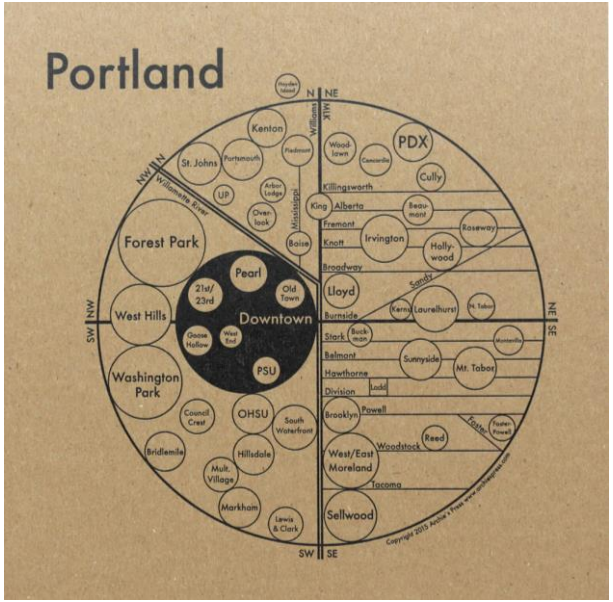
- Review and evaluate recent impactful literature in the practice of Hospital Medicine.
- Specifically, evidence-based medicine for the decisions we make when things go wrong.
- Develop a plan for how this data may: confirm, inform, or perhaps change your practice.
- Save you some time and keep you entertained.

Updates in Hospital Medicine 2022

Road Map

- New literature from 2021-2022
- No COVID-19 studies
- High level review
  - Case based approach

- Articles selected based on likelihood to:
  - ✓Change practice
  - ✓Inform/Modify practice
  - ✓Confirm practice



Case 1: The Inpatient with Acute Hypertension

A 52yo was admitted 72hrs ago for management of diabetic toe ulcer. Patient is not septic; antibiotics are on hold pending surgical debridement in the AM the following day. You are paged at 2300 that, “FYI patient’s BP 195/110, on past three checks. Asymptomatic.” They are not currently on any antihypertensive medications.

Do you:

A) Delete the page and “continue to monitor.”

B) Give hydralazine IV 10mg x1.

C) Start a PO antihypertensive medication and titrate as needed.

D) Write a complex, comprehensive order set for IV and PO medications based on multiple BP ranges and mic drop.

Treatment Outcomes of Inpatient Hypertension

Severe inpatient hypertension prevalence and blood pressure response to antihypertensive treatment

Multi-hospital retrospective observational cohort study of adults admitted for reasons other than HTN, who developed severe HTN as an inpatient. One of the largest studies to date.

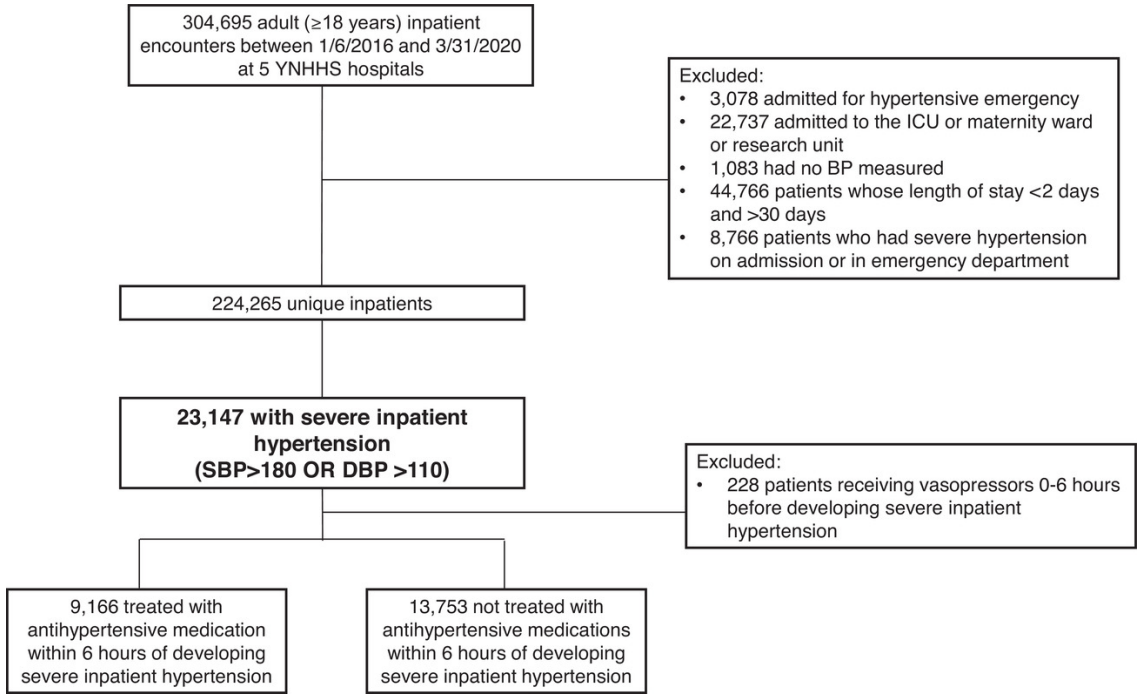
- Severe HTN defined as 2 consecutive measurements >180/>110 within 3 hours, at least 1 hour after admission.
  - Treatment defined as receiving antihypertensives within 6h of BP elevation.
  - Longitudinal data sets from EHRs from 5 separate hospitals.
  - Patients limited to LOS 2-30 days.

  - Outcome: Primary outcome was time to MAP drop >30% within 6 hours of onset of HTN.

Ghazi et al JCH Feb 2022

Treatment Outcomes of Inpatient Hypertension

Study Design



Ghazi et al JCH Feb 2022

- Antihypertensive interventions studied included PO and IV formulations:
  - ACEi/ARB
  - CCBs
  - Beta blockers
  - Diuretics
  - Renin inhibitors
  - Vasodilators (ie hydralazine)
- Treatment defined as a *new* medication.

Treatment Outcomes of Inpatient Hypertension

Results

- Model 1: unadjusted data.

- Model 2: adjusted for age, sex, race, ethnicity, ward, **confounding comorbidities**, baseline labs, NSAID/steroid/crystalloid/narcotic use within 6 hours of HTN episode.

- Model 3: same as model 2 but **All comorbidities.**

MAP drop >30% Hazard ratio (95% CI)	Model 1 (unadjusted)	Model 2 (Confounding comorbidities)	Model 3 (Fully adjusted)
Treated vs untreated	0.86 (0.80-0.94)	0.89 (0.82-0.96)	0.89 (0.80-0.99)
Treated with oral only	0.59 (0.53-0.66)	0.61 (0.54-0.68)	0.69 (0.61-0.79)
Treated with IV only	1.49 (1.33-1.68)	1.49 (1.32-1.68)	1.38 (1.15-1.67)
Treated with IV vs oral	2.57 (2.22-2.98)	2.48 (2.13-2.91)	2.06 (1.65-2.57)

Treatment Outcomes of Inpatient Hypertension

Discussion

- MAP drop >30% within 6 hours of severe inpatient HTN was observed in both untreated and treated patients.
- Treatment with PO medications was associated with lower rates of MAP drop >30%.
  - ➢ Thought likely secondary to pharmacological modulation of sympathetic baroresponse, limiting reflexive drops.
- In contrast, treatment with IV medications had a 38% higher rate of MAP drop >30%.
- MAP drop >30% was also significantly higher among patients treated with IV vs PO.

Treatment Outcomes of Inpatient Hypertension

Caveats

- No data on how BP was measured, what the patient was doing or how they were acting (ie in pain, delirious, agitated).
- Study assessed the effect of treatment irrespective of treatment indication, dose, and whether antihypertensive was a home medication.
- Clinical decision-making reasons for treatment or no treatment were not captured.

Take aways

- Treatment with PO antihypertensive agents might be safer than no treatment at all.
- IV treatment has significant risk of MAP drop >30%.
- Confirms and supports multiple other multicenter studies showing risk of harm and real harm from IV BP treatment.
- **Change my practice: severe inpatient HTN is best treated with PO medications, IV best avoided. PO antihypertensives may prevent unsafe swings in BP by better modulating autonomic reflexes.**

Case 2: The Patient with Frequent Falls

A 78yo with multiple chronic medical issues and dementia has been admitted for three days for syncope workup after a fall getting out of bed at home. You are paged at 1030, “FYI patient fell. Please come assess.” This is their third fall since admission. Workup so far suggests issues with poor sympathetic tone due to age and debility.

What do you do to prevent another fall:

A) Order a 1:1 sitter and/or place in a Posey bed.

B) Start Midodrine to improve adrenergic tone.

C) Give an IV fluid bolus.

D) Reinforce the use of bed alarms,
and ask the RNs to increase night-time checks to q2hrs.

Midodrine to Prevent Falls

Midodrine for Prevention of Vasovagal Syncope

- In 2010 Midodrine was FDA approved for the treatment of orthostatic hypotension. Now, novel research is being done into its use for vasovagal/neurocardiogenic syncope.

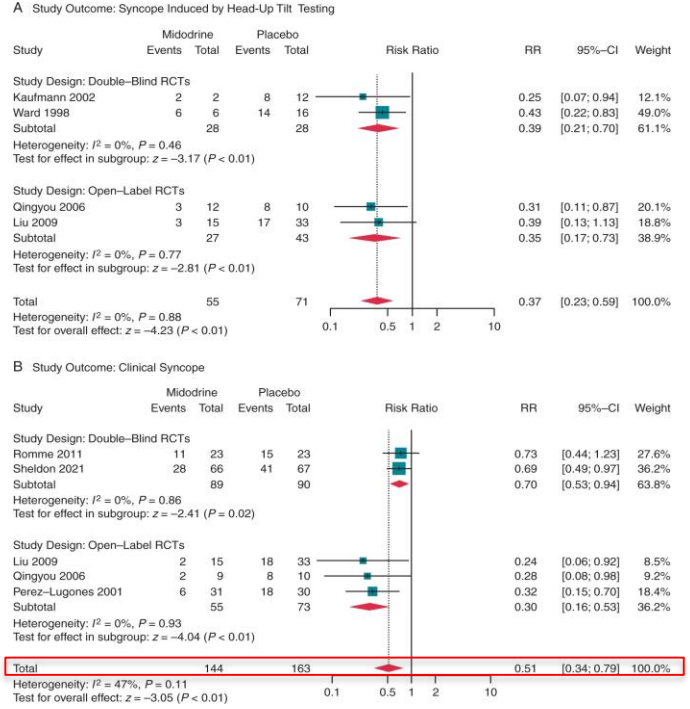
- 1:1 double blind placebo-controlled study following syncope rates for Midodrine vs placebo for 12 months.
  - Syncope rates were 42% in the Midodrine group vs 61% in the placebo group.
  - Relative risk 0.69 (CI 0.49–0.97 *P=0.035*). Absolute risk reduction was 19% (CI 2-36%).
  - Number needed to treat to prevent 1 patient from having syncope was 5.3 (CI, 2.8-47.6).

- Results also supported by recent systematic review and meta-analysis (Lei et al Europace 2022).

Sheldon et al Ann IM Oct 2021;

Midodrine to Prevent Falls

Midodrine prevents syncope induced by heads up tilt testing



Lei et al Europace July 2022

Midodrine to Prevent Falls

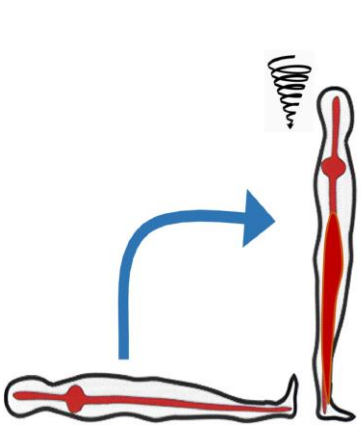
<u>Management of Orthostatic Hypotension in the Hospitalized Patient</u>

- Describes an inpatient management plan based on literature review and clinical pharmacology.

- Most falls that are not strictly mechanical are caused by similar physiology to orthostatic hypotension and/or vasovagal syncope.

+ Remove factors contributing to orthostasis, avoid bed rest, postprandial hypotension, utilize Midodrine and other PO pressor agents 30-60 minutes before activity.

Wahba et al AJM jan 2022



Gravitational venous pooling
500 – 1000 mL
splanchnic circulation >> lower limbs

- Abdominal binder
- Compression Stockings
- Leg muscle pump

↓ Venous Return
↓ Cardiac Output

Baroreflex Response:
↑ Sympathetic tone
↓ Parasympathetic tone

- Norepinephrine "enhancers"
- Pyridostigmine
- Atomoxetine

Cardiac output recovery
Vasoconstriction
Restoration of blood pressure

- Norepinephrine "replacers"
- Midodrine
- Droxidopa

Modern Uses of Midodrine in the Hospital

<u>Take aways</u>

- Strong evidence shows Midodrine is a safe and effective treatment for both orthostatic and vasovagal/neurocardiogenic types of syncope.

- Patients at high risk of falls due to low adrenergic tone (age, LoS, deconditioning, chronic illnesses, dementia/delirium, etc.) can benefit significantly from Midodrine.

- Change my practice:

- Midodrine can be used as primary treatment for patients who present with, and/or suffer from, vasovagal syncopal episodes.

- Midodrine can be used as part of a multimodal treatment to prevent falls in these patient populations in the hospital.

Case 3: The *Really* Hypotensive Patient

A 60yo patient is admitted for management of multifocal pneumonia. You are paged at 1600 that patient's BPs are 70/30 x2 and they are lethargic. At bedside, 3 IV fluid boluses do not improve their BP. They have a 20g PIV in their R forearm. ICU fellow on-call is contacted but they state, "we have no beds."

Do you:

A) Bolus 2 more liters.

B) Start levophed through the 20g PIV.

C) Contact the ICU Attending and demand a bed.

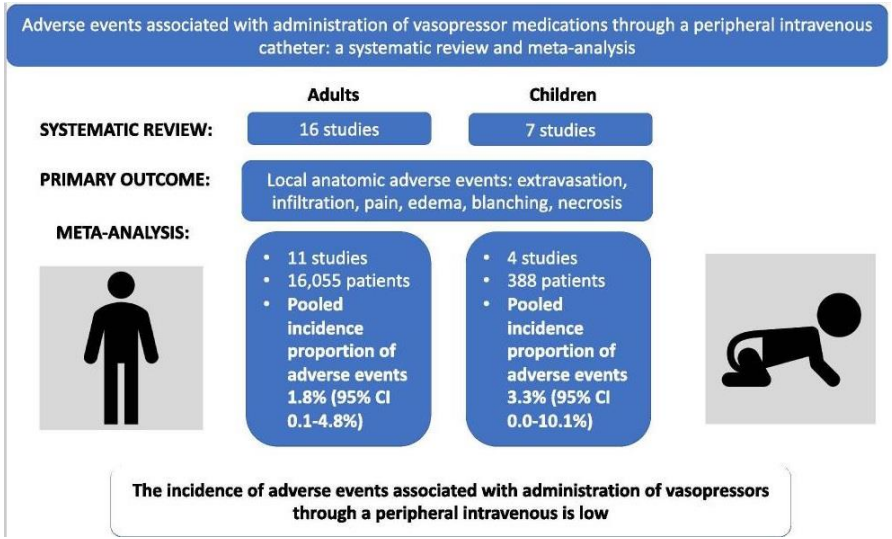
D) Hold off on any further treatments until a central line is placed.

Initiating Vasopressors through a Peripheral IV

Adverse events associated with administration of vasopressor medications through a peripheral IV (PIV)

- A systematic review and meta-analysis.
- Studies included were cohort, quasi-experimental, or randomized controlled trial study designs.

- Last major systematic meta-analysis was in 2015 (predominately case reports) did show significant rates of skin necrosis up to 40%!
- Since 2015, several single center retrospective and prospective studies have shown PIV vasopressor use to be safe.



Owen et al Crit Care Apr 2021 *Cardenas-Garcia et al J Hosp med 2015; Datar J IC Med 2018; Pancaro Anesth 2020*

Initiating Vasopressors through a Peripheral IV

Patient, route, and vasopressor characteristics

- Adult age ranged from 36-81 years, 53% male.
- 88% of PIVs were 16-20g with 61% being 20g. 64% in forearm, 27% in hand or wrist.
- Vasopressin was most used (15,584 cases in 9 studies), followed by phenylephrine, epinephrine, and dopamine (151 cases in 6 studies).
- Average PIV vasopressor infusion duration was 12-24 hours in most studies.

Adverse events included

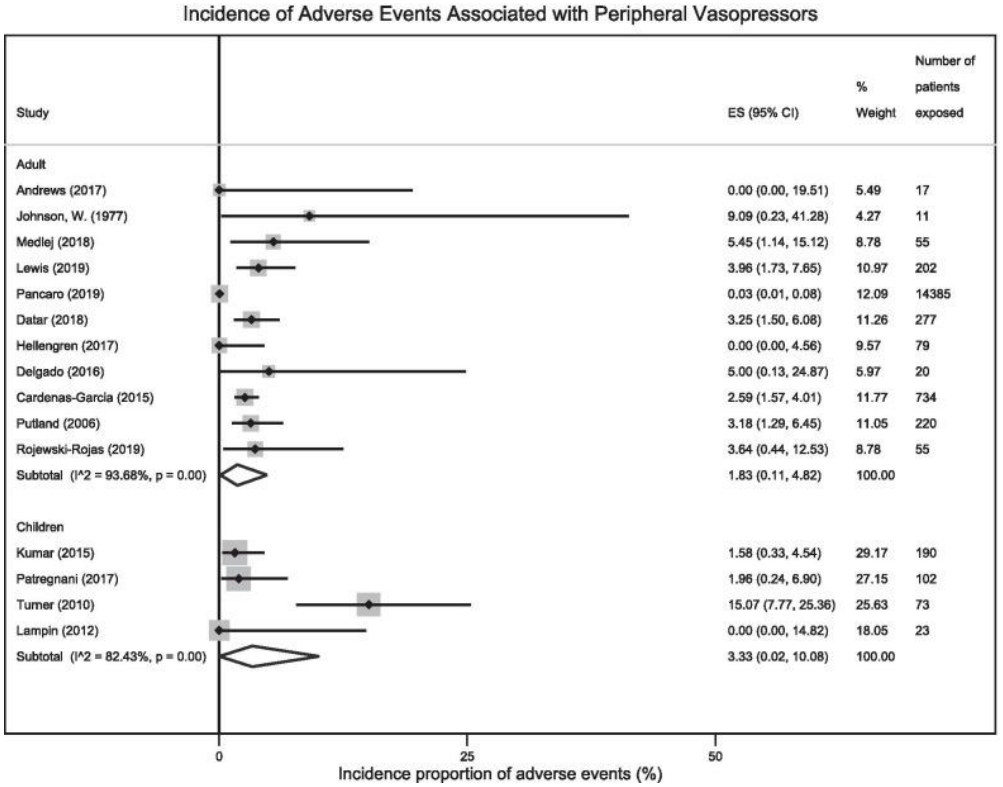
- Mild events included infiltration or extravasation leading to mild tissue reactions (edema, erythema, discomfort).
- Moderate events included cutaneous discoloration (can be long term complication).
- Severe events included thrombophlebitis, slough, and ischemia with skin necrosis.

Owen et al Crit Care Apr 2021

Initiating Vasopressors through a Peripheral IV

Incidence of adverse events

- Meta-analysis of pooled data showed adverse rate of 1.8% (95% CI 0.1-4.8%).
- Vast majority were mild requiring no treatment.
- No statistically significant differences in subgroup analysis of heterogeneity (ie ICU vs Wards, anatomic site of infusion, pressor type, IV size).
- Limitations in published data did not allow for subgroup examination based on pressor dose.



Initiating Vasopressors through a Peripheral IV

Subgroup analysis (adults)

Subgroup	Number of patients	Pooled incidence of adverse events	Test of heterogeneity between groups
Short stay unit	14,732	1.47%(0.00-6.4%)	p=0.75
ICU/Stepdown	1,323	1.85%(0.67-3.42%)	
Less than 24hrs	15,255	1.57%(0.37-3.11%)	P=0.73
Greater or equal 24hrs	800	1.50%(0.37-3.11%)	
16-20g PIV	1051	2.04%(1.04-3.27%)	P=0.31
22g or smaller PIV	105	8.50%(0.00-90.63%)	
Hand	101	3.05%(0.21-7.92%)	P=0.42
Arm/forearm	307	1.19%(0.00-5.13%)	

Initiating Vasopressors through a Peripheral IV

Caveats

- Difficult to make clinical recommendations without direct comparison to CVCs.
    - Imagine a head-to-head comparison of adverse event rate study between PIV vs CVC.
- Most included studies were single-center, retrospective cohort studies, at risk of bias.
- Significant interstudy heterogeneity. Caused mostly by clinical factors.

Take aways

- This is the largest study in adults to date and reflects the true state of current literature.
- CVCs carry their own risk of adverse outcomes, many often worse than those of PIVs (ie pneumothorax, infection, etc).
- **Change my practice: Do not wait for CVC or an ICU bed to begin vasopressors in a hypotensive patient. (Cautious with 22g PIV and/or hand placement).**

Case 4: The Pancreatitis Patient

An 50yo patient is admitted with severe abdominal pain and anorexia due to acute edematous pancreatitis. In addition to standard IV pain medications and clear liquid diet as tolerated, you are trying to decide on an IV fluid resuscitation rate. Your nocturnist is tired of getting paged about acute pulmonary edema in all your patients on IV fluid.

Do you:

A) Follow the standard aggressive IV hydration protocol.

B) Use a more modest IV hydration approach.

Fluid Resuscitation in Acute Pancreatitis

Aggressive or Moderate Fluid Resuscitation in Acute Pancreatitis

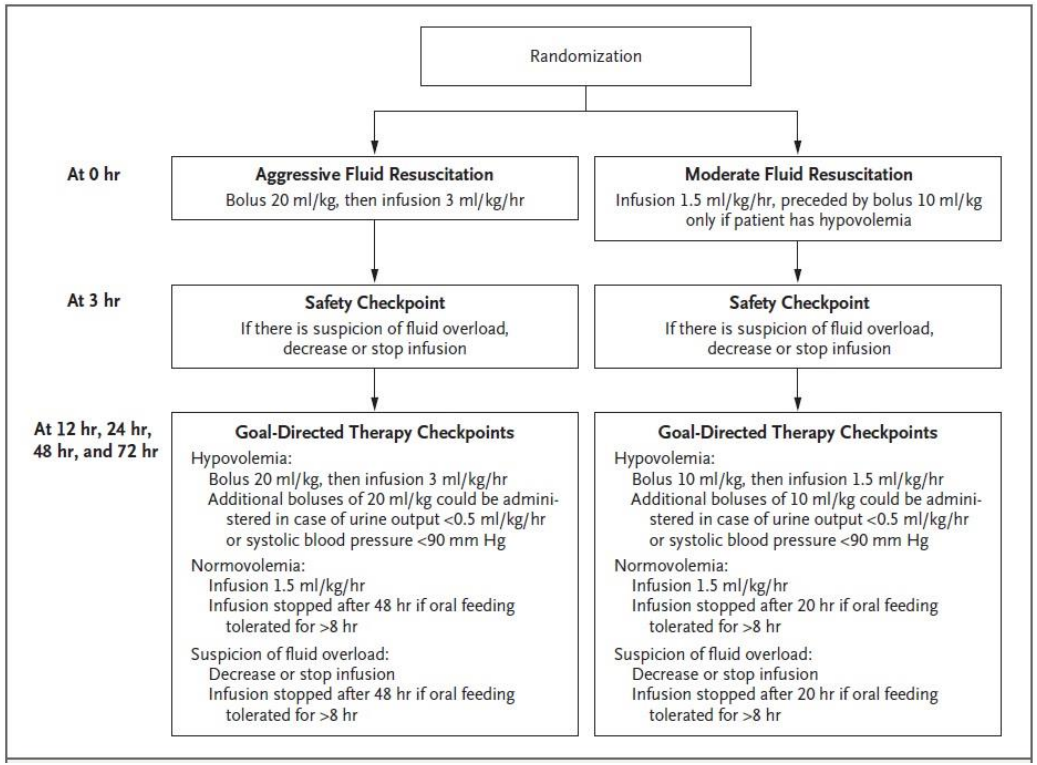
- Multicenter (18 centers) open-label, parallel-group, randomized, controlled superiority trial. "WATERFALL" trial.

- Measured outcomes were:
  a) Development of moderately severe or severe pancreatitis.
  b) Volume overload.

- 249 patients total. The trial was halted early and unanimously owing to "between-group differences in safety outcomes without a significant difference in the incidence of moderately severe or severe pancreatitis."

De-Madaria E. et al NEJM September 15 2022

Fluid Resuscitation in Acute Pancreatitis



De-Madaria E. et al NEJM September 15 2022

Per 70kg adult:

Aggressive resuscitation:

- 1,400cc bolus, then 210cc/hr
  - Stopped after 48hr if tolerating PO.
  - Median of 7.8 liters in first 48hrs.

Moderate resuscitation:

- 700cc bolus, then 105cc/hr
  - Stopped after 20hr if tolerating PO.
  - Median of 5.5 liters in first 48hrs.

Fluid Resuscitation in Acute Pancreatitis

Results

Outcome	Aggressive resuscitation (n=122)	Moderate resuscitation (n=127)	Adj. relative risk (95% CI)
Moderately severe or severe pancreatitis	22.1%	17.3%	1.30(0.78-2.18)
Fluid overload	20.5%	6.3%	2.85(1.36-5.94) p 0.004
Organ failure	7.4%	3.9%	1.23(0.47-3.23)
Respiratory failure	7.4%	2.4%	2.19(0.63-7.64)
Median PAN PROMISE (pain) score (48hrs)	10	8	1.29(1.01-1.66)
ICU admission	8%	2%	2.71(0.64-11.51)
Median hospital stay	6	5	1.31(0.98-1.75)

Fluid Resuscitation in Acute Pancreatitis

Discussion

- Aggressive fluid resuscitation increased the risk of volume overload without any clear benefit, leading to unanimous early termination of this trial by their monitoring board.

- Conclusions add to growing evidence that aggressive hydration is linked to worse outcomes in critically ill patients. Aggressive hydration can worsen intra-abdominal pressures in acute pancreatitis.

Caveats

- Early termination limits this study's power for overall efficacy.

- Open-label architecture introduces bias but was required for sequential exams and fluid rate adjustments.

- Was IV hydration in the aggressive group, *too aggressive? (upwards of 7L in 48hrs).*

Fluid Resuscitation in Acute Pancreatitis

Take aways

- These findings do not support our current treatment guidelines which recommend early aggressive hydration.

- Very strong, high-quality evidence suggesting no benefit from aggressive hydration and significant harm.
- Supported by several recent studies showing worse outcomes with aggressive IV resuscitation.

- Change my practice: **IV hydration for the treatment of acute pancreatitis will use a moderate fluid resuscitation approach.**

- 10ml/kg bolus followed by 1.5ml/kg/hr IVF infusion (70kg: 1L IVF followed by 100cc/hr).

Your nocturnist will be much happier.

Case 5: The Awake Patient

A 65yo patient with DM2, HTN, CAD, HFpEF is admitted for management of community acquired pneumonia with a 2-4L O2 requirement by NC. Their RN pages you at 2300, “Patient unable to sleep, can you write for something?”

Do you:

A) Write orders for no-vitals overnight, mute IV pumps, and place ‘Do Not Disturb’ orders for the patient?

B) Order Melatonin and Trazodone qHS.

C) Titrate on and up Seroquel.

D) The ward is loud, Propofol is the only answer.

Improving Sleep in the Hospital

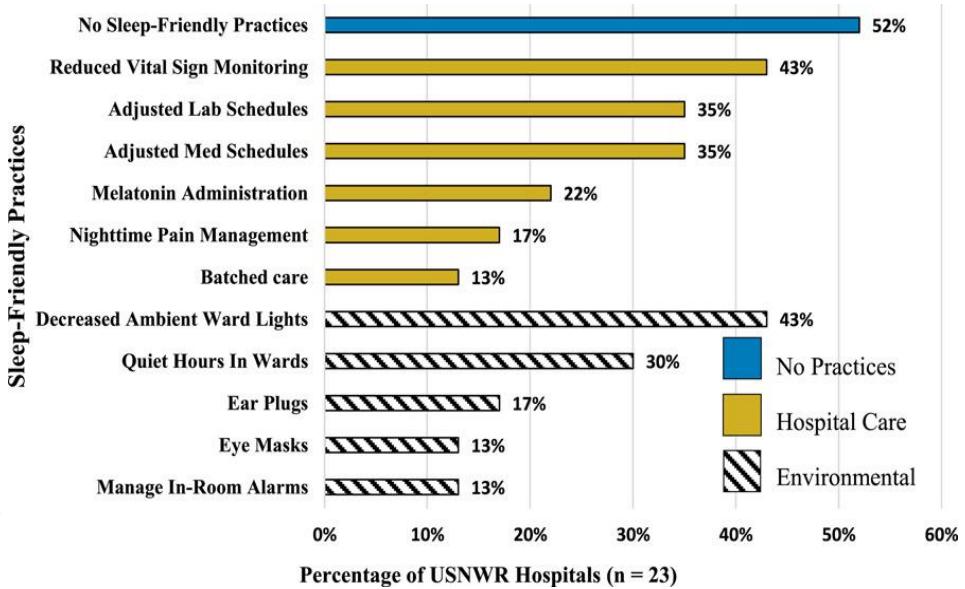
<u>Defining existing practices to support the sleep of hospitalized patients</u>

- Survey of 20 hospitals via interviews of hospitalist section chiefs.

- 96% rated patient sleep as important.

- Only 43% were satisfied with their institution's efforts to improve patient sleep.

- Fewer than half (48%) of top hospitals have sleep friendly practices.



Affini M et al JAMA July 2022

Improving Sleep in the Hospital

Effectiveness of an analytics-based intervention for reducing sleep interruption

- Randomized clinical trial to assess harm if patients do not have overnight vitals. Inpatient encounters randomized 1:1 to intervention vs usual care. 1699 patients in study.
- Intervention: An epic-based logistic regression model used real-time patient data to determine if patients had a high likelihood of stable nighttime vital signs.
- If yes, a clinical decision support notification asked the physician to discontinue night-time vitals.

966 patients in intervention group	Intervention	Control/usual Care	P-value
Nighttime vitals checks (mean)	0.97	1.41	P<0.001
ICU transfers	49(5%)	47(5%)	P=0.92
Code Blue	2(0.2%)	9(0.9%)	P=0.07
Delirium	108(11%)	123(13%)	P=0.32

Najafi N et al JAMA Feb 2022

Improving Sleep in the Hospital

Caveats

- Changes to physician culture and fears regarding leaving patients without vitals or overnight checks is the hardest part of any of these studies.
- Many effective changes require institution-wide improvements.
- Do we need an “epic-based logistic regression model and notification system” to make this decision for us?

Take aways

- Patient sleep is a top priority of 96% of physicians and hospitals, but only 43% of hospitals are proactive toward improving patient sleep.
- A lack of nighttime vitals, and likely Do Not Disturb orders, will not lead to a Code Blue.
- **Change my practice: All low and moderate risk patients should have no nighttime vitals, DND, batch labs and medication times at 0700 and 1900, and managed in-room alarms.**

Case 6: What About Us

A 38yo hospitalist has 17 patients on their list. They have been working for 6 days straight. Is this affecting their patient outcomes?

Multiple choice:

A) Yes, absolutely yes.

B) No, no way. In fact, give them more patients.

<u>Association between hospitalist physician workload, LOS, and return to hospital:</u>

- Out of 38,141 hospitalizations, comparing hospitalists with <13 patients to those with >16 patients.

- LOS was prolonged by only 0.05 days (95% CI 0.02-0.08 p=0.001)

- No association between workload and ED visits or readmissions within 7 to 30 days.

- The answer is B.

Djulbegovic M et al JHM June 2022

“Do This, Don’t Do That”

Summary Take Aways

1. Do use PO antihypertensives for inpatient hypertension. Avoid IV antihypertensives.

2. Do use Midodrine in patients at high risk of falls due to vasovagal syncope, orthostasis, debility, poor autonomic tone, etc.

3. Do feel confident that using a PIV for pressors in the crashing patient carries a low risk of harm.

4. Do use a moderate fluid resuscitation strategy for treatment of acute pancreatitis.

5. Do strive to be proactive regarding patient sleep quality. We can all do better.

6. Do. Not. Worry. About. Your. Workload!

Updates in Hospital Medicine 2022

Thank you!