Automated Identification of Hospital-Acquired Venous Thromboembolism

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Introduction

- Venous thromboembolism (VTE)
- Present on admission
- Hospital-acquired ← potentially preventable complication
- Decrease of hospital-acquired VTE indicates success of efforts to prevent inpatient VTE
Medium-high expositional risk
non-surgical
- infection or acute inflammation with immobilization
- acute heart failure (NYHA III-IV)
- acute decompensation of chronic obstructive pulmonary disease
- stroke with lower limb paresis
- sepsis
- mechanical ventilation
- severely ill patient in the intensive care unit
surgical
- immobilization of the lower limbs
- arthroscopic surgery of the lower limbs
- major surgery
- major trauma
- cancer surgery

Low expositional risk
non-surgical
- infection or acute inflammation without immobilization
- central venous line or port catheter
surgical
- minor surgery
- trauma with minor tissue damage

Medium-high dispositional risk
- previous thromboembolism
- first grade relatives with thromboembolism
- age ≥60 years
- obesity (BMI ≥30 kg/m²)
- immobilization
- congestive heart failure or previous myocardial infarction
- cancer or myeloproliferative disorder

Low dispositional risk (according to type, substance)
- thrombophilia
- therapy with or inhibition of sex hormones

With or without the following dispositional risk factors
- pregnancy and childbirth
- nephrotic syndrome
- significant varicosity

Anticoagulant thromboprophylaxis (if not contraindicated)

Basic measures:
- early mobilisation
- mobilisation exercises
- When indicated: additional physical methods can be administered for prophylaxis

Contraindications to standard anticoagulant thromboprophylaxis:
- hypersensitivity to unfractionated or low molecular weight heparin
- heparin induced thrombocytopenia
- anti-coagulant medication
<table>
<thead>
<tr>
<th>Event</th>
<th>ICD-10 diagnosis codes</th>
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</thead>
<tbody>
<tr>
<td>Bleeding due to anticoagulants</td>
<td>D68.3*</td>
</tr>
<tr>
<td>Other bleeding events</td>
<td>D69.9*, H11.3*, H31.3*, H35.6*, H43.1*, H45.0*, I60.<em>, I61.</em>, I62.<em>, K22.8</em>, K62.5*, K66.1*, K92.0*, K92.1*, K92.2*, M25.0*, R04.<em>, R23.3</em>, R31, R58</td>
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<tr>
<td>Heparin-induced thrombocytopenia</td>
<td>D69.53</td>
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<tr>
<td>VTE</td>
<td>I26.<em>, I80.1</em>, I80.2*, I80.3*, I80.8*, I80.9*, I82.1*, I82.2*, I82.3*, I82.8*, I82.9*, 022.3*, 087.1*, 088.2*</td>
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</tbody>
</table>

The * character is used as a wildcard that matches zero or more numeric digits. ICD, International Classification of Diseases; VTE, venous thromboembolism.

Clinical outcome assessment

<table>
<thead>
<tr>
<th>Intervention group</th>
<th>Baseline period</th>
<th>Reminder period</th>
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<tbody>
<tr>
<td></td>
<td># of patients</td>
<td>%</td>
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<tr>
<td>Bleeding due to anticoagulants</td>
<td>6</td>
<td>0.18</td>
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<tr>
<td>Other bleeding event</td>
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<td>0.87</td>
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<td>Heparin-induced thrombocytopenia</td>
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<td>VTE event</td>
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<td>Total number of patients</td>
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<table>
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<th>Control group</th>
<th>Baseline period</th>
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<td>4256</td>
<td>100</td>
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</tbody>
</table>

Hospitalized patients

- Admission
  - VTE present on admission (may be reason for admission)
- Intravenous heparin
- Order entry
- Hospital-acquired VTE (complication)
- Discharge
Hospitalized patients

Order entry

Admission

VTE present on admission (may be reason for admission)

Hospital-acquired VTE (complication)

Discharge
Inclusion criteria

- Inpatients
- Discharged from Brigham and Women’s Hospital between January 2009 and April 2014
- Length of stay ≥24 hours
- With acute venous thrombosis or pulmonary embolism (ICD-9 codes)
- In “admitting diagnosis field” (i.e. “present on admission”), or in one of up to 50 discharge diagnoses
- Patients received either heparin, dalteparin, enoxaparin, alteplase, rivaroxaban or fondaparinux
Structured predictors

- Drug orders (heparin, dalteparin, enoxaparin, alteplase, rivaroxaban, fondaparinux)
- Route of administration
- Dose information (high vs. low vs. “on median”)
- Time from admission to order entry for each considered drug therapy
- Demographics (age, gender, race, language)
- Length of stay
- Admission service
- Discharge service
- Transfer destination of the patient after discharge
- Patient is alive or died during hospitalization or within 30 days after discharge
Modeling

- Single decision tree using all available predictors
- First random forest (5000 trees) using prospective predictors only (demographics, admission service, time to order a drug, route and dose information for each drug)
- Second random forest (5000 trees) using all available predictors
- Half of the data served as calibration set, half as validation set
- R version 3.1.0 (R Foundation for Statistical Computing, Vienna, Austria)
- Presentation of accuracy and positive predictive value (PPV)
Results

- A total of 5374 patients were included

VTE present on admission:
- 1262 patients (23.5%)
- Median time to order drug therapy was 2.5h (IQR 1.3-5.0)

Hospital-acquired VTE:
- 4112 patients (76.5%)
- Median time to order drug therapy was 4.2h (IQR 1.7-18.2)
Decision tree

- Using all available predictors
- Accuracy of 78.8%
- PPV of 83.3% for the classification of hospital-acquired VTE
Heparin IV (no unit), ordering time >8h after admission, or no such order

- yes: Hospital-acquired VTE
- no (heparin IV <8h)
  - Length of stay <6.8d
    - yes: VTE present on admission
    - no (length of stay >6.8d)
      - Hospital-acquired VTE

PPV of 83.3%
First random forest

- Only prospective predictors, available in real time (i.e. demographics, admission service, time to order a drug, route and dose information for each drug)
- Accuracy of 79.7%
- PPV of 85.3% for the classification of hospital-acquired VTE
Second random forest

- Using all available predictors
- Accuracy of 81.7%
- PPV of 87.8% for the classification of hospital-acquired VTE
Conclusions

- The presented decision tree, considering the first order for intravenous heparin and the length of stay, could immediately be implemented as a first step to identifying patients with hospital-acquired VTE.

- Random forests could help to evaluate interventions to improve VTE prophylaxis regimens for inpatients, where costly chart reviews are needed to differentiate between VTE present on admission and potentially preventable complications.