Prediction of Cerebral Venous Thrombosis with D-dimer levels and a new clinical score

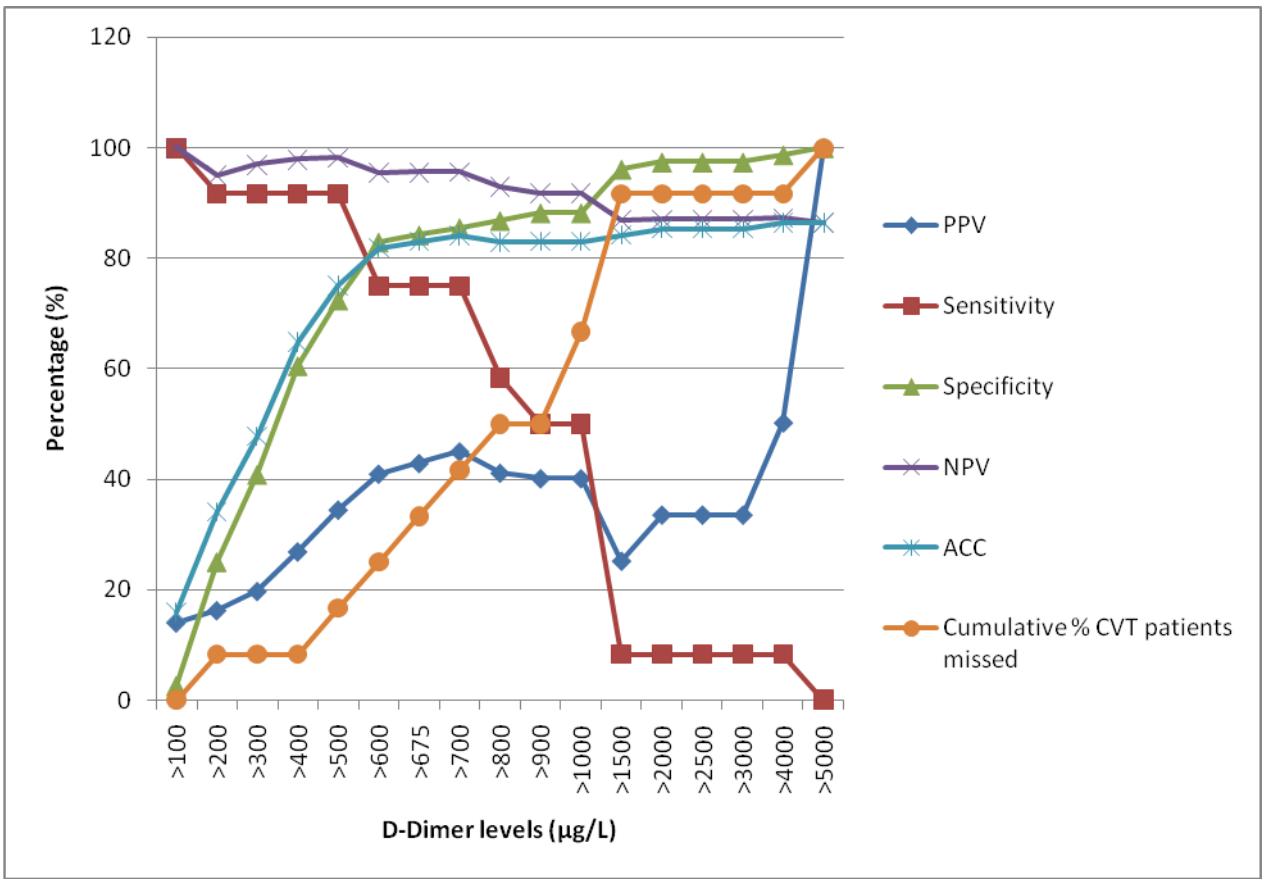
Methods 1. Baseline characteristics, demographic data, risk factors and clinical findings.

	Further description
Age (median, range)	NA
Sex (female)	NA
BMI (median, range)	NA
Time from symptom onset to admission (days, median, range)	NA
Symptom duration • **>6 days**	NA
Ethnic race • **Caucasian** • **Non-Caucasian** – **African** – **Asian** – **Other**	NA
Headache	Pain in the head
Headache, worst ever	Pain in the head, worst ever
Headache, unilateral	Pain in the head, on one side only
Headache, after valsalva	Pain in the head, within minutes after valsalva
Focal neurological deficits	Neurological impairment of a specific area of the body
Seizure(s)	Focal, tonic-clonic and/or status epilepticus
Decreased consciousness	GCS ≤14 points
GCS admission	3-15 points
Visual acuity decreased	Less than 6/6 vision (at 6 meters, a human eye with that performance is able to separate contours that are approximately 1.75 mm apart)
Visual positive phenomena	False visual images
Diplopia or other visual disturbance	Double vision or any other visual disturbance other than decreased visual acuity or visual positive phenomena
Nausea	Feeling of sickness with an inclination to vomit
Vomitus	Matter from the stomach that has come up into and may have been ejected beyond the mouth
Fever	Body temperature >38°C degrees Celsius (>37.5°C if measured axillary)
Infection, local	Infection, in the region of the head or neck
Infection, systemic	Infection, affecting the entire body, rather than a single organ or body part
Previous CVT	NA
Previous DVT	NA
Previous PE	NA
Previous CVT/DVT/PE, ≥ 2 events	NA
Known thrombophilia	Mutations of factor V Leiden and prothrombin, antithrombin III deficiency, protein C or S deficiency, antiphospholipid syndrome, positive Lupus anticoagulant, heparin-induced thrombozytopenia, platelet dysfunction, myeloproliferative disorders, unspecified thrombotic diathesis with recurrent venous thrombotic events
Pregnancy	NA
Recent birth (<1y)	NA
Smoking, present	NA
Smoking, previous	Smoking, not at present but in the past
Malignancy *	Active cancer: treated within 6 months or palliative
Malignancy, active or previous	Active cancer: treated within 6 months or palliative, previous: any previous diagnosis
Vasculitis and/or systemic inflammatory disease	Any inflammation of vessels and/or affecting the entire body, rather than a single organ or body part
Steroids	NA
Hormone replacement	Treatment with hormones to replace natural hormones
Oral contraception	Any birth control estrogen/progesterone intake/application
Head trama (<2w)	Any head contusion, concussion, compression
Neurosurgery (<2w)	Any neurosurgery
Major surgery (<3m)	Any surgery under general anesthesia
Fracture (<1m)	Any fracture
Bedridden (>3d in <2w)	Bound to bed
Thyroid dysfunction	Hypothyroidism or hyperthyroidism
Hypothyroidism	Disorder of the endocrine system in which the thyroid gland does not produce enough thyroid hormone
Hyperthyroidism	Disorder of the endocrine system in which the thyroid gland does produce too much thyroid hormone
Known intracranial hypotension/ LP (<2w)	Negative pressure within the brain cavity, <7 mmHg

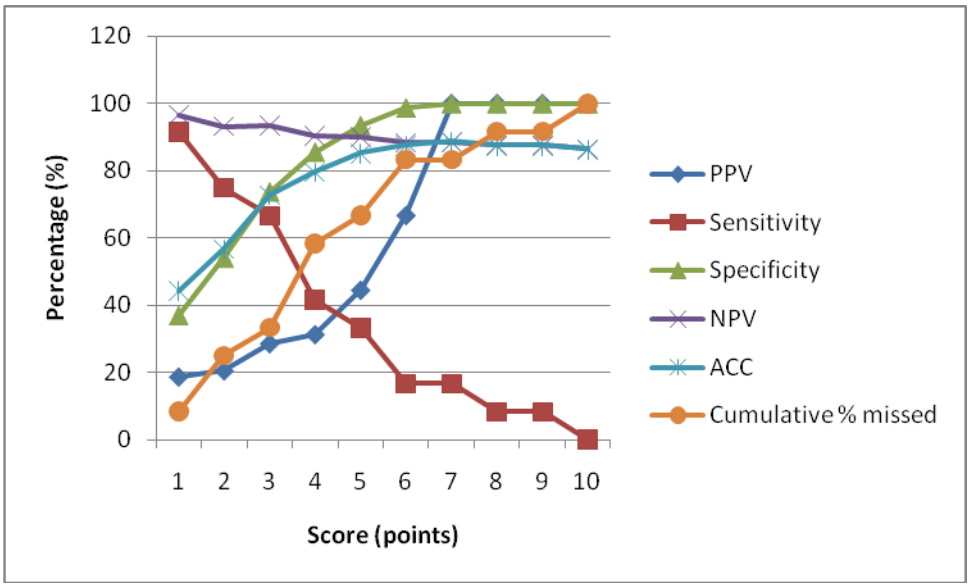
*according to Wells criteria

Figure 1. Subgroup analyses for isolated headache (non-CVT n=76, CVT n=12)

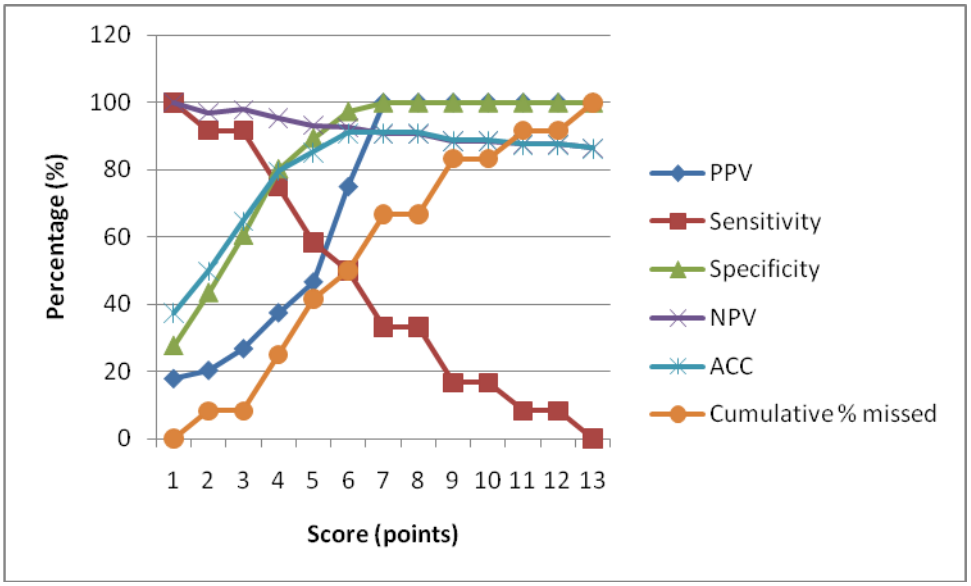
a) Validity of D-dimer levels predicting CVT and cumulative percentage of patients with CVT missed at various D-dimer levels.



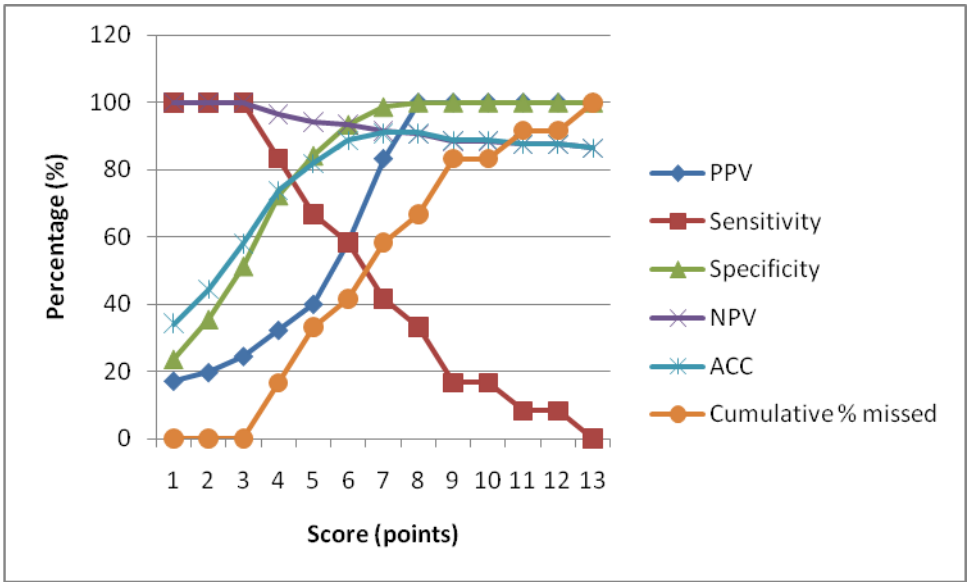
b) Validity of CVT score predicting CVT and cumulative percentage of patients with CVT missed at various score values.



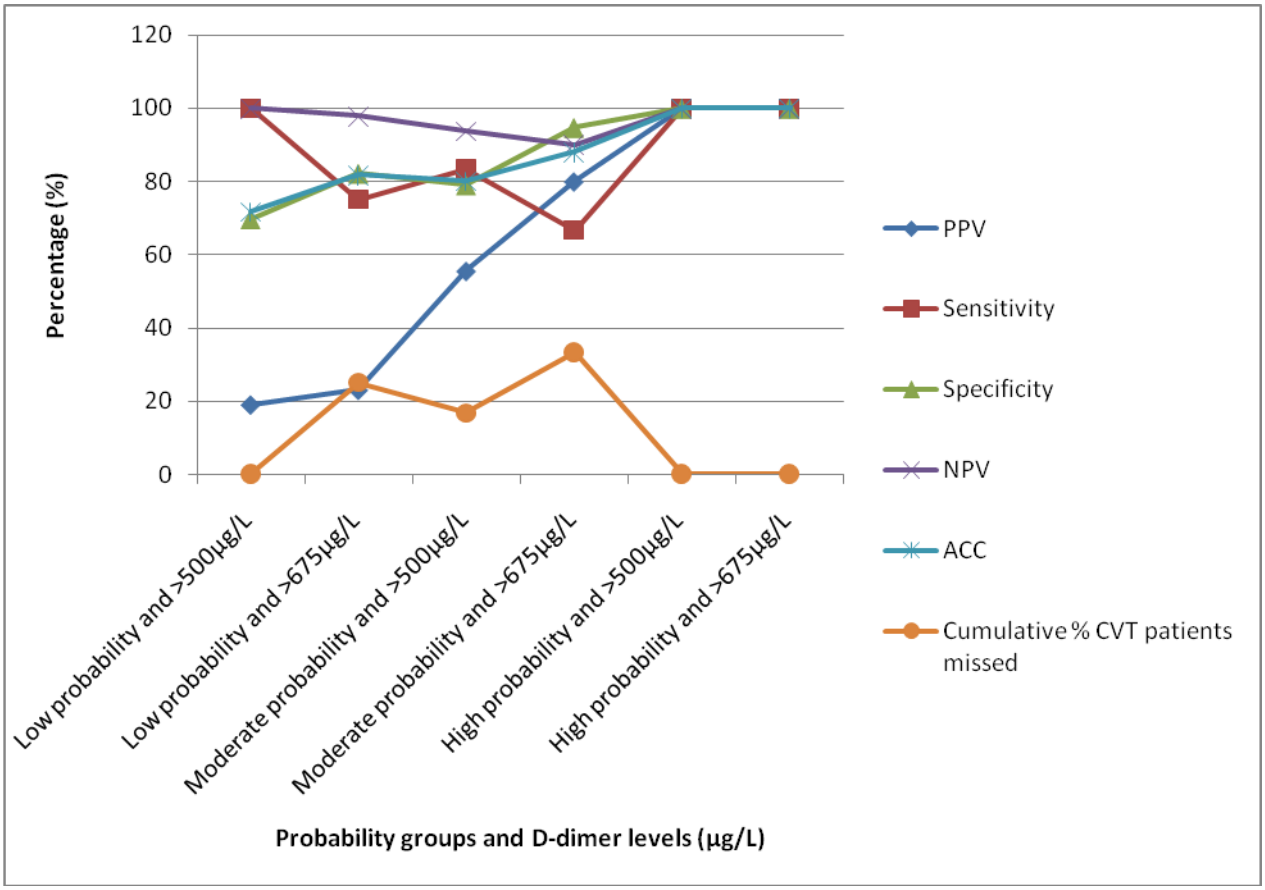
c) Validity of CVT D-dimers (>675µg/L) score predicting CVT and cumulative percentage of patients with CVT missed at various score values.



d) Validity of CVT D-dimers (>500µg/L) score predicting CVT and cumulative percentage of patients with CVT missed at various score values.



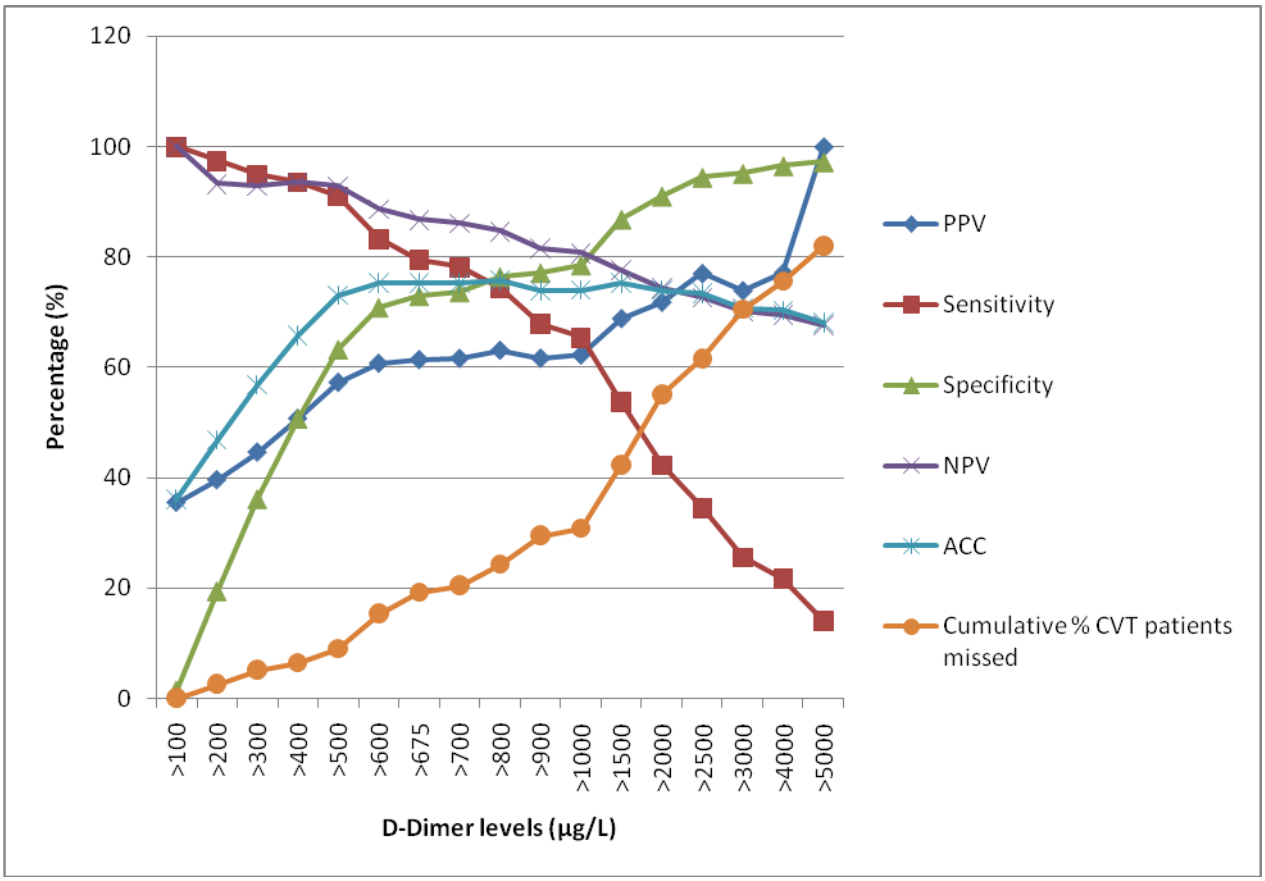
e) D-dimer level cut-offs (>500µg/L and >675µg/L respectively) applied to the different low, moderate and high CVT probability groups for prediction of CVT.



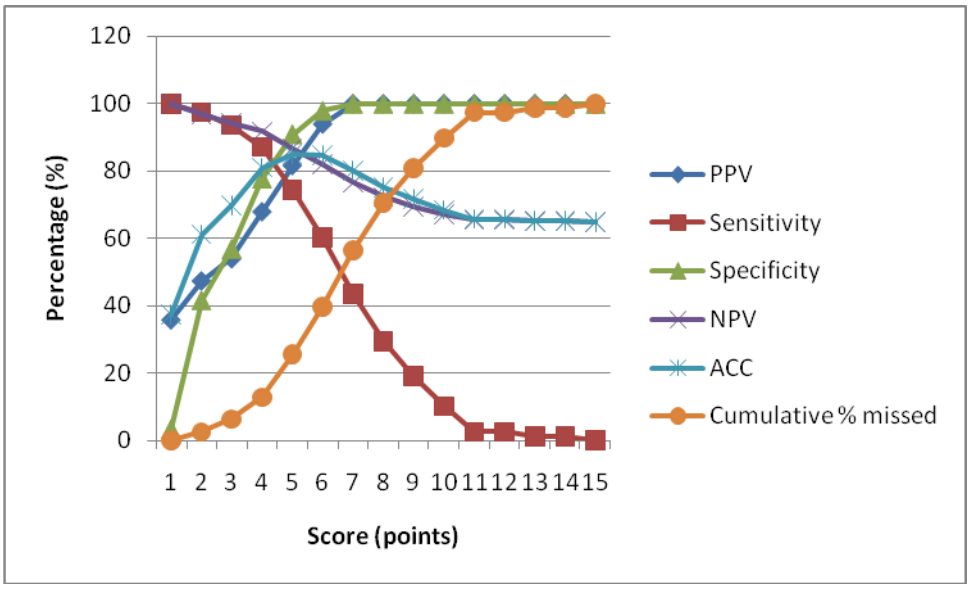
Cut-off (µg/L)	PPV	Sensitivity	Specificity	NPV	ACC	Cumulative % CVT patients missed	Cumulative CVT patients missed
Low probability and >500µg/L	19	100	69.6	100	71.7	0	0
Low probability and >675µg/L	23.1	75	82.1	97.9	81.7	25	1
Moderate probability and >500µg/L	55.6	83.3	78.9	93.8	80	16.7	1
Moderate probability and >675µg/L	80	66.7	94.7	90	88	33.3	2
High probability and >500µg/L	100	100	100	100	100	0	0
High probability and >675µg/L	100	100	100	100	100	0	0

Figure 2. Subgroup analyses for focal neurological deficits and/or seizure(s) and/or disturbed consciousness (non-CVT n=144, CVT n=78)

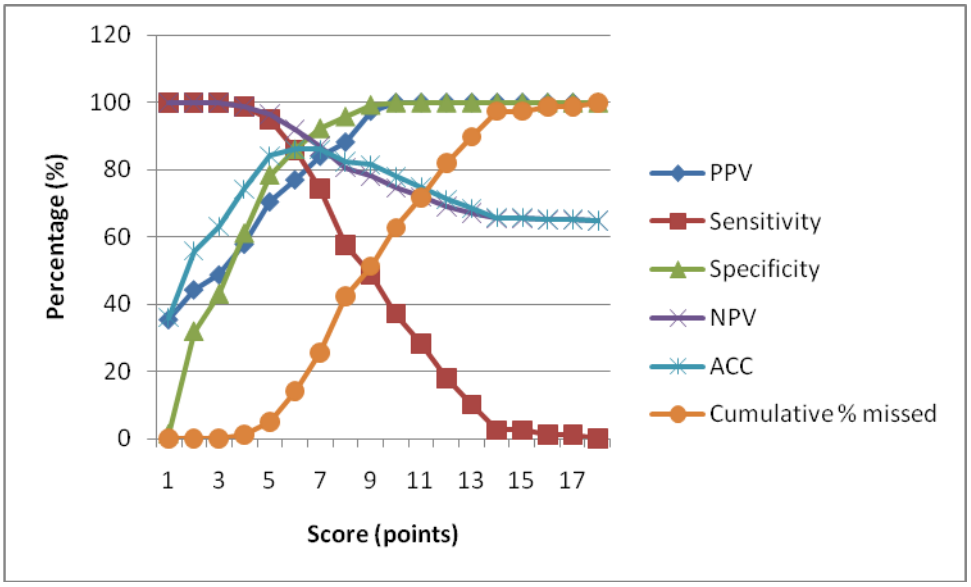
a) Validity of D-dimer levels predicting CVT and cumulative percentage of patients with CVT missed at various D-dimer levels.



b) Validity of CVT score predicting CVT and cumulative percentage of patients with CVT missed at various score values.



c) Validity of CVT D-dimers (>675µg/L) score predicting CVT and cumulative percentage of patients with CVT missed at various score values.



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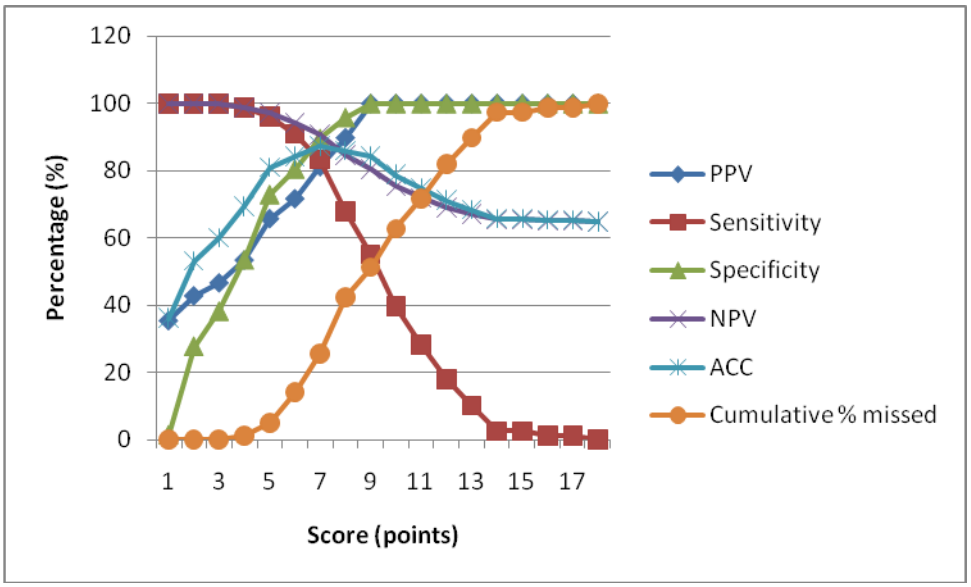
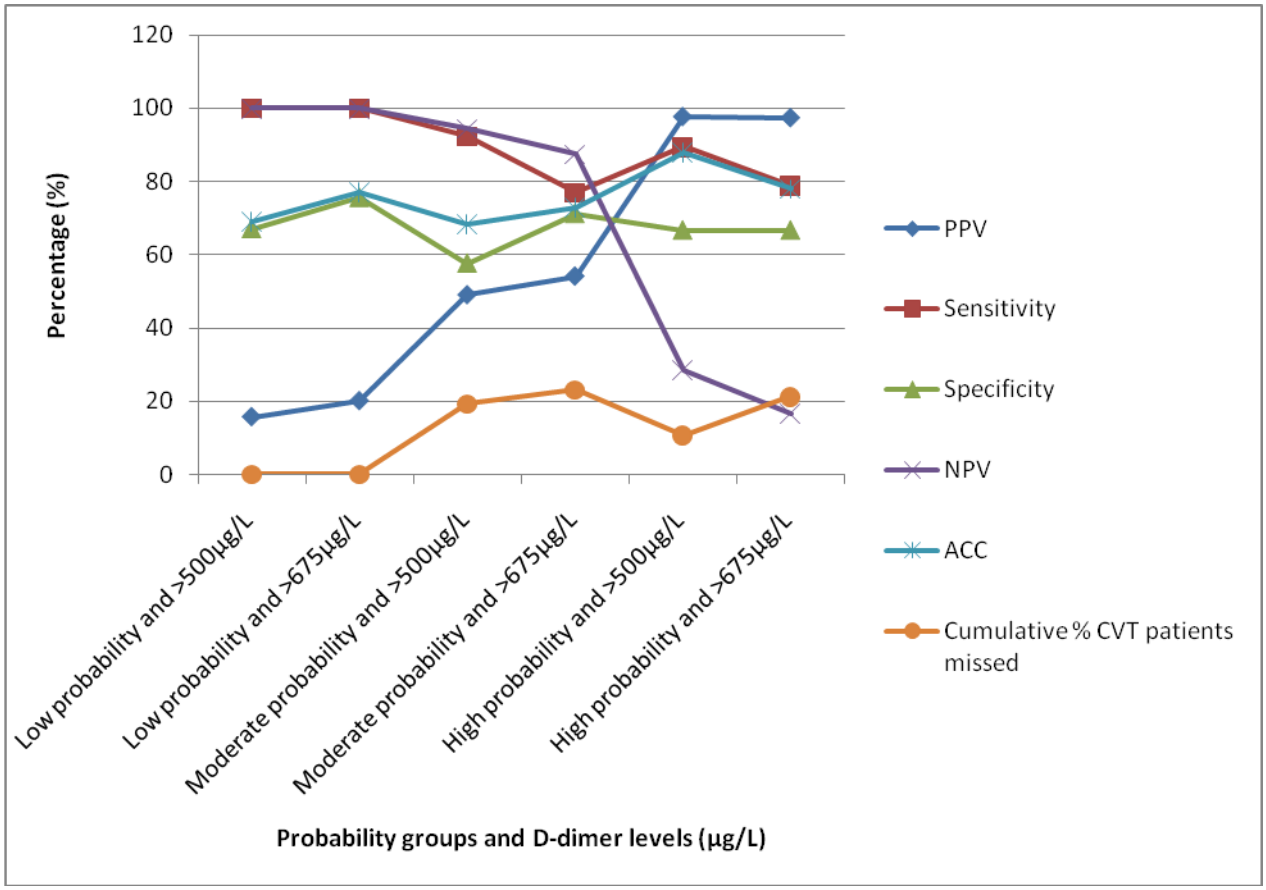


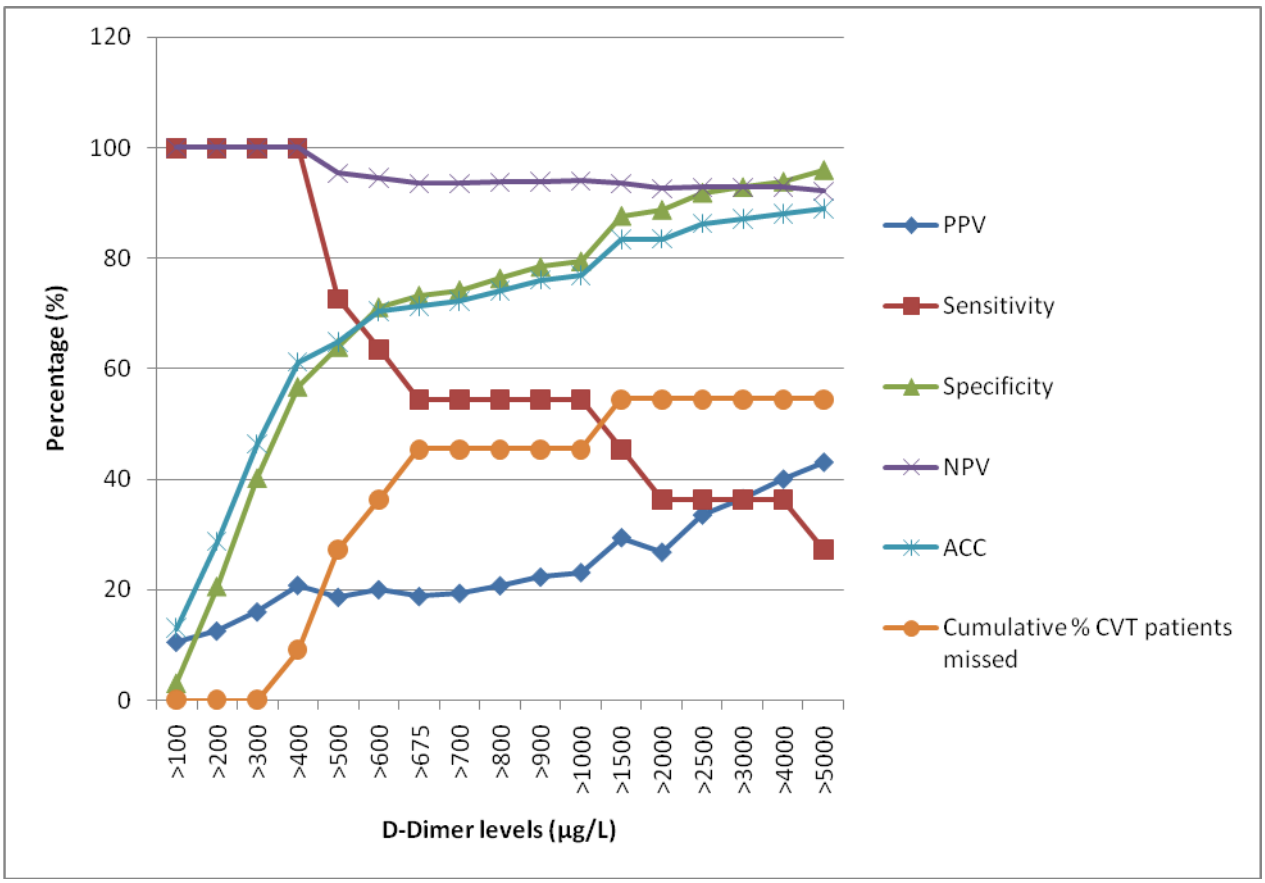
e) D-dimer level cut-offs (>500µg/L and >675µg/L respectively) applied to the different low, moderate and high CVT probability groups for prediction of CVT.



Cut-off (µg/L)	PPV	Sensitivity	Specificity	NPV	ACC	Cumulative % CVT patients missed	Cumulative CVT patients missed
Low probability and >500µg/L	15.6	100	67.1	100	69	0	0
Low probability and >675µg/L	20	100	75.6	94.4	77	0	0
Moderate probability and >500µg/L	49	92.3	57.6	94.4	68.2	19.2	5
Moderate probability and >675µg/L	54.1	76.9	71.2	87.5	72.9	23.1	6
High probability and >500µg/L	97.7	89.4	66.7	28.6	88	10.6	5
High probability and >675µg/L	97.4	78.7	66.7	16.7	78	21.3	10

Figure 3. Subgroup analyses for acute symptoms (<48 h) (non-CVT n=97, CVT n=11)

a) Validity of D-dimer levels predicting CVT and cumulative percentage of patients with CVT missed at various D-dimer levels.



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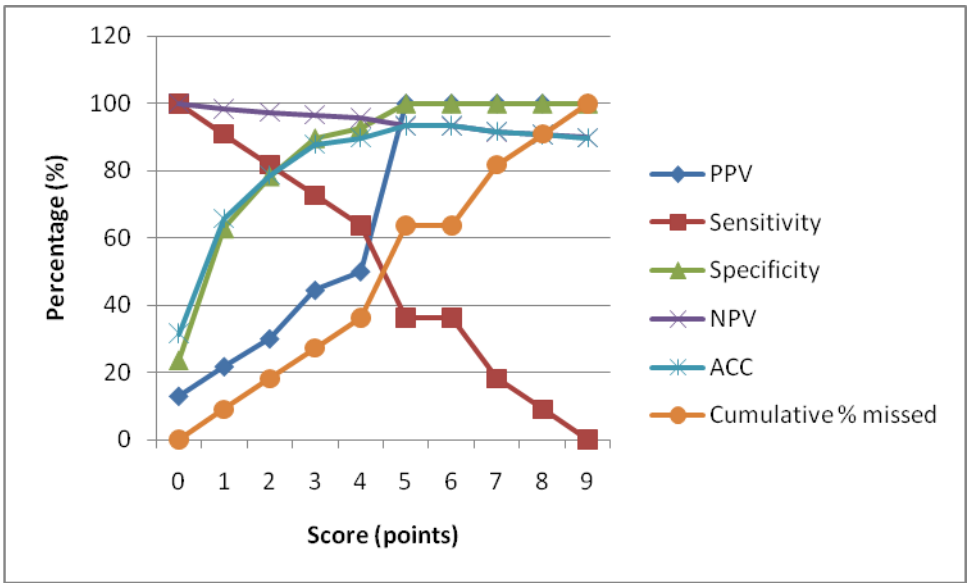
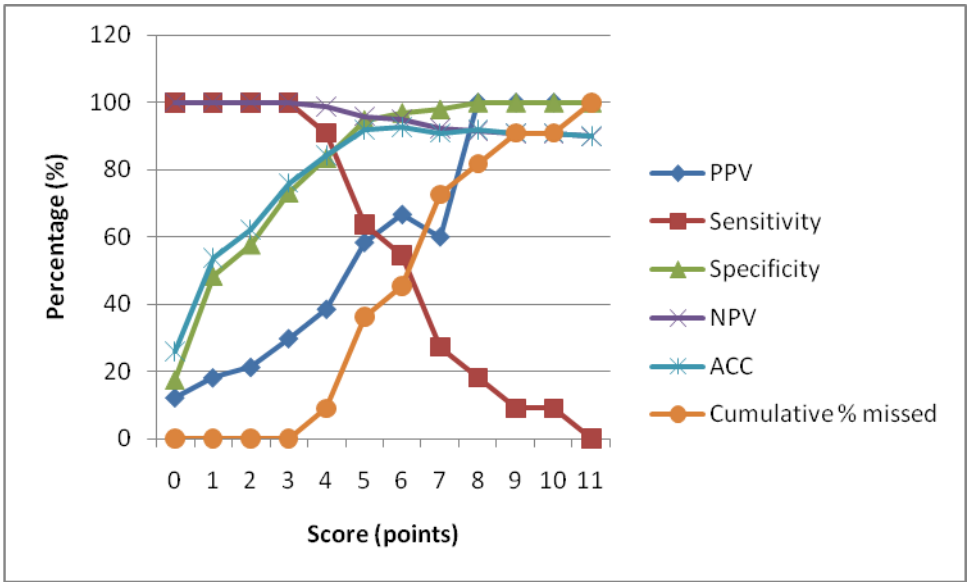


c) Validity of CVT D-dimers (>675µg/L) score predicting CVT and cumulative percentage of patients with CVT missed at various score values.



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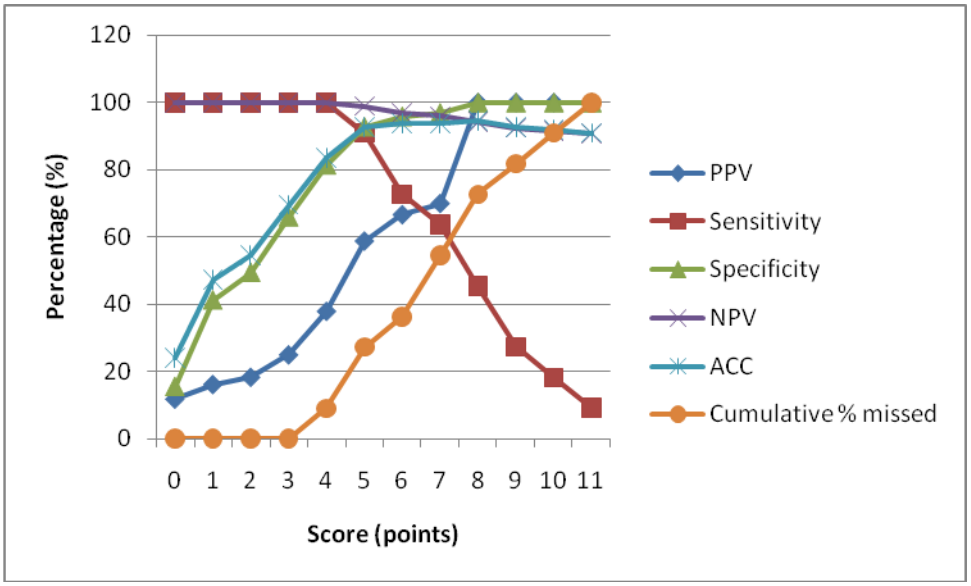

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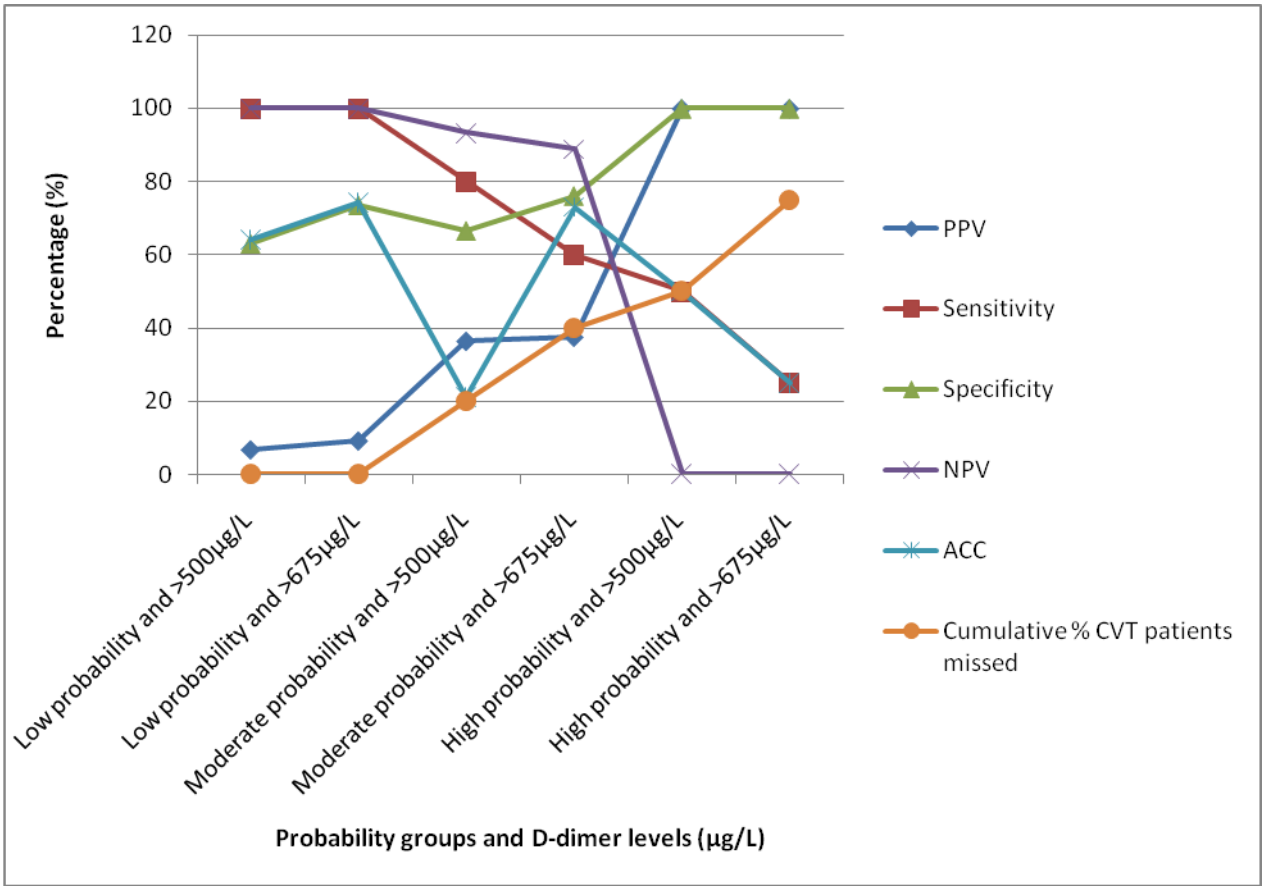

Cut-off (µg/L)	PPV	Sensitivity	Specificity	NPV	ACC	Cumulative % CVT patients missed	Cumulative CVT patients missed
Low probability and >500µg/L	6.7	63.2	63.2	100	64.1	0	0
Low probability and >675µg/L	9.1	73.7	73.7	100	74.4	0	0
Moderate probability and >500µg/L	36.4	66.7	66.7	93.3	21.2	20	1
Moderate probability and >675µg/L	37.5	76.2	76.2	88.9	73.1	40	2
High probability and >500µg/L	100	100	100	0	50	50	2
High probability and >675µg/L	100	100	100	0	25	75	3