DEM Journal Club

Article Appraisal

Article: Prediction of cerebral venous thrombosis with a new clinical score and D-dimer levels

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Background and Study Objective(s):

- Cerebral Venous Thrombosis (CVT) is a difficult diagnosis to make due to the broad presentation spectrum, and necessity for specialized imaging (CT venogram, MR venogram)
- Clinical syndromes vary with anatomic location of CVST and diagnosis requires high pre-test probability
- The goal of this study was to develop a clinical score to stratify patients into low, moderate, and high risk of CVT, and assess predictive value of D-dimer levels for CVT both alone and combined with clinical score.
- The secondary goals were to assess prevalence of CVT (and anatomic location thereof) vs mimics in symptomatic patients.

Study Design:

This was a prospective multi-centre study, enrolling consecutive patients identified at neurologic emergency departments at UH Bern and Amsterdam.

Inclusion Criteria

- >= 18yo
- Deemed by neurologist to have 1 or more of:
    - Isolated unexpected headache,
    - Headache + focal deficits,
    - Headache + altered level of consciousness,
    - Headache + seizure,
    - Unexplained papilledema

Exclusion Criteria

- Anticoagulation
- Prior deep vein thrombosis, pulmonary embolism, ischemic stroke, or myocardial infarction within 3 months

Protocol

ED patients were seen and evaluated by trained neurologists. Demographic, clinical, and historic features were identified. Patients had labs drawn for D-dimer (ELISA sample), and underwent neuroimaging with MR venogram or CT venogram.

Results:

- 359 patients were enrolled in the study
- 94 were found to have CVT (prevalence of 26%)
- The score was developed with 6 variables that provided the "ideal fit" for the model, scored out of 14 points. Components were weighted according to regression coefficients.
    - Seizure at presentation (4)
    - Known thrombophilia (4)
    - OCP (2)
    - Symptoms greater than 6 days (2)
    - Worst HA ever (1)
    - Focal neuro (1)
- 0-2 pts: low risk, 5.9% had CVT (NPV 94.1%)
- 3-5 pts: moderate, 28.3% had CVT
- 6-14: high, 92.5% had CVT (PPV and spec. 100% for CVT if in 7-14 range)

D-Dimer alone

- D-Dimer sensitivity/specificity crossover at 675. Miss rate 21.3% at this cut-off.
- Youden index best at D-Dimer level of 533. Level of 500 was used due to existing DVT/PE dimer cutoffs. 10.6% of CVTs were missed at this level when used alone.
    - Within clinical low risk group, D-Dimer had NPV 100, sensitivity 100.
    - Within clinical high risk group, 5 patients had negative dimer but imaging + CVT.

Combined

- + Dimer (using either cutoff) adds 3 pts to the clinical score for a total of 17.
- Combined scores with Dimer cutoff of 675 had a CVT miss rate of 10.6% at score of 5
    - Sens 89.4, Spec 83, PPV 65.1, NPV 95.7
- With score of 500, CVT miss rate 17% at score of 6
    - Sens 83, Spec 86.8, PPV 69, NPV 93.5
    - No CVTs missed at low or high ends (0-2, 9-17)

Comments:

- 26% of enrolled patients had CVT - this is far higher than the general ED headache population.
    - Bern and Amsterdam hospitals in trial are tertiary CVD centers.
- 5.9% had CVT in low risk group - this is still unacceptably high for most ED docs.
    - When combined with negative dimer <500, no misses though (in the low probability group)
- Known thrombophilia was identified as a 4-point risk factor, but anticoagulated patients were excluded for an unclear reason. Similar, patients with known clinical manifestations of thrombosis were excluded from the study.

Validity of Results:

- This was a derivation study using a combination of demographic, historic, laboratory, and clinical findings.
- There has not been a validation study done using this clinical prediction score in any set of patients.

Generalizability of Results:

- This is a very different population from what we see in Canadian EDs
- Patients were seen in a “neurologic ED”, resulting in a potential selection bias as patients were directed to specialist-centered EDs by family doctors and internists
- Patient population with 26% prevalence of CVST is much higher than what we see in our EDs
- All patients evaluated by trained neurologists, unlike general headache patients in most EDs

The Bottom Line:

- Mainly clinically scary inclusion criteria - (aLOC/seizures/focal neuro/papilledema) - these patients are likely going to get CTs in most EDs. Non-contrast CT-head may satisfy most searches, but this score may be useful in reaching for the venogram in the high-risk group (9-17 in combined score). Non-contrast CT head has been cited as only 70% sensitivity for CVST.
- Very different population from what we see in Canadian EDs
- Clinical prediction rule has not been validated
- This prediction rule is likely not ready for prime-time, but may be worth re-visiting after validating performance in different clinical context/setting.