The Pharmacist's Role in Pandemic Planning in the Emergency Department

What to Do When You Don't Know What to Do!

Erin M Lingenfelter, PharmD
Inpatient Clinical Pharmacist, Emergency Medicine
PGY2 Emergency Medicine Pharmacy Coordinator
University of Utah Health, Salt Lake City, UT

Disclosure

Instructions:
The speaker has no conflicts of interest to disclose.
The speaker will not be discussing any off-label uses of drugs.

Learning Objectives

At the conclusion of this activity, pharmacists should be able to successfully:
1. Articulate the various roles of pharmacists in an interdisciplinary team creating pandemic plans in the emergency department.

What is Disaster Response?

- WHO defines a disaster as a sudden phenomenon of sufficient magnitude to overwhelm the resources of a hospital, region, or location requiring external support
- A thoughtful fast approach in response to a disaster is critical.
- The emergency medicine approach is quite similar to Dr. Michael Ryan, Executive Director, WHO Health Emergencies Program

Learning Objectives

At the conclusion of this activity, pharmacy technicians should be able to successfully:
1. Explain why frequent changes in product selection, policy, and procedures during a pandemic or disaster management response occur.
How can we mitigate this situation to be less bad than it could possibly be?

Are we prepared for something bad if it happens?

Do we have the resources to respond?

How will we recover from this?

We all have emergency preparedness skills

Preparedness Cycle
- Preparedness
- Prevention
- Response
- Recovery
- Mitigation

How can we **mitigate** this situation to be less bad than it could possibly be?

Are we **prepared** for something bad if it happens?

Do we have the **resources** to respond?

How will we **recover** from this?
Disaster Role(s) of a Pharmacist in the ED

ASHP Guideline on Emergency Medicine Services

“It is essential that Emergency Medicine Pharmacists (EMP), in conjunction with the department of pharmacy, participate in emergency preparedness planning.”

“Planning and involvement should occur at a minimum at the institutional level….knowledge of local, state, and national emergency preparedness plans, programs, and support systems is paramount.”

Support Documents for Pharmacy Involvement

- ASHP Statement on the Role of Health-System Pharmacists in Emergency Preparedness
- Emergency and Disaster Preparedness and Response Planning: A Guide for Boards of Pharmacy
- A Pharmacist’s Guide to Pandemic Preparedness
- Pharmacist as Front-Line Responders for COVID-19 Patient Care
- Joint Executive Summary by all major Rx orgs
- ASHP Guidelines on Emergency Medicine Pharmacist (EMP) Services
- Pharmacy Leader’s Role in Hospital Emergency Preparedness Planning

Other Training for Pharmacist and Technician Involvement

- Emergency Preparedness
- Basic Disaster Life Support
- Advanced Disaster Life Support
- National Incident Management System
- Free online training @ www.FEMA.gov
- Disaster Medical Assistance Teams
- Emergency Medication Assistance Program

Assess the Scene:

Jan 22, 2019: Received first communication from our ED Code Bio Coordinator

- Mask the patient, limit contact, place in airborne precautions…
Assess the Scene:
January 23, 2020: Chinese government locks down Wuhan

Assess the Scene:
January 30, 2020
- WHO declares a "global health emergency"
February 4, 2020
- The "Diamond Princess" is quarantined off the coast of Yokohama, Japan

Assess the Scene:
March 3, 2020
- First official communication from management
March 6, 2020
- First patient in Utah

Disaster Role(s) of an EMP: Patient Care
ED: Still open for business
- "Normal" patient care
- Resuscitation
- Medication management, safety, and optimization
- Response to critical events or procedures
  - Rapid Sequence Intubation
  - ACLS

Disaster Role(s) of an EMP: Drug Information
- Drug cures, drugs to avoid
- Drugs to stockpile, don’t stockpile it’s bad
- Reported, perceived, actual, felt at user level shortages
- Med Twitter Ideas, both good and bad
- Literature review and dissemination
- Rumor management and follow up

Disaster Role(s) of an EMP: Regulation
- Rapid changes from the CDC, local, state, and national government
- Protecting yourself & others from health care exposure
- Emergency Medical Treatment & Labor Act (EMTALA)
Disaster Role(s) of an EMP: Operations

- ADC inventories in treatment areas
- Medication preparation at bedside/room
- Inpatient pharmacy delivery facilitation
- Safe drug return to central operations

Disaster Role(s) of an EMP: Problem solving

- Everything takes longer AND keeps changing
- Changes coming from the top down takes time
- Avoiding over use of PPE
- Communication and space issues
- Surges and inventory lag
- Disagreements in care management
- Hard to keep up with information flying around
- Non-adherence to safety practices and protocols
- Recognizing yourself as a non-redundant resource

Disaster Role(s) of an EMP: Administration and Medication Management

Administrative
- P.A.C.E planning
- Education
- Policies, guidelines and procedures updates
- Resource management
- Protocol development

Disaster Role(s) of a Technician in the ED

Medication Procurement & Preparation Experts
- Emergency kits
- Experts in automated dispensing cabinets
- Optimizing ADC par levels
- Shortages and formulary change management
- Best Use Date champions
- Responding to emergency requests

Disaster Role(s) of an EMP: Operations

- ADC inventories in treatment areas
- Medication preparation at bedside/room
- Inpatient pharmacy delivery facilitation
- Safe drug return to central operations
The ED intubation and airway management protocol went through 4.1! reiterations to keep up with changes, drug stock and expert suggestions.

Tips and Tricks
- Have a working understanding of the local, state, and federal response and command systems
- Living communication tools
- Did I hear you say a drug name or “pharmacy”?
- A “no” today does not mean “no” tomorrow
- Back up plans, don’t be afraid to be creative
- Don’t over extend yourself or your team

Tips and Tricks
- Have your own emergency kit, snacks, comfort items, and sleeping needs
- Have a robust phone # list
- Maintain physical and mental health
- Obtain your own PPE if needed
- Phone charger, battery bank
- Find a quiet place and mantras
- Timer for cleaning
- Support team
- Make friends with ambiguity

Test Questions
- Which of the following roles in action should an EM pharmacist not participate in during a pandemic?
  A) Creating tools for fast decision making and dosing by nursing staff?
  B) Daily literature upload and dissemination
  C) Patient care like drug-disease interaction and error prevention
  D) Daily routine, keep the status quo
  E) Collaborate with operations for ADC optimization
Test Questions
 Why is yesterday’s brand new standard operating procedure (SOP) changed today already?

A) Drug formulation shortage announced overnight
B) Clinical practice for best care supports research or use of a new drug
C) Key personnel are now out on leave due to quarantine
D) Best Use Date allows for best inventory use
E) All or any of the above, because disasters aren’t predictable and we made the best SOP with the knowledge we had yesterday. Today’s a new day!

COVID-19 Medication Controversies:
-Do you have an ACE (Inhibitor) up your sleeve?
-WHO said WHAT? Some things better left NSAID

Cole Sloan Pharm.D., BCPS, BCGP
Emergency Medicine Pharmacist
Program Director, PGY2 EM Pharmacy
University of Utah Health

References

Disclosure
Instructions:
No relevant relationships or conflicts of interest, financial or otherwise, to disclose
We will discuss off-label use(s) of medications

Learning Objectives
At the conclusion of this activity, pharmacists should be able to successfully:
1. Evaluate available literature regarding risks and/or benefits of ACE-I, ARB, NSAID use during an acute COVID-19 infection
2. Formulate a recommendation based on available literature when discussing the ACE-I/ARB/NSAID conundrum with providers and patients

Learning Objectives
At the conclusion of this activity, pharmacy technicians should be able to successfully:
1. List medications in the ACE-I, ARB, and NSAID class of medications
2. Identify patients who may have concerns regarding continued use of ACE-I, ARB, and NSAID during the COVID-19 pandemic
Road Map

Discuss controversy regarding ACEi (Angiotensin Converting Enzyme – Inhibitor) & ARB (Angiotensin Receptor Blocker) use in COVID-19 patients
Biologic mechanisms and relevant literature for various hypotheses
Current recommendations for patients taking these medications
Repeat for NSAIDs (Non-Steroidal Anti-Inflammatory Drugs)
Touch on other pertinent classes of medications

Controversy! RAS Inhibitor Use During COVID-19

- Lancet publishes correspondence March 11th (updated March 19th): "The expression of ACE2 is substantially increased in patients with type 1 or type 2 diabetes, who are treated with ACEi & ARBs... Consequently, the increased expression of ACE2 would facilitate infection with COVID-19. We therefore hypothesise (sic) that diabetes and hypertension treatment with ACE2-stimulating drugs increases the risk of developing severe and fatal COVID-19."
- Panic ensues from patients and medical providers hoping to do the right thing in this rapidly emerging situation

RAS = Renin-Angiotensin System

Hypothesis – RAS Inhibition = Harmful
No RAS Inhibitor

SARS-CoV-2

\[ \downarrow \]

ACE2 Receptor

Simplified from Nature Reviews April 2020

RAS Inhibitor

SARS-CoV-2

\[ \downarrow \]

ACE2 Receptor

Simplified from Nature Reviews April 2020

Hypothesis – RAS Inhibition = Beneficial
No RAS Inhibitor

SARS-CoV-2

\[ \downarrow \]

ACE2 Receptor

Simplified from Nature Reviews April 2020

RAS Inhibitor

SARS-CoV-2

\[ \downarrow \]

ACE2 Receptor

Simplified from Nature Reviews April 2020

ACEi, ARB Use & Confounders?
Perhaps the issue in COVID-19 is not ACEi or ARB use, but potential confounders including increasing age, hypertension (or other underlying indication for ACEi or ARB treatment)

- Many studies have been completed and are ongoing attempting to answer this question
- Nothing conclusive (yet), design limitations, population confounders, when/how to adjust analyses, etc

Should we ‘play it safe’ and switch patients to another medication for HTN (e.g. amlodipine)?

- Association between RAS inhibition and COVID-19 remains unknown
- RAS inhibition affects much more than blood pressure (kidney protective, etc)
- Switching medications may require additional monitoring (difficult whilst physically distancing)
- If RAS inhibition affects COVID-19, not sure in what direction and how robustly

MA ↓ Mortality – Hypertension Aug 2020

Odds Ratio

M-H, Fixed, 95% CI

Favours [ACEi/ARB] vs. [Non-ACEi/ARB]
Current Atherosclerosis Reports Aug 2020

Dx COVID-19: Continue ACEi or ARB?

- Retrospective, multi-center study including 1128 adult patients w/ hypertension diagnosed with COVID-19, where 188 using ACEI/ARB and 940 not using ACEI/ARB
- Admitted to 9 hospitals in Hubei Province, China from December 31, 2019 to February 20, 2020
- All-cause mortality was lower in the ACEI/ARB group versus the non-ACEI/ARB group (adjusted hazard ratio, 0.42 [95% CI, 0.19–0.92]; P=0.03)
- Subgroup compared use of other antihypertensive meds, ACEI/ARB associated w/ decreased mortality (adjusted hazard ratio, 0.30 [95% CI, 0.12–0.70]; P=0.01)

“Interim” Final Word

Recommend / Strongly Encourage (and many other synonyms) continuing ACEi/ARB treatment.

Not just my opinion...

American College of Physicians, American Heart Association, American College of Cardiology, European Society of Hypertension, ESC Council on Hypertension, and many others.

American Diabetes Association didn’t have an official statement I was able to find, but publications in their society journal were congruent with the recommendation to continue treatment with an ACEi/ARB or other cardiovascular/diabetes medication that has been implicated with increased ACE2 expression

Controversy! NSAID Use During COVID-19

- Lancet publishes letter March 11th (updated March 19th): “ACE2 can also be increased by thiazolidinediones and ibuprofen... We therefore hypothesise [sic] that diabetes and hypertension treatment with ACE2-stimulating drugs increases the risk of developing severe and fatal COVID-19.
- March 14th French Minister of Health recommends against anti-inflammatory medications (e.g. ibuprofen, cortisone) and in the event of fever recommends taking acetaminophen (paracetamol)
- March 18th WHO ‘clarifies’ stance via Tweet, “WHO does not recommend against the use of ibuprofen”

NSAID Use Caveats

This question does not have the same level of evidence as the previous therapeutic conundrum (ACEi/ARB). Much of this section is based on hypotheses, broad derivations and outright speculation. It is also more difficult to study as Over-The-Counter use makes it hard to establish usage. Not to mention individual patient dosing can vary widely, as anyone performing medication histories can attest

NSAIDs are much broader from a chemical structure standpoint (e.g. COX 1 & COX 2 inhibition differences, varying prostaglandin effects, PK parameters) relative to other medication classes discussed in the context of COVID-19 controversy; some differences may yet be elucidated.

E.g. certain NSAIDs may be harmful while others may be equivocal or beneficial.
Why Might NSAIDs be Harmful?

- Ibuprofen upregulates ACE2, potentially increasing viral load and/or likelihood SARS-CoV-2 enters cells via increased chances to bind ACE2
- In bacterial soft tissue infections, patients on NSAIDs experienced more severe infections, thought to be due to either immune-depressive effects or initial symptom suppression resulting in delayed treatment initiation
- Fever is a natural physiologic response to viral infection and reduces viral activity; antipyretics, such as NSAIDs, could reduce the body’s natural defense systems against viruses
- Centre for EBM notes, “NSAIDs do not significantly reduce total symptoms or duration of illness in Acute Respiratory Infections.” Note: this summary was not looking at COVID-19 respiratory infections specifically [March 24th 2020 Link]

Why Might NSAIDs be Beneficial?

Or at least not as harmful as initially thought

- Ibuprofen upregulating ACE2 enzyme was found in a single study in diabetic rats; perhaps more robust evidence is needed in this area. It’s unclear how long NSAIDs would need to be taken before upregulation of ACE2 would occur in humans, if at all. Not to mention ACE2 upregulation has not been linked to worse outcomes in COVID19 (see ACEi/ARB section)
- NSAIDs masking symptoms would be unlikely to cause problems as widespread and robust treatments of COVID-19 are currently lacking; wouldn’t be appreciably delaying treatment as there are no time-sensitive outpatient therapies to start at present*
- As the sequelae of COVID-19 severe respiratory infections are still being elucidated, perhaps the immune-depressive effects of NSAIDs may be helpful (akin to corticosteroid use)
- Mortality from COVID-19 may be worsened during ‘surges’ so if an NSAID is able to keep patients out of the hospital that may have downstream benefits*

NSAID Literature

- Much of it derived from respiratory infections in general, not specifically COVID-19
- Naproxen as part of a medication cocktail was effective in treating influenza A (H1N1) [link]
- Recent systematic review of six clinical trials (included study above) recommends caution until more data are available; the authors suggest naproxen may be a good choice for future study [link]
- LIBERATE trial is underway looking at ibuprofen as a potential treatment for COVID-19 and reduction of lung injury in acute hypoxic respiratory failure [lipid ibuprofen NCT04346629]
- Case-control survey study underway: Role of Ibuprofen and Other Medicines on Severity of Coronavirus Disease 2019 (RISC) NCT04383899

What about other med classes?

Due to time constraints and limited data relative to ACE-I, ARB and NSAID use we will not dive deep into these classes today

- Thiazolidinediones (TZDs)
  - Harmful? [upregulates ACE2 in Rats] [5/6 World J 2014]
- HMG-CoA Reductase Inhibitors (Statins)
  - ↓ Risk of mortality: [link] Cell Metab Aug 2020
- Proton Pump Inhibitors (PPIs)
  - ↑ Risk of severe clinical outcomes: [link] Gut July 2020
Test Questions

T/F: There exists clear and convincing evidence regarding which medications should be discontinued if a patient is at all concerned about COVID-19

A. True
B. False

Test Questions

MC: Which of the following medications has not been subject to controversy in patients infected with COVID-19

A. Ibuprofen
B. Telmisartan
C. Docusate
D. Lisinopril

Coagulopathies in COVID

Laura Steffens, PharmD, BCCCP, MS
September 12, 2020
USHP Winter Meeting

IMPLICATIONS FOR VTE PROPHYLAXIS AND TREATMENT

Disclosure

Relevant Financial Conflicts of Interest

- The presenter, Laura Steffens, has no financial conflicts of interest to disclose.

Off-Label Uses of Medications

- The use of tPAs for empiric treatment of microthrombi associated with COVID will be discussed.

Learning Objectives

Pharmacists

- Describe coagulopathies associated with COVID infections and apply guideline recommendations for venous thromboembolism (VTE) prophylaxis and treatment.

Technicians

- Distinguish between oral, intravenous (IV), and subcutaneous (SQ) medications for VTE prophylaxis and treatment.

Background

- High risk for VTE development in COVID (+) admitted to a hospital
- Similar coagulopathy pattern as seen in SARS and MERS
- Incidence of VTE 1.1-69% in COVID patients
- Higher morbidity and mortality in those who develop VTE
- Practicality of diagnosis can be challenging
Pathophysiology

Coagulopathy in ARDS
- Permeability of alveolar-capillary junction
- Infiltration of various inflammatory and coagulation factors
- Tissue factor exposed on damaged epithelium
- Increased production of fibrinogen
- Increased PAI-1 release (hypofibrinolytic state)
- Unrestricted inflammation and fibrin deposits
- High risk for clot development
- Concern in later stages for mass fibrin deposits

Various Thrombi Formations

Overall Effects
Of note, uncommon to see:
- Thrombocytopenia
- Hemolytic anemia

Additional Risk Factors
- Intense inflammatory response
- Critical illness
- Traditional risk factors (immobility, venous stasis)
- Drugs interactions with investigational therapies
- Unjustified fears about medications
Progression of Disease and Coagulopathy

Disseminated intravascular coagulation
Consumptive coagulopathy

Lab characteristics
- PT
- PTT
- Fibrinogen
- D-dimer
- Red cells – schistocytes

Single center study in China (N=183)
- 71% of those who died developed DIC
- 0.6% of those who lived developed DIC


Implications for Prevention and Treatment

<table>
<thead>
<tr>
<th>Medication</th>
<th>Mechanism of Action</th>
<th>Typical Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unfractionated Heparin (UFH)</td>
<td>Enhances action of anti-thrombin III to inactive thrombin, Factor Xa, and other clotting factors</td>
<td>Prophylaxis: 5000-7500 units SQ Q8-12 h Treatment: 80 units/kg bolus, 18 units/kg/hr IV, or other variations</td>
</tr>
<tr>
<td>Low Molecular Weight Heparin (LMWH)</td>
<td>Same as UFH, but higher affinity for Factor Xa; Some postulated benefits in COVID as UFH</td>
<td>Prophylaxis: 10 mg daily, 30 mg BID SQ Treatment: 1 mg/kg BID SQ *Adjusted for renal function</td>
</tr>
<tr>
<td>Fondaparinux</td>
<td>Binds antithrombin III to specifically inhibit Factor Xa; Unknown supplemental benefits in COVID at this time or if confers the benefits as UFH and LMWH</td>
<td>Prophylaxis: 2.5 mg daily SQ Treatment: 5-10 mg per day SQ (weight-based) *Adjusted for renal function</td>
</tr>
</tbody>
</table>

Warfarin
- Inhibition of vitamin K activation, which is required for synthesis of clotting factors II, VII, IX, and X
- Unknown supplemental benefits in COVID at this time

DOACs
- Rivaroxaban, Apixaban
- Direct inhibition of Factor Xa
- Unknown supplemental benefits in COVID at this time

Tissue plasminogen activator (tPA)
- Converts plasminogen to plasmin to break down fibrin
- Proinflammatory cytokines leading to further alveolar-capillary permeability

Warfarin: Vari, but typical starting dose of 5 mg daily PO Adjust with INR
DOACs: Adjusted for renal function
Tissue plasminogen activator (tPA): Typically 50-100 mg IV over various times, usually 2 hours Can be given as catheter-directed therapy

Question 1
Which of the following medications do not currently have additional postulated benefits beyond prevention of VTE in COVID positive patients admitted to the hospital?

A. Enoxaparin
B. UFH
C. Rivaroxaban
D. tPA

COVID Lab Value Trends

<table>
<thead>
<tr>
<th>Lab Value</th>
<th>Effects in COVID</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>D-dimer</td>
<td>Elevated</td>
<td>Higher risk of ICU admission, mechanical ventilation, and/or death</td>
</tr>
<tr>
<td>PT</td>
<td>Elevated</td>
<td>Increased in high plasmin and fibrinolytic activities (diabetes, cardiovascular disease, hypertension; challenging to attribute solely to clot</td>
</tr>
<tr>
<td>PTT</td>
<td>Elevated</td>
<td>Not as elevated relative to PT</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>Elevated</td>
<td>Major role in DIC development assessment</td>
</tr>
<tr>
<td>CRP</td>
<td>Elevated</td>
<td>Augments tissue factor exposure, further promoting coagulopathy</td>
</tr>
<tr>
<td>PCT</td>
<td>Neutral to mild decrease</td>
<td>Not usually a significant finding, unless severe illness</td>
</tr>
<tr>
<td>IL-6</td>
<td>Elevated</td>
<td>Proinflammatory cytokines leading to further alveolar-capillary permeability</td>
</tr>
</tbody>
</table>

PT = prothrombin time; PTT = partial thromboplastin time; CRP = C-reactive protein; PCT = procalcitonin

Typically less dramatic than in bacterial infections
Literature about how labs used

* Many studies assessing labs to predict risk of VTE development, mostly surrounding D-Dimer
* High D-dimers noted in severe COVID patients admitted to the ICU

Per the American College of Cardiology:
No great data to support diagnosis of VTE based off D-Dimer alone

- Many studies assessing labs to predict risk of VTE development, mostly surrounding D-Dimer
- High D-dimers noted in severe COVID patients admitted to the ICU


Detection of VTE with D-Dimer >1,5000 ng/mL: sensitivity 85%, specificity 88%
Small sample size, not validated, not replicated

Practicality of diagnosis can be challenging

- Infection risk
- Patient instability

Ideally: Imaging and Labs
- D-Dimer not specific but can have a high negative predictive value
- CTPA
- VQ Scan
- ECHO assessing new right heart strain
- Ultrasound

Assess signs and symptoms:
- DVT manifestations
- Disproportionate hypoxemia
- New right ventricular dysfunction
- Consider empiric treatment if high concern

Ideally:
Imaging and Labs
- D-Dimer not specific but can have a high negative predictive value
- CTPA
- VQ Scan
- ECHO assessing new right heart strain
- Ultrasound

Assess signs and symptoms:
- DVT manifestations
- Disproportionate hypoxemia
- New right ventricular dysfunction
- Consider empiric treatment if high concern

Imaging not possible

Professional Societies

- International Society on Thrombosis and Haemostasis (ISTH)
- American Society of Hematology (ASH)
- World Health Organization (WHO)
- American College of Cardiology (ACC)
- Several more coming out!

Bikdeli B. et al. J Am Coll Cardiol 2020;75(23)2950-2973. (JACC)


Professional Societies

Statements on VTE Treatment in COVID patients

<table>
<thead>
<tr>
<th>ISTH</th>
<th>ASH</th>
<th>WHO</th>
<th>ACC</th>
</tr>
</thead>
<tbody>
<tr>
<td>No comment</td>
<td>Consider drug-drug interactions with selection of agents</td>
<td>No comment</td>
<td>Exoxaparin may be favored if no contraindications acutely</td>
</tr>
<tr>
<td>Prefer heparin or LMWH for hospitalized patients for shorter half life and less drug interactions</td>
<td>Consider underlying conditions, valves, etc</td>
<td>Consider systemic fibrinolysis vs catheter-directed therapy in massive PE</td>
<td></td>
</tr>
</tbody>
</table>

Largely support pre-COVID VTE treatment guidance

<table>
<thead>
<tr>
<th>Implications for Prevention and Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medication</strong></td>
</tr>
<tr>
<td>UFH</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>LMWH</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Fondaparinux</td>
</tr>
<tr>
<td>Warfarin</td>
</tr>
<tr>
<td>DOACS</td>
</tr>
<tr>
<td>IMA</td>
</tr>
</tbody>
</table>

Useful drug-drug interaction resource: https://covid19-druginteractions.org/checker
Prophylaxis

Assessment of Severity
- Risks Assessment Methods to Consider:
  - PADUA scores in medically ill patients
  - Caprini scores in surgically ill patients
  - Sepsis-Induced Coagulopathy score
  - No specific score validated in COVID patients

This has led many institutions to develop individual risk assessments and approaches

Approaches to therapy
- Significant controversy surrounding dosage for VTE prophylaxis

- Standard Dosing
  - Hospitalized patients with COVID

- Intermediate Dosing
  - Therapeutic Dosing

- Therapeutic Dosing

Standard Dosing Approach
- COVID patients are typically adult, medically ill patients
- Initial and potential ongoing concern that this may not be enough

- 3 Dutch hospitals, 184 ICU patients with COVID
- 25 symptomatic VTEs
- 2 ICUs used lower than recommended doses for prophylaxis

Unclear implications with inappropriate dosing

Intermediate Intensity Prophylaxis
- No specific studies available currently
- Several institutions have developed individualized approaches
- Empiric twice daily dosing
- Elevated Anti-Xa targets
  - Recommendations are currently just expert opinion
  - Not yet well supported by the literature

Empiric Full Dose Anticoagulation
- Several hospitals have published protocols incorporating empiric full dose anticoagulation

- Single center retrospective observational study
- Improved mortality and median survival days in mechanically ventilated patients with full anticoagulation vs rest

- No report of prophylactic dosing
- No account for baseline characteristics
- Did state if just prophylactic anticoagulation or none at all in the comparator group

Not well supported by the literature at this time
Empiric tPA

- In the setting of presumed microthrombi in the lungs

- 3 case reports
- Improvement in oxygenation and P/F ratio
- Response was short lived, <12 hours

Not well studied or justified currently

Professional Societies

<table>
<thead>
<tr>
<th>Name</th>
<th>LMWH</th>
<th>UFH</th>
<th>FONDAPARINUX</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISTH</td>
<td>Prophylactic: LMWH in all hospitalized patients with no contraindications</td>
<td>Administer in all hospitalized patients</td>
<td>Mechanical prophylaxis when chemical not available or contraindicated</td>
</tr>
<tr>
<td>ASH</td>
<td></td>
<td>Administer LMWH or heparin 5000 units SQ SID</td>
<td>Unknown if intermediate-intensity or full empiric anticoagulation beneficial</td>
</tr>
<tr>
<td>WHO</td>
<td></td>
<td></td>
<td>Unknown if post-discharge prophylaxis beneficial</td>
</tr>
<tr>
<td>ACC</td>
<td></td>
<td></td>
<td>No known benefit of empiric therapeutic anticoagulation in setting of elevated D-Dimer</td>
</tr>
</tbody>
</table>

- Risk scores for VTE prophylaxis
- Weight-based dosing needs to be further studied
- Unknown benefit of empiric full anticoagulation
- Pregnancy needs further studies for correct approach
- Individual risk/benefit stratification for prophylactic post-discharge anticoagulation <45 days

Current Studies

**Full Dose Vs Prophylactic Dose Heparin in High Risk COVID-19 Patients**

**Design:** Prospective, randomized active-comparator trial

**Population:** Adult high-risk hospitalized patients with COVID diagnosis with O_2 requirement

**Intervention**
- For VTE prophylaxis:
  - Therapeutic LMWH
  - Prophylactic or intermediate-dose LMWH or UFH

**Outcome**
- Composite: venous or arterial thrombotic events, all-cause mortality

  - **Full Dose Vs Prophylactic Dose Heparin in High Risk COVID-19 Patients**

Question 2

69 year old female presents to your ED with cough, shortness of breath, and positive COVID nasal swab 4 days prior to arrival. She is requiring high flow nasal cannula 70 L 100% with oxygen saturations ~85%. The team decides to intubate and she is admitted to the medical ICU. They are working to enroll her in clinical trials for COVID therapies. Patient reports no current home medications, but had recently moved here from Argentina. She is found to have an A1c of 14% on arrival. Some presenting data are as follows: WBC 13, D-dimer 115, CrCl ~75 mL/min (making appropriate urine), BMI 45 kg/m^2.

**What do you recommend for DVT prophylaxis in this patient?**

A. Enoxaparin 40 mg SQ daily
B. Enoxaparin 40 mg SQ BID
C. Heparin 80 units/kg bolus, followed by 18 units/kg/hr
D. Warfarin 5 mg day

Take Home Points

- COVID patients, particularly critically ill tend to be at high risk for development of VTE
- Unknown significance of D-dimer, except that potentially high risk for clot, and still carries good negative predictive value
- VTE diagnosis in COVID patients can be challenging
- Treatment is per usual, but mindful of drug-drug interactions and nurse contact time
- Prophylaxis definitive statements are still challenging and more data is needed

Coagulopathies in COVID

**IMPLICATIONS FOR VTE PROPHYLAXIS AND TREATMENT**

Laura Steffens, PharmD, BCCCP, MS

September 12, 2020

USHP Winter Meeting