POST-ISTH:
Novità dal meeting di Toronto
Terapia del tromboembolismo venoso

Walter Ageno

Università dell'Insubria - Varese

Conflitti di interesse

- Supporto alla ricerca: Bayer Healthcare, Boehringer Ingelheim
- Advisory Boards: Bayer Healthcare, Boehringer Ingelheim, Daiichi Sankyo, BMS-Pfizer, Italfarmaco, ONO
- Fees per letture a congressi: Bayer Healthcare, Boehringer Ingelheim, Daiichi Sankyo, BMS-Pfizer, Stago

Abstract selezionati

- Stratificazione del rischio nei pazienti affetti da embolia polmonare
- Terapia della trombosi venosa distale
- Modelli predittivi di recidiva di TEV

Stratificazione del rischio nei pazienti affetti da embolia polmonare

- Acute PE: external validation of the 2014 risk stratification model of the ESC (Becattini C et al PO626-MON)
- Efficacy and safety of outpatient treatment based on the hestia clinical decision rule with or without pro-BNP testing in patients with acute PE: a randomized trial (den Exter et al OR 257)
- Prognostic significance of asymptomatic DVT in patients presenting with acute PE (Jimenez et al OR 321)

Classification of patients with acute PE

Early mortality risk	Shock or hypotension	High risk PESI score	RV dysfunction	Myocardial injury
High risk	+	(+)	(+)	(+)
Intermediate high risk	-	+	+	+
Intermediate low risk	-	+ -	+ -	+ -
Low risk	-	-	(-)	(-)

Konstantinides S et al. Eur Heart J 2014

PESI score

Variable	Points
Age	1/year
Male sex	10
Cancer	30
Heart failure	10
Chronic lung disease	10
Heart rate >110/min	20
Systolic blood pressure <100 mmHg	30
Respiratory rate ≥30/min	20
Body temperature <36°C	20
Disorientation, lethargy, stupor, coma	60
SaO_2 <90%	20

Data are from reference 214.
Risk categories (30-day all-cause mortality, %): class I, <65 points (0%); class II, 66–85 points (1%); class III, 86–105 points (3.1%); class IV, 106–125 points (10.4%); class, V >125 points (24.4%). Low risk = classes I and II (0–1%).
SaO_2 = pulsoximetry.

Aujesky et al; Eur Heart J 2006

Simplified PESI

Age > 80	1 point
Cancer	1 point
Cardiopulmonary disease	1 point
HR $\geq$ 110/min	1 point
SBP < 100 mm Hg	1 point
O_2 saturation < 90%	1 point

Jiménez D, Arch Intern Med 2010

Hestia criteria for the outpatient treatment of PE patients

1. Hemodynamically unstable?
2. Thrombolysis or embolectomy necessary?
3. Active bleeding or high risk of bleeding?
4. Oxygen supply to maintain sO2 >90%>24 h?
5. PE during anticoagulant treatment?
6. Intravenous pain medication >24 h?
7. Medical or social reason for treatment in the hospital >24 h?
8. Creatinine clearance of less than 30 mL/min?
9. Severe liver impairment?
10. Pregnant?
11. Documented history of HIT?

If one of the questions is answered with YES, the patient can NOT be treated at home

External validation of the 2014 risk stratification model of the ESC

- METHODS

Consecutive patients with symptomatic, objectively confirmed PE and available information about sPESI score, RVD (by either echocardiography or CT) and troponin levels were included

Outcomes: Overall mortality and PE-related death at 30 days

Becattini C et al PO626-MON

External validation of the 2014 risk stratification model of the ESC

- RESULTS

906 hemodynamically stable patients

Overall incidence of death: 7.2%

Overall incidence of PE-related death: 4.1%

196 patients defined at low risk (21.6%)

Deaths at 30 days: 1 (0.5%)

Becattini C et al PO626-MON

External validation of the 2014 risk stratification model of the ESC

CONCLUSIONS:

The 2014-ESC model avoids further testing in about 20% of the patients preserving a high negative predictive value (c-statistic for overall death 0.71; 95% CI 0.65-0.77; for PE-related death 0.77;95% CI 0.70-0.85)

Becattini C et al PO626-MON

Outpatient treatment based on the Hestia with or without pro-BNP

AIM: To investigate the safety of selecting PE patients for outpatient treatment by clinical criteria alone compared to clinical criteria combined with NT-proBNP testing

Outpatient treatment based on the Hestia with or without pro-BNP

METHODS:

- RCT, non-inferiority design, 17 centers

R:

- Direct discharge based on Hestia or
- Hestia + NT-proBNP (discharge if <500 ng/L)

Primary outcome: 30-days PE, bleeding-related death, CP resuscitation, intensive care admission

Outpatient treatment based on the Hestia with or without pro-BNP

RESULTS:

550 patients, 34/275 (12%) with positive NT-pro BNP in the BNP group

Primary outcome:

- Direct discharge: 3/275 (1.1%, 95% CI 0.2-3.2%)
- BNP: 0/275 (0%, 95% CI 0-1.3%), p: 0.08

Outpatient treatment based on the Hestia with or without pro-BNP

CONCLUSIONS:

Outpatient treatment of PE patients selected by the Hestia criteria alone is safe. Additional prognostic assessment based on NT-proBNP levels would only change therapeutic management in 12% of patients, without affecting the 30-day prognosis.

Prognostic significance of asymptomatic DVT

AIM:

To assess whether PE patients with concomitant asymptomatic DVT have an increased risk of short-term complications

Prognostic significance of asymptomatic DVT

METHODS:

820 consecutive normotensive patients with PE underwent bilateral C-CUS.

Primary outcome: all cause mortality at 30-day

Secondary outcome: PE-related mortality at 30-day

Jimenez D OR321

Prognostic significance of asymptomatic DVT

RESULTS:

375/820 (46%) PE patients had concomitant DVT

193/375 (51%) were asymptomatic

Overall mortality: 37/820 (4.5%), 11 died from PE

Patients with asymptomatic DVT had increased all cause mortality (OR 2.77;95% CI 1.35-5.67) and PE-related mortality (OR 7.11;95% CI 1.42-35.5)

Jimenez D OR321

Prognostic significance of asymptomatic DVT

CONCLUSIONS:

In stable patients with an episode of acute symptomatic PE, the presence of concomitant asymptomatic DVT is an independent predictor of death in the ensuing month after diagnosis

Jimenez D OR321

Terapia della trombosi venosa distale

- Anticoagulant therapy for symptomatic distal deep vein thrombosis: the CACTUS randomized placebo-controlled trial (Righini et al AS 137)

Antithrombotic therapy for VTE disease – AT 9 2012

In patients with acute isolated distal DVT

of the leg and without severe symptoms or risk factors for extension, we suggest serial imaging of the deep veins for 2 weeks over initial anticoagulation (Grade 2C) .

In patients with acute isolated distal DVT

of the leg and severe symptoms or risk factors for extension, we suggest initial anticoagulation over serial imaging of the deep veins (Grade 2C) .

Antithrombotic therapy for VTE disease – AT 9 2012

In patients with acute isolated distal DVT of the leg who are managed with initial anticoagulation, we recommend using the same approach as for patients with acute proximal DVT (Grade 1B)

Risk factors for extension: positive D-dimer, thrombosis that is extensive or close to proximal veins, no reversible provoking factors, active cancer, history of VTE, inpatient status.

Anticoagulant therapy for symptomatic IDDVT

AIM:

To assess the superiority of full anticoagulation vs. placebo for distal DVT treatment

Anticoagulant therapy for symptomatic IDDVT

METHODS:

Patients with a first distal DVT were randomized:

1) Nadroparin 170 IU/kg once daily for 42 days
2) Placebo for 42 days

Primary outcome: symptomatic proximal DVT or PE at 42 days

CUS at day 3 to 7 and at 6 weeks

Righini et al AS137

Anticoagulant therapy for symptomatic IDDVT

RESULTS:
746 screened, 259 included (male 51%, mean age 52.8)

Primary outcome:
Nadroparin 4/122 (3.3%)
Placebo 7/130 (5.4%) p value 0.54

Major and non-major clinically relevant bleeding:
Nadroparin 5/122 (4.1%)
Placebo 0/130 (0%) p value 0.03

Righini et al AS137

Anticoagulant therapy for symptomatic IDDVT

RESULTS:

Efficacy outcomes at 3 months

Nadroparin 4/122 (3.3%)

Placebo 8/130 (6.1%)

Righini et al AS137

Anticoagulant therapy for symptomatic IDDVT

Conclusions:

No difference in the risk of symptomatic VTE; full-dose anticoagulation was associated with a significantly increased risk of bleeding

Caveat: low risk patients included (young, 2% with cancer, none with previous VTE)

Righini et al AS137

Modelli predittivi di recidiva di TEV

- Long-term follow-up of a prospective cohort of unprovoked venous thromboembolism patients off anticoagulants-risk stratification evaluation (REVERSE) (Rodger MA et al AS139)

Risk stratification models to identify patients at low risk for recurrence

From Kyrle and Eichinger Thromb Haemost 2012

	Men continue and HER DOO2	Vienna Prediction Model	DASH-Score
Author (reference)	Rodger et al. (24)	Eichinger et al. (25)	Tosetto et al. (26)
Number of patients	646	929	1818
Design	Prospective cohort	Prospective cohort	Patient level meta-analysis
Predictive variables	Men: none Women: Age ≥60 years Signs of PTS BMI ≥30 kg/m^2 D-dimer ≥250 µg/l during anticoagulation	Sex Location of first VTE D-Dimer after anticoagulation	Abnormal D-Dimer after anticoagulation Age < 50 years Male sex Hormonal therapy
Recurrence risk Low risk	≤1 point 1.6% (95% CI 0.3%–4.6%) 52% of women	≤180 points (according to nomogram) 4.4% (95% CI 2.7%-6.2%)	≤1 point 3.1% (95% CI 2.3 – 3.9) 51% of patients

HER DOO2

1) Hyperpigmentation
2) Edema
3) Redness
4) D-dimer >250 ug/ml (Vidas)
5) Obesity (BMI >30 kg/m2)
6) Older than 65

REVERSE study

AIMS

To confirm the high risk of recurrent VTE in high risk patients and the low risk in low risk women over long term follow-up

REVERSE study

METHODS

Multicenter prospective cohort study of first unprovoked VTE patients recruited 2001-2006

Outcome:

Symptomatic suspected VTE off OAC

REVERSE study

RESULTS

647 participants, mean age 53 years, 49% female

Mean follow-up 5.1 years

Annual risk of recurrence: 4.9% (4.2-5.7%)

Rodger MA AS139

REVERSE study

RESULTS

VTE in men: 7.4% (6.1-9.0%)

Low risk women (1 or 0 HERDOO points): 1.1% (0.6-2.0%)

High risk women: 5.9% (4.2-8.1%)

Men with HER: 10.6% (7.9-13.9)

Rodger MA AS139

REVERSE study

Conclusions:

Men and high risk women with unprovoked VTE should be considered for long-term OAC therapy. HER is a strong predictor of recurrent VTE.