Welcome

Trish Tennill, RN, BSN
Welcome: Trish Tennill, RN, BSN

COVID-19 Coagulopathy: Manila Gaddh, MD

Anticoagulation Evidence in COVID-19: Deepak Pradhan, MD, FCCP

Institutional Protocols: Vikram Mukherjee, MD

NETEC Resources: Trish Tennill, RN, BSN

Questions and Answers with NETEC
National Emerging Special Pathogens Training and Education Center

Mission Statement
To increase the capability of the United States public health and health care systems to safely and effectively manage individuals with suspected and confirmed special pathogens

For more information
Please visit us at www.netec.org or email us at info@netec.org
**NETEC Overview**

### Assessment
- Empower hospitals to gauge their readiness using **Self-Assessment**
- Measure facility and healthcare worker readiness using **Metrics**
- Provide direct feedback to hospitals via **On-Site Assessment**

### Education
- Provide self-paced education through **Online Trainings**
- Deliver didactic and hands-on simulation training via **In-Person Courses**
- COVID-19 focused **Webinars**

### Technical Assistance
- **Onsite & Remote Guidance**
- Compile **Online Repository** of tools and resources
- Develop customizable **Exercise Templates** based on the HSEEP model
- Provide **Emergency On-Call Mobilization**

### Research Network
- **Online Repository**
  - Built for rapid implementation of clinical research protocols
- Develop Policies, Procedures and Data Capture Tools to facilitate research
- Create infrastructure for a **Specimen Biorepository**

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**Cross-Cutting, Supportive Activities**

- COVID-19 focused Webinars
COVID-19 Coagulopathy

Manila Gaddh, MD
COVID-19 Coagulopathy

- Mild Thrombocytopenia
- Mild elevation of Prothrombin Time
- Elevated fibrinogen
- Elevated D-dimer
- Increased risk of thrombosis
- Overt disseminated intravascular coagulopathy (DIC), with hyperfibrinolytic/bleeding phenotype is rare and develops in late stages of the disease

N Tang et al. JTH 2020; 18(4): 844-847
# COVID-19 and Thrombotic Disease

## Table 2: Association Between Coagulation Abnormalities or Markers of Thrombosis and Hemostasis and Clinical Outcomes in Patients With COVID-19

<table>
<thead>
<tr>
<th>Study</th>
<th>Platelet count</th>
<th>D-dimer</th>
<th>Prothrombin time</th>
<th>Troponin (hs-TnI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Setting of comparison</td>
<td>Setting of comparison</td>
<td>Setting of comparison</td>
<td>Setting of comparison</td>
</tr>
<tr>
<td></td>
<td>ICU vs. non-ICU</td>
<td>Severe vs. nonsevere</td>
<td>ICU vs. non-ICU</td>
<td>ICU vs. non-ICU</td>
</tr>
<tr>
<td>Han et al.,</td>
<td>ICU vs. non-ICU</td>
<td>Dead vs. alive</td>
<td>ICU vs. non-ICU</td>
<td>Dead vs. alive</td>
</tr>
<tr>
<td>2020 (24)</td>
<td>(N = 94)</td>
<td>2.4 (0.6-14.4)</td>
<td>5.2 (1.5-21.1)</td>
<td>12.7 (11.2-13.4)</td>
</tr>
<tr>
<td>(N = 41)</td>
<td></td>
<td>vs. 0.5 (0.3-1.0)</td>
<td>vs. 0.6 (0.3-1.0)</td>
<td>vs. 10.7 (9.8-12.1)</td>
</tr>
<tr>
<td>Zhou et al.,</td>
<td>Dead vs. alive</td>
<td>12.9 (2.9)</td>
<td>12.1 (11.2-13.7)</td>
<td>12.2 (11.2-13.4)</td>
</tr>
<tr>
<td>2020 (19)</td>
<td>(N = 191)</td>
<td>vs. 10.9 (10.4-12.6)</td>
<td>vs. 11.4 (10.4-12.6)</td>
<td>vs. 10.7 (9.8-12.1)</td>
</tr>
<tr>
<td>(N = 138)</td>
<td></td>
<td>(2.7)</td>
<td>(1.2)</td>
<td>(2.7)</td>
</tr>
<tr>
<td>Wu et al.,</td>
<td>Dead vs. alive</td>
<td>11.3 (1.4)</td>
<td>13.2 (12.3-14.5)</td>
<td>15.5 (14.4-16.3)</td>
</tr>
<tr>
<td>2020 (10)</td>
<td>(N = 201)</td>
<td>vs. 12.0 (12.0)</td>
<td>vs. 12.9 (12.3-13.4)</td>
<td>vs. 11.8 (11.0-12.5)</td>
</tr>
<tr>
<td>(N = 183)</td>
<td></td>
<td>(1.2)</td>
<td>(13.4)</td>
<td>(11.0-12.5)</td>
</tr>
<tr>
<td>Lippi et al.,</td>
<td>Dead vs. alive</td>
<td>0.5 (0.3-0.9)</td>
<td>0.4 (0.2-1.3)</td>
<td>11.6 (11.1-12.5)</td>
</tr>
<tr>
<td>2020 (22)</td>
<td>(N = 1,779)</td>
<td>vs. 0.2 (0.2-0.3)</td>
<td>vs. 0.2 (0.1-0.3)</td>
<td>vs. 11.8 (11.0-12.5)</td>
</tr>
<tr>
<td>(N = 553)</td>
<td></td>
<td>(0.2-0.3)</td>
<td>(0.1-0.3)</td>
<td>(11.0-12.5)</td>
</tr>
<tr>
<td>Lippi and</td>
<td>Severe vs. nonsevere</td>
<td>4.0 (1.0-11.0)</td>
<td>2.1 (1.0-5.3)</td>
<td>13.6 (13.0-14.0)</td>
</tr>
<tr>
<td>Favaoro, 2020</td>
<td>3.0 (2.5-3.5)*</td>
<td>vs. 0.5 (0.3-1.2)</td>
<td>vs. 0.6 (0.4-1.3)</td>
<td>vs. 13.6 (13.0-14.0)</td>
</tr>
<tr>
<td>(N = 341)</td>
<td></td>
<td>(0.3-1.2)</td>
<td>(0.4-1.3)</td>
<td></td>
</tr>
</tbody>
</table>

*Mean difference, results from meta-analysis data. **Subgroup analysis of 3 studies.
COVID-19 = coronavirus disease-2019; DIC = disseminated intravascular coagulation; hs-TnI = high-sensitivity troponin I; other abbreviations as in Table 1.
## COVID-19 Coagulopathy

### Burden of Thrombosis

<table>
<thead>
<tr>
<th>STUDY, COUNTRY</th>
<th>DESIGN</th>
<th>POPULATION</th>
<th>N</th>
<th>TPX</th>
<th>SCREENING</th>
<th>VTE RATE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cui, China</strong></td>
<td>Retrospective</td>
<td>ICU</td>
<td>81</td>
<td>No</td>
<td>No</td>
<td>25%</td>
</tr>
<tr>
<td><strong>Helms, France</strong></td>
<td>Prospective</td>
<td>ICU</td>
<td>150</td>
<td>Yes</td>
<td>No</td>
<td>16.7%* vs 2.1%</td>
</tr>
<tr>
<td><strong>Klok, The Netherlands</strong></td>
<td>Retrospective</td>
<td>ICU</td>
<td>184</td>
<td>Yes</td>
<td>No</td>
<td>31%</td>
</tr>
<tr>
<td><strong>Llitjos, France</strong></td>
<td>Retrospective</td>
<td>ICU</td>
<td>26</td>
<td>Yes</td>
<td>Yes</td>
<td>69%</td>
</tr>
<tr>
<td><strong>Lodigiani, Italy</strong></td>
<td>Retrospective</td>
<td>Inpatient</td>
<td>388</td>
<td>Yes</td>
<td>No</td>
<td>21%</td>
</tr>
<tr>
<td><strong>Poissy, France</strong></td>
<td>Retrospective</td>
<td>ICU</td>
<td>107</td>
<td>Yes</td>
<td>No</td>
<td>20.6%* vs 6.1%</td>
</tr>
<tr>
<td><strong>Thomas, United Kingdom</strong></td>
<td>Retrospective</td>
<td>ICU</td>
<td>63</td>
<td>Yes</td>
<td>No</td>
<td>29%</td>
</tr>
</tbody>
</table>

*Pulmonary Embolism only*
Autopsy Evidence

D. Wichmann et al., Germany

Prospective Study

Compare clinical findings with data from autopsy

Results

7/12 patients had unsuspected bilateral DVT
4/7 died from PE
6/9 men had fresh thrombi in prostatic venous plexus

<table>
<thead>
<tr>
<th>Marker (Median)</th>
<th>No thrombotic/bleeding complication (n=347)</th>
<th>Thrombotic complication (n=38)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>D-dimer</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Initial</td>
<td>891</td>
<td>1538</td>
</tr>
<tr>
<td></td>
<td>Minimum</td>
<td>760</td>
<td>1336</td>
</tr>
<tr>
<td></td>
<td>Peak</td>
<td>1377</td>
<td>4001</td>
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<tr>
<td><strong>Fibrinogen</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Initial</td>
<td>579</td>
<td>696</td>
</tr>
<tr>
<td></td>
<td>Minimum</td>
<td>549</td>
<td>669</td>
</tr>
<tr>
<td></td>
<td>Peak</td>
<td>662</td>
<td>828</td>
</tr>
<tr>
<td><strong>C-Reactive Protein</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Initial</td>
<td>63.3</td>
<td>124.7</td>
</tr>
<tr>
<td></td>
<td>Minimum</td>
<td>35.4</td>
<td>94.2</td>
</tr>
<tr>
<td></td>
<td>Peak</td>
<td>130.3</td>
<td>277.7</td>
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<tr>
<td><strong>ESR</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Initial</td>
<td>38</td>
<td>47</td>
</tr>
<tr>
<td></td>
<td>Minimum</td>
<td>36</td>
<td>43</td>
</tr>
<tr>
<td></td>
<td>Peak</td>
<td>56</td>
<td>91</td>
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<tr>
<td><strong>Ferritin</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Initial</td>
<td>504</td>
<td>825</td>
</tr>
<tr>
<td></td>
<td>Minimum</td>
<td>453</td>
<td>750</td>
</tr>
<tr>
<td></td>
<td>Peak</td>
<td>707</td>
<td>1182</td>
</tr>
</tbody>
</table>
Endotheliitis

- Postulated to be a central feature of pathophysiology
- SARS CoV-2 binds to host cells via the ACE-2 receptor
- High density of ACE 2 receptors on endothelial cells
- Endotheliitis and viral inclusions in endothelial cells have been reported in COVID-19 autopsy series

M Ackermann et al. NEJM 2020
Goshua et al:

- Single center study studied markers of endothelial cell and platelet activation
- Higher levels associated with more severe disease (ICU admission) and mortality

<table>
<thead>
<tr>
<th></th>
<th>Standard reference range, or measurements from the control cohort (n=13)</th>
<th>ICU (n=48)</th>
<th>Non-ICU (n=20)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>D-dimer, mg/L FEU</td>
<td>&lt;0.55</td>
<td>4.2 (2.6–6.9)</td>
<td>0.7 (0.4–1.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>TAT, μg/L</td>
<td>&lt;4</td>
<td>10.6 (7.1–18.4)</td>
<td>7.2 (4.7–11.3)</td>
<td>0.020</td>
</tr>
<tr>
<td>Antithrombin activity</td>
<td>70–133%</td>
<td>102% (32)</td>
<td>111% (13)</td>
<td>0.12</td>
</tr>
<tr>
<td>Protein C activity</td>
<td>81–145%</td>
<td>121% (97–150)</td>
<td>106% (92–130)</td>
<td>0.46</td>
</tr>
<tr>
<td>Protein S activity</td>
<td>62–166%</td>
<td>100% (30)</td>
<td>93% (22)</td>
<td>0.32</td>
</tr>
<tr>
<td>α2-antiplasmin activity</td>
<td>72–122%</td>
<td>112% (24)</td>
<td>113% (10)</td>
<td>0.77</td>
</tr>
<tr>
<td>PAI-1, ng/mL</td>
<td>4–43</td>
<td>58 (47–88)</td>
<td>54 (44–89)</td>
<td>0.65</td>
</tr>
<tr>
<td>VWF antigen</td>
<td>62–175%</td>
<td>565% (199)</td>
<td>278% (133)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>VWF activity</td>
<td>58–163%</td>
<td>390% (390–390)</td>
<td>260% (145–323)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Factor VIII activity</td>
<td>66–143%</td>
<td>398% (111)</td>
<td>251% (90)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Soluble P-selectin, ng/mL*</td>
<td>9.5 (8.5–11.3)†</td>
<td>15.9 (4.8)</td>
<td>11.2 (3.1)</td>
<td>0.0014</td>
</tr>
<tr>
<td>Soluble thrombomodulin, ng/mL*</td>
<td>2.5 (2.2–3.3)†</td>
<td>4.2 (2.6–6.5)</td>
<td>3.0 (2.6–3.2)</td>
<td>0.23</td>
</tr>
<tr>
<td>sCD40L, pg/mL*</td>
<td>67 (33–98)†</td>
<td>136 (82–228)</td>
<td>157 (85–211)</td>
<td>0.80</td>
</tr>
</tbody>
</table>

Data are mean (SD) or median (IQR), unless specified otherwise. p values are for comparison between ICU and non-ICU patients. ICU=intensive care unit. FEU=fibrinogen equivalent units. TAT=thrombin-antithrombin complex. PAI-1=plasminogen activator inhibitor-1. VWF=von Willebrand factor. sCD40L=soluble CD40 ligand. *Measured in 40 ICU and ten non-ICU patients. †Median values measured in the control cohort (n=13).
Neutrophils (to a lesser extent, monocytes and eosinophils), release extracellular traps in response to strong stimulation

NETs cause endothelial cell, platelet and factor XII activation resulting in thrombosis

NETs Inhibit anticoagulant activity of TFPI >> thicker fibrin strands resistant to fibrinolysis

Neutrophil aggregates and NETs occlude pulmonary microvasculature

Virchow’s Triad IN COVID-19

Vascular Endotheliitis

Platelet Activation
Viral RNA
DNA-NETS
VWF
Factor Xla
Thrombin-Fibrin

Endothelial Dysfunction
Altered Blood Flow

https://doi.org/10.1007/s11239-020-02134-3
Anticoagulation Evidence in COVID-19

Deepak Pradhan, MD, FCCP
Anticoagulation Evidence in COVID-19

Received: 20 March 2020 | Accepted: 24 March 2020
DOI: 10.1111/jth.14817

ORIGINAL ARTICLE

Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy

Ning Tang¹ | Huan Bai¹ | Xing Chen¹ | Jiale Gong¹ | Dengju Li² | Ziyong Sun¹

Single center retrospective cohort study at Tongji Hospital in Wuhan, China

449 hospitalized severe COVID adult patients (RR≥30, Sao2 ≤93% at rest, P/F ≤300)

Methods:
- 99 patients received prophylactic heparin/LMWH for 7 days or more
  - authors do not specify why DVT prophylaxis is not their standard of care for hospitalized patients, just that DVTs occur less in Asians.

Results:
- 28-day mortality was the same for heparin-users and non-users (30% for both groups)
  - If patients were re-stratified by D-dimer level >3000 ng/mL, then heparin users had a lower 28-day mortality rate (33 vs. 52%, p=0.017).
Limitations:

- Single center, retrospective design
- No mortality difference in less sick patients
- Minority (only 22%) received thromboprophylaxis; don’t know how/why these patients received it [potential selection bias]
- Prophy was ≥ 7 days [introduces immortal time bias]
- Not controlled for confounders
Association of Treatment Dose Anticoagulation With In-Hospital Survival Among Hospitalized Patients With COVID-19

Design:
• Single-center retrospective cohort study at Mount Sinai Health System, NYC, 03-4/11/2020
Results:

- 2773 patients, median 5 days hospitalization
- 28% received therapeutic AC, median duration 3 days of AC
- In-hospital mortality 23% for both groups
- Median survival 21 days (AC group), 14 days (non-AC group)
- Mechanical ventilation 30% (AC group), 8% (non-AC group), p<0.001  [n= 395]
  - In-hospital mortality 29% and median survival 21 days (AC group), 63% and 9 days (non-AC group)
- Multivariate Cox proportional hazards model: longer duration of AC associated with reduced mortality risk (adjusted HR 0.86/day, p<0.001)
- Major bleeding in 3% (AC group), 1.9% (non-AC group)
Limitations:

- Single center, retrospective design
- Unknown indication for AC (indication bias)
- AC agents and dosing not defined
- Duration of therapeutic AC only 3 days?!
- Prophylactic AC not articulated
- Patients not classified regarding illness severity
- Immortal time bias
- Confounders
Anticoagulation Evidence in COVID-19

Design:

• Two-center (Western Connecticut) retrospective cohort study 4/1/2020 - 4/25/2020
**Methods:**

- Patients received either prophy or therapeutic AC (heparin/LMWH) started at the time of hospital admission
- Of note, excluded therapeutic AC for thrombotic indication
- Prophy group received only prophy dosing for whole inpatient duration

**Results:**

- 374 patients (299 prophy group, 75 therapeutic group)
- Article does not mention why these 75 received therapeutic AC
Results (continued):

• Logistic model included: AC dosage, age, ethnicity, diabetes, history of cancer or heart disease, hyperlipidemia, peak CRP, intensive care, mechanical ventilation, and antibiotic use

• Risk of mortality was higher (aRR = 2.3, 95% CI = 1.0, 4.9, p = 0.04) for patients on therapeutic AC as compared to prophylactic AC

Limitations:

• Retrospective design
• Western Connecticut (older population, majority white) [questions generalizability]
• Unknown indication for therapeutic AC (indication bias)
• Duration of therapeutic AC not defined
• Patients not classified regarding illness severity; Prophy group 12% ICU and 7% mechanical ventilation; Therapeutic group 36% ICU and 31% mechanical ventilation
• No report of bleeding complications
• Confounders

Anticoagulation Evidence in COVID-19

Thromboprophylaxis

Acutely ill hospitalized COVID-19 patients (in the absence of contraindications) should receive anticoagulant thromboprophylaxis

- LMWH, UFH, Fondaparinux

American Society of Hematology
International Society on Thrombosis and Haemostasis
American College of Cardiology
National Institute of Health
CHEST

Areas for Future Research

- Outpatients (no trials yet addressing thromboprophylaxis in COVID-19 outpatients)
- Better defining the subpopulation at-risk for both macro and micro thrombi, and thus identifying subgroup most to benefit from therapeutic AC
- Validating bleeding risk scores in COVID-19 patients, and thus identifying subgroups at greatest risk of harm from therapeutic AC
- Dose of therapeutic AC/target goals
- Role for antiplatelet therapy
- Post-discharge therapeutic or prophylactic AC


Institutional Protocols

Vikram Mukherjee, MD
# Institution #1’s Approach

## D-dimer <500

**Prophylactic Anticoagulation**

- **Enoxaparin subp preferred**
  - Dose w/CrCl ≥ 30 mL/min
    - <150 kg: 40 mg daily or 30 mg q12h
    - BMI 40-50: 40 mg q12h
    - BMI > 50: 60 mg q12h
- **Dose w/CrCl <30 mL/min**
  - <150 kg: 30 mg daily
  - BMI 40-50: 40 mg daily
  - BMI > 50: 60 mg daily
- **Heparin subq** If anuric/ESRD/AKI
  - 50-150kg: 5000 units q8h
  - <50kg: 5000 units 12h
  - BMI >40: 7500 units q8h

## D-dimer 500-2000

**Equipoise**

- **Consider RCT: PROTECT-COVID-19**
  - Prophylactic AC vs. therapeutic AC
  - Refer to Study Protocol
  - Prophylactic AC as reflected in D-dimer <500 box
  - **Therapeutic AC:**
    - Enoxaparin 1 mg/kg q12h
    - IV Heparin at 10 u/kg/hr titrate to antiXa 0.3-0.5 U/mL

*If not in trial, use Prophylactic Anticoagulation as reflected in D-dimer <500 box*

**Therapeutic AC may be considered if HIGH suspicion for DVT/PE**

## D-dimer >2,000 & <10,000

**Consider Therapeutic AC**

- **Enoxaparin subp preferred**
  - Dose w/CrCl ≥ 30 mL/min
    - <150 kg: 1mg/kg q12h
    - BMI >40: 0.75 mg/kg q12h - consider antiXa peak monitoring
  - **Dose w/CrCl <30 mL/min**
    - <150 kg: 1mg/kg Qday
    - BMI > 40: 0.75 mg/kg Qday

**If enoxaparin contraindicated**

- IV Heparin at 10 units/kg/hr titrate to antiXa 0.3-0.5 U/mL – avoid bolus dose
  - **Alternatively**
    - Consider RCT: PROTECT-COVID-19
      - Prophylactic vs. therapeutic AC

## D-dimer >10,000

**Therapeutic AC Preferred**

- **Enoxaparin subp preferred**
  - Dose w/CrCl ≥ 30 mL/min
    - <150 kg: 1mg/kg BID
    - BMI >40: 0.75 mg/kg BID - consider antiXa peak monitoring
  - **Dose w/CrCl <30 mL/min**
    - <150 kg: 1mg/kg Q24h
    - BMI > 40: 0.75 mg/kg Q24h

**If enoxaparin contraindicated**

- IV Heparin at 10 units/kg/hr titrate to antiXa 0.3-0.5 U/mL – avoid bolus dose if PE not confirmed by CT
Institution #2’s Approach

Prophylactic anticoagulation in all patients unless absolute contraindication

Threshold for initiation of therapeutic anticoagulation:
- Objective evidence of clot
- D-Dimer >5000
- D-Dimer >3000
  - That is also increasing by >1,000 in the prior 24 hours
- D-Dimer >1000
  - Beside DVT study

Daily risk/benefit assessment
<table>
<thead>
<tr>
<th>LEVEL 1</th>
<th>For patients without known thrombus AND a D-dimer &lt; 3,000:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Standard prophylaxis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>LEVEL 2</th>
<th>For patients without known thrombus AND a D-dimer ≥ 3,000*:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Intermediate dosing</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>LEVEL 3</th>
<th>For patients with known or suspected VTE, or otherwise unexplained increase in oxygen requirement, dead space, or organ failure (e.g., AKI, MSOF) with concern for microvascular thrombi</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Therapeutic dosing</td>
</tr>
<tr>
<td>Condition</td>
<td></td>
</tr>
<tr>
<td>---------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Venous or arterial thrombosis</td>
<td></td>
</tr>
<tr>
<td>Disseminated intravascular coagulation</td>
<td></td>
</tr>
<tr>
<td>Advanced age</td>
<td></td>
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<tr>
<td>Recent surgery or trauma</td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td></td>
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<tr>
<td>Pregnancy or puerperium</td>
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</tr>
<tr>
<td>Infection</td>
<td></td>
</tr>
<tr>
<td>Chronic inflammation</td>
<td></td>
</tr>
<tr>
<td>Liver disease</td>
<td></td>
</tr>
<tr>
<td>Renal disease</td>
<td></td>
</tr>
<tr>
<td>Thrombolytic therapy</td>
<td></td>
</tr>
</tbody>
</table>

Venous or arterial thrombosis
Disseminated intravascular coagulation
Advanced age
Recent surgery or trauma
Cancer
Pregnancy or puerperium
Infection
Chronic inflammation
Liver disease
Renal disease
Thrombolytic therapy

Table 1. Diagnoses on discharge of patients with an extremely elevated D-dimer

<table>
<thead>
<tr>
<th>Diagnosis (multiple diagnoses possible in a single case)</th>
<th>Total</th>
<th>5000 - &lt;20,000 µg/l</th>
<th>&gt;20,000 µg/l</th>
<th>Mean D-dimer µg/l (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category</td>
<td>n %</td>
<td>n = 587</td>
<td>n = 459</td>
<td>n = 122</td>
</tr>
<tr>
<td>Disorders known to cause diffuse intravascular coagulation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td>168 (28.9%)</td>
<td>25.9% (119)</td>
<td>40.7% (49)</td>
<td>22.957 (120.321)</td>
</tr>
<tr>
<td>Infection</td>
<td>143 (24.4%)</td>
<td>24.6% (110)</td>
<td>26.6% (34)</td>
<td>18.64 (85.354)</td>
</tr>
<tr>
<td>Total</td>
<td>272 (46.8%)</td>
<td>45.2% (200)</td>
<td>50.9% (70)</td>
<td>20.037 (25.885)</td>
</tr>
<tr>
<td>Venous thromboembolism</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>183 (31.5%)</td>
<td>35.3% (165)</td>
<td>16.4% (20)</td>
<td>14.414 (99.797)</td>
</tr>
<tr>
<td>DVT</td>
<td>73 (12.6%)</td>
<td>12.9% (39)</td>
<td>11.5% (14)</td>
<td>13.721 (15.865)</td>
</tr>
<tr>
<td>Total</td>
<td>256 (44.1%)</td>
<td>35.3% (203)</td>
<td>21.6% (10)</td>
<td>11.313 (11.419)</td>
</tr>
<tr>
<td>Trauma/surgery</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trauma</td>
<td>87 (15.0%)</td>
<td>12.4% (57)</td>
<td>24.6% (10)</td>
<td>24.218 (13.444)</td>
</tr>
<tr>
<td>Recent surgery</td>
<td>58 (10.0%)</td>
<td>9.8% (49)</td>
<td>10.7% (13)</td>
<td>17.399 (17.720)</td>
</tr>
<tr>
<td>Total</td>
<td>145 (25.0%)</td>
<td>14.3% (101)</td>
<td>33.6% (41)</td>
<td>20.188 (27.818)</td>
</tr>
<tr>
<td>Dissection / aneurysm</td>
<td>35 (6.0%)</td>
<td>5.7% (26)</td>
<td>7.4% (9)</td>
<td>19.793 (19.519)</td>
</tr>
<tr>
<td>Thrombotic microangiopathies</td>
<td>15 (2.6%)</td>
<td>2.0% (9)</td>
<td>4.9% (6)</td>
<td>24.846 (33.449)</td>
</tr>
<tr>
<td>Stroke</td>
<td>3 (0.5%)</td>
<td>0.3% (1)</td>
<td>-</td>
<td>6230 (8.841)</td>
</tr>
<tr>
<td>Total</td>
<td>15 (2.5%)</td>
<td>1.5% (7)</td>
<td>6.6% (8)</td>
<td>25.544 (23.331)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>14 (2.4%)</td>
<td>3.1% (14)</td>
<td>-</td>
<td>9610 (8.32)</td>
</tr>
<tr>
<td>Auto-immune diseases</td>
<td>14 (2.4%)</td>
<td>1.7% (8)</td>
<td>4.9% (6)</td>
<td>16.813 (14.687)</td>
</tr>
<tr>
<td>Acute coronary syndrome</td>
<td>11 (1.9%)</td>
<td>2.4% (13)</td>
<td>-</td>
<td>10.975 (4.820)</td>
</tr>
<tr>
<td>Arterial thrombus</td>
<td>8 (1.4%)</td>
<td>1.7% (5)</td>
<td>-</td>
<td>9720 (4577)</td>
</tr>
<tr>
<td>Pre-eclampsia</td>
<td>4 (0.7%)</td>
<td>0.9% (4)</td>
<td>-</td>
<td>14445 (7148)</td>
</tr>
<tr>
<td>Other**</td>
<td>30 (5.2%)</td>
<td>5.4% (24)</td>
<td>4.9% (6)</td>
<td>11.880 (13.595)</td>
</tr>
<tr>
<td>No diagnosis</td>
<td>4 (0.7%)</td>
<td>0.7% (3)</td>
<td>0.8% (1)</td>
<td>22.970 (38.413)</td>
</tr>
</tbody>
</table>

*The diagnosis ‘Infection’ was registered for patients with a diagnosis of an infectious disease together with a systemic inflammatory response.
**Other includes severe liver failure, childbirth, bleeding or haemorrhage (e.g. subdural haematoma), allergic (anaphylactic) reaction and multiorgan failure (not otherwise specified).
NETEC Resources

Trish Tennill, RN, BSN
NETEC will continue to build resources, develop online education, and deliver technical training to meet the needs of our partners.

**NETEC is Here to Help**

**Ask for help!**

- Send questions to [info@netec.org](mailto:info@netec.org) - they will be answered by NETEC SMEs.
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