Thrombotic markers – VTE risk assessment

post

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- Risk factor / marker for increased risk of first VTE

- Diagnosis of VTE

- Risk factor / marker for increased risk of recurrent VTE or death

post

Increased circulating DNA, calprotectin and mieloperoxidase, as neutrophil extracellular trap markers, are risk factors for deep vein thrombosis

Martos L, Navarro S, Ramon LA, Ferrando F, Cid AR, Bonanad S, España F and Medina
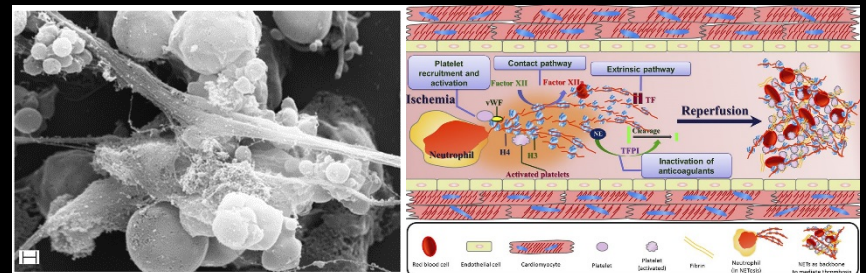
To measure the levels of circulating DNA, calprotectin and myeloperoxidase in plasma from 193 DVT patients and 198 healthy controls in order to assess the role of NETs on the risk of DVT in vivo.

DNA was measured with PicoGreen (Life Technologies). CP (Hycult Biotech) and MPO (Abnova) were measured by ELISAs.

Odds Ratios (ORs) were adjusted for age, sex and the presence of genetic thrombophilic defects.

PO534

	DVT Patients	controls
DNA (ng/mL)	1616 ± 296	1327 ± 228
CP (ng/mL)	121 ± 60	88 ± 54
MPO (ng/mL)	2116 ± 1335	1752 ± 1393

Multivariate analysis including the 4th Q of DNA, CP and MPO showed a significantly increased OR only for DNA (15.6; 1.2–203.0).

These results support the potential use of DNase as a new therapeutic tool for DVT prevention or thrombolysis.

post

DNA in plasma indicates disease extent and predicts mortality in patients with venous thromboembolism

Fuchs T, Jiménez-Alcazar M, Limacher A, Mean M, Renne T, Aujesky D and Lämmle B

Elevated levels of DNA in plasma from patients or animals with DVT. The diagnostic and prognostic value of plasma DNA in VTE is not known.

We hypothesized that levels of plasma DNA or DNase1 correlate with the extent of VTE at diagnosis and are indicative of the clinical outcome.

863 patients from a prospective multicenter cohort study in consecutive patients aged ≥ 65 years with acute, symptomatic VTE (SWITCO65+).

extracellular DNA and DNase1 activity (zymography) measured in patient plasma.

Data analyzed in competing risk and Cox-regression models, adjusting for relevant risk factors and periods of anticoagulation as a time-varying co-variant.

Plasma DNA and DNase1 were positively (P < 0.001) and negatively (P < 0.022) correlated with the extent of VTE at enrollment, respectively.

	median DNA/DNase1 ratio
distal DVT (n = 71),	231 ng/mU
proximal DVT (n = 195),	410 ng/mU
non-massive PE (n = 589)	667 ng/mU
massive PE (n = 8)	1546 ng/mU

DNA and DNase1 were not associated with VTE recurrence or major bleeding.

High DNA levels (top quartile) were predictive for mortality within 12 months post VTE diagnosis (adjusted HR 2.40, 95% CI 1.53–3.75, P < 0.001).

Increased DNA and decreased DNase1 in plasma are associated with the extent of VTE at time of diagnosis.

Quantification of DNA in plasma may help identifying patients at risk of dying within months after acute VTE

PO582

The use of an age-adjusted cut-off for D-dimer in screening patients for suspected DVT in the community can safely decrease the need for compression ultrasonography

Hughes AS, Hall B, Jennings K, Webb V, Page G, Smith C, Charova F

To determine whether the use of AADD in a primary care setting could safely decrease the number of CUSs required.

2-year retrospective analysis of patients > 50 of age with suspected DVT to a single community-based clinic.

All patients assessed using Wells score and quantitative Point of Care DD. CUS carried out as per standard diagnostic pathways.

All patients discharged with DVT excluded had a 3-month follow (3 m-FU).

PO582

669 patients with suspected DVT and age >50.

**160/669
non-high Wells score and DD > 500 mcg/L.**

3 m-FU in CUS negative patients showed
1 DVT (0.7% failure rate).

PO582

669 patients with suspected DVT and age >50.

**160/669
non-high Wells score and DD > 500 mcg/L.**

69 (43%) had an AADD <cut off (age in years x10 mcg/L)

AT 3-month follow up none developed a DVT

An AADD cut off with a non-high Wells score can safely exclude a DVT in patients > 50 years and decrease the need for CUS by approximately 40%.
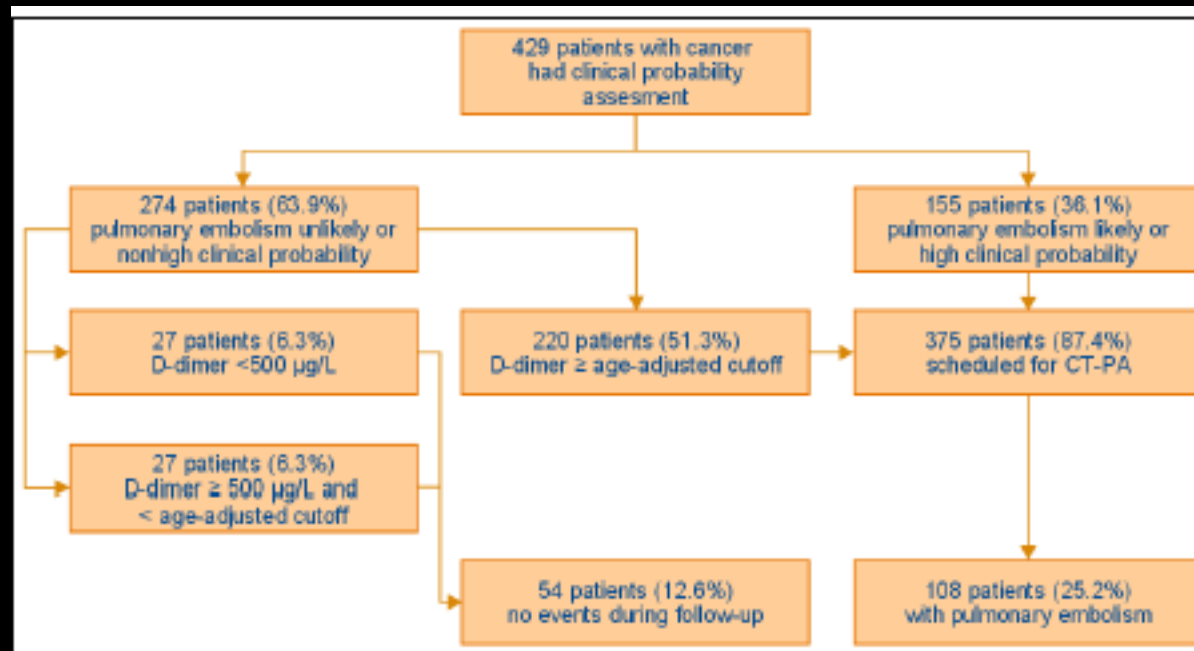
PO597

Age-adjusted D-Dimer cut-off level increases the number of cancer patients in who pulmonary embolism can be safely excluded without CTPA imaging: the adjust-PE Cancer substudy

Wilts D, Gal GL, den Exter PL, van Es J, Carrier M, Planquette B, Büller HR, Righini M, Huisman MV and Kamphuisen PW

429 (12.9%) patients with cancer and suspected PE. Among cancer patients with an unlikely CDR, 27/274 (9.9%) had a Ddimer <500 Ig/L as compared with 19.7% using the age-adjusted D-dimer cut-off;

429 patients with cancer had clinical probability assesment

274 patients (63.9%) pulmonary embolism unlikely or nonhigh clinical probability

155 patients (36.1%) pulmonary embolism likely or high clinical probability

27 patients (6.3%) D-dimer <500 µg/L

220 patients (51.3%) D-dimer ≥ age-adjusted cutoff

375 patients (87.4%) scheduled for CT-PA

27 patients (6.3%) D-dimer ≥ 500 µg/L and < age-adjusted cutoff

54 patients (12.6%) no events during follow-up

108 patients (25.2%) with pulmonary embolism

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…In cancer patients

post

Prospective evaluation of risk assessment models and biological markers of hypercoagulability for the identification of high VTE risk patients with lung adenocarcinoma. The roadmap study

Evmorfiadis I, Paraskevi B, Rousseau A, Charpidou A, Dreden PV, Giozos G, Syrigos K, Spanoudaki A, Grusse M, Elalamy I and Gerotziafas G

In patients with lung adenocarcinoma (LA), metastasis
(MTS), advanced stage and chemotherapy (CTx) are risk factors
for VTE. Routine thromboprophylaxis is not recommended but
individualized risk assessment is encouraged.

Aims: The selection of the most relevant hypercoagulability
biomarkers for incorporation into the risk assessment models
(RAM) for VTE

PO102

Patients with documented LA eligible for CTx were included after at least 3 months from surgery or hospitalization.

They were either CTx naive (NG) or had received CTx (OTG). Control group (CG) consisted of 30 healthy age & sex-matched individuals.

Thrombin generation (TG), P-Selectin, heparanase (HPA), procoagulant phospholipids (PPL), factor VIIa, D-Dimers (DDi) and Tissue Factor activity (TFa) were assessed.

PO102

Increased PPL, TF pathway up regulation, DDimer and HPA increase were observed in LA patients.

Chemotherapy has an impact on TGT and HPA levels.

Baseline values of TGT, PPL, HPA, DDimer were related with mortality and thrombosis.

Incorporation of hemostatic biomarkers in VTE-RAMs is being studied on an ongoing trial.

A new generic risk score for predicting venous thromboembolic events in cancer patients receiving Chemotherapy

Muñoz A, Ziyatdinov A, Souto JC, Soria JM and Soria JM

PO126

Thrombo inCode (TiC) is a new tool for VTE risk prediction using an algorithm that combines a genetic risk score (GRS) with subject's VTE clinical risk parameters (cancer type and cancer disease status 'CDS', included).

PO126

Prospective, observational study in 111 patients

with locally advanced or metastatic cancer (colon,

stomach, pancreas and lung) receiving systemic

outpatient chemotherapy.

Patients followed-up for 6 months.

TiC is composed of

- Genetic variants : FVL, PT, F5 rs118203906 and rs118203905, F12 rs1801020, F13 rs5985, SERPINC1 rs121909548, SERPINE10 rs2232698 and A1 blood group rs8176719, rs7853989, rs8176743, rs8176750.

- Clinical risk factors: age, sex, family history of VTE, BMI, smoking, diabetes, type of cancer and CDS

Khorana score, Khorana score plus CDS and TiC were compared.

The incidence of VTE at 6 months was 26% (Mainly in patients with pancreas cancer, followed by colorectal).

	AUC
Korana score	0.509 (95% CI 0.386–0.633)
Khorana score + CDS	0.64 (95% CI 0.513–0.767)
TiC	0.80 (95% CI 0.699 – 0.897)

TiC predicts chemotherapy-associated VTE risk significantly better than Khorana score with CDS

post

Prediction of cancer associated thrombosis.

A prospective biomarker study.

Tafur A, Mansfield A, Cherry M, Comp P, Rathbun S and Stoner J

PO157

Prospective sample collection, retrospective blinded evaluation study.

Outpatient adults with solid tumors planning to start chemotherapy.

Blood samples for D Dimer, Protein C, Factor VIII, thrombin-activatable fibrinolysis inhibitor, fibrin monomers were collected prior to chemotherapy.

VTE and death were periodically adjudicated. Biomarkers were categorized by quartiles. Data analysis with death as competing event.

PO157

234 patients evaluated: 60 years (median), 72% female,

22% low Khorana risk, 10.4 months follow up.

30 patients (13%) developed VTE and 32 (14%) died.

In the univariate biomarker analysis

	Hazard Ratio	95% CI	P value
DD > 1.5 mcg/mL	2.7	1.1-6.8	0.03
PC <119 mcg/mL	3.1	1.5-6.7	<0.01
FVIII > 262 IU/dL	4.5	2.1–9.6	< 0.001

were associated with incident VTE

Results remained significant when adjusting for

Khorana score, or functional status, or metastatic disease.

When Khorana score and the three biomarkers were in the model,

PC (HR 2.6, 95% CI 1.2-5.6, p 0.01) and

FVIII (HR 2.9, 95% CI 1.2-6.8, p 0.01)

remained strongly associated with VTE.

PO157

Conclusion: High D Dimer, Factor VIII as well as low Protein C levels are predictors of cancer associated VTE and can provide added stratification value when used in combination

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Tissue factor (TF) as predictor of recurrent VTE: risk factor and biomarker analysis from the catch trial of treatment of cancer associated VTE with tinzaparin or warfarin

Khorana AA, Kamphuisen PW, Meyer G, Bauersachs R, Janas MS, Jarner MF, Lee AYY on behalf of the CATCH Investigators

AS081

CATCH was a randomized, multicenter trial of 900 patients comparing tinzaparin 175 IU/kg once daily or dose-adjusted warfarin for 6 months in patients with cancer and acute, symptomatic VTE.

Assays included TF ELISA and sP-selectin (R&D Systems), D-dimer (Roche), FVIII and CRP (Siemens).

Competing risk regression analysis was then conducted accounting for multiple variables.

AS081

805 patients with available biospecimens; 72 developed rVTE.

Univariate analysis for VTE recurrence

	RR	95% CI	p
highest quartile of TF	3.3	2.1–5.1	< 0.0001
Elevated CRP (> 75 mg/L)	2.3	1.3–4.2	0.007
elevated D-dimer (> 5800 mcg/)	1.6	1.0–2.5;	0.08

sP-selectin and FVIII were not significantly associated.

AS081

In competing risk regression analysis, adjusting for treatment assignment, region, history of VTE and metastatic disease, TF continued to be strongly associated with risk of rVTE (adjusted HR 3.4; 95% CI 2.1–5.5; P < 0.001).

Post

A prospective evaluation of the prothrombotic and prognostic potential of circulating microparticles in glioblastoma multiforme(GBM), pancreatic adenocarcinoma (PAC) and esophageal-gastric cancer (EGC)

Campello E, Radu CM, Spiezia L, Gavasso S, Woodhams B and Simioni P

Conclusion

- Novel biomarkers for VTE risk and VTE severity have been proposed.

- Age-adjusted D-dimer is currently the new most validated thrombotic marker, with a role in diagnostic algorithm for VTE.

- The use of biomarkers is proliferating in cancer patients.

- In order to achieve a clinical value for everyday practice biomarkers should be easy to be determined and rapidly available.