P1622
Risk factors for development of postthrombotic syndrome in patients with deep venous thrombosis: from the COMMAND VTE Registry

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Background/Introduction: Postthrombotic syndrome (PTS) is the most common chronic complication of deep venous thrombosis (DVT), which increases healthcare costs and reduces quality of life. Identifying high-risk patients of developing PTS would be useful for expecting prognosis and preventing PTS. However, risk factors for development of PTS have not been adequately characterized yet.
Purpose: The purpose of this study is to investigate PTS risk factors apparent at the time of DVT diagnosis in a large observational study in Japan.
Methods: The COMMAND VTE Registry is a multicenter registry enrolling consecutive patients with acute symptomatic venous thromboembolism (VTE) objectively confirmed by imaging examination or by autopsy among 29 centers in Japan between January 2010 and August 2014. Among 3027 consecutive patients with acute symptomatic VTE enrolled in the registry after screening of the consecutive 19634 patients with suspected VTE for eligibility through chart review by the physicians at each institution, we excluded 381 patients without DVT and 1315 patients with mortality or loss to follow-up within 3 years after diagnosis, and the current study population consisted of 1331 DVT patients with 3 years of follow-up data. Consistent with previous reports, we selected the 13 clinically relevant risk-adjusting variables (age, sex, obesity, history of DVT, DVT symptoms at diagnosis [leg swelling, pain, erythema, warmth, tenderness pain upon dorsiflexion of the foot for DVT], proximal DVT, varicose vein, absence of a transient risk factor for VTE, and thrombophilia), and we used a multivariable logistic regression analysis to estimate the odds ratio (OR) and 95% confidence intervals (CI) of variables for the presence of PTS at 3-year after DVT diagnosis.
Results: Of entire 1331 patients, 173 (13%) patients were diagnosed as PTS within 3 years. Mean age and proportion of female sex were not significantly different between patients with and without PTS (64.9 vs. 65.6 years, P=0.63; 60% vs. 62%, P=0.59). Patients with PTS had history of DVT, DVT symptoms at diagnosis, proximal DVT, chronic kidney disease, active cancer, and absence of a transient risk factor for VTE more frequently (9.8% vs. 5.4%, P=0.02; 95% vs. 79%, P<0.001; 79% vs. 72%, P=0.04, 27% vs. 16%, P<0.001; 27% vs. 10%, P<0.001; 79% vs. 62%, P<0.001). The multivariable logistic regression analysis showed that leg leg swelling (OR 4.64 [95% CI 2.61–8.25, P<0.001] and absence of a transient risk factor (OR 2.56 [95% CI 1.71–3.84], P<0.001) were independently associated with the presence of PTS.
Conclusion: In real-world DVT patients, leg swelling and absence of a transient risk factor for VTE at the time of DVT diagnosis were independent risk factors for development of PTS.
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P1623
Association of low hemoglobin with venous thromboembolism in acutely ill hospitalized medical patients: findings from the APEX trial

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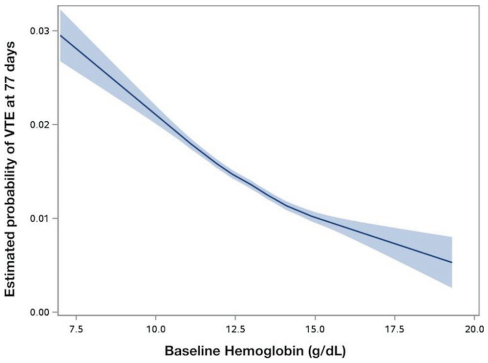
Background: Anemia is a common finding and independent predictor for adverse outcomes in hospitalized patients with medical illness. It remains unclear whether anemia is a risk factor for venous thromboembolism (VTE) and whether the presence of anemia can refine risk assessment for prediction of VTE, thereby adding incremental utility to a validated VTE model.
Methods: In the APEX trial, 7,513 hospitalized medical patients were randomized to receive either betrixaban or standard-of-care enoxaparin for thromboprophylaxis. Baseline hemoglobin concentrations were obtained in 6,861 patients with a follow-up of 77 days. Symptomatic VTE events, including symptomatic deep vein thrombosis (DVT), pulmonary embolism (PE), and VTE-related mortality, were compared between low hemoglobin and normal hemoglobin group (normal range: 12.5 to 17.0 g/dL for males and 11.0 to 15.5 g/dL for females). The relationship between anemia and VTE events was assessed by fitting a univariable and multivariable logistic regression model composed of thromboprophylaxis and VTE risk factors. VTE risk refinement by hemoglobin measurement was evaluated in the IMPROVE risk assessment model.
Results: Low hemoglobin at baseline was associated with a greater risk of symptomatic VTE (RR=1.94 [95% CI: 1.27–2.98]; p=0.002), symptomatic DVT (RR=2.29 [1.12–4.68]; p=0.019), and non-fatal PE (RR=2.63 [1.22–5.65]; p=0.010) but not VTE-related mortality (RR=1.47 [0.71–3.04]; p=0.30). After adjusting for thromboprophylaxis, history of previous VTE, intensive or coronary unit admission and D-dimer, low hemoglobin (as a categorical or continuous variable) remained associated with an increased likelihood of VTE (adjusted OR=1.71 [1.09–2.69]; p=0.020). Low hemoglobin also improved VTE risk discrimination and reclassification after inclusion in the IMPROVE model.

The risk of VTE in patients with low vs. normal hemoglobin levels

End point	Low Hemoglobin (N=1,390)	Normal Hemoglobin (N=5,315)	RR (95% CI)	P-value
Symptomatic VTE	31 (2.23)	61 (1.15)	1.94 (1.27 to 2.98)	0.0020
Symptomatic DVT	12 (0.86)	20 (0.38)	2.29 (1.12 to 4.68)	0.0190
Non-fatal PE	11 (0.79)	16 (0.30)	2.63 (1.22 to 5.65)	0.0102
VTE-related mortality	10 (0.72)	26 (0.49)	1.47 (0.71 to 3.04)	0.30



Baseline hemoglobin and VTE risk at 77 d

Conclusions: Anemia was independently associated with a greater risk of symptomatic VTE among acutely ill medical patients despite the provision of thromboprophylaxis. Hemoglobin measurement also improved risk stratification by the IMPROVE VTE risk score.
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P1624
Intravenous iron substitution improves pulmonary diffusion capacity in patients with iron deficiency and precapillary pulmonary hypertension

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Background: Iron deficiency is a well-known phenomenon in patients with heart failure and in patients with pulmonary arterial hypertension. Intravenous iron substitution is an effective therapy. To date, little is known about the effects of iron substitution on lung function and pulmonary diffusion capacity (DLCO). Pathophysiological considerations suggest that DLCO may improve by an increase in Hemoglobin concentration (cHB).
Purpose: We analyzed whether intravenous iron substitution had a significant influence on DLCO in patients with pulmonary hypertension (PH), and whether changes in DLCO were mainly dependent on an increase in cHb.
Methods: We analyzed 60 patients (44f, 16m) with confirmed precapillary PH (groups I and IV of the NICE classification) and iron deficiency, who received intravenous iron due to clinical indication. All patients were stable, with unchanged medication for at least 3 months. Relevant laboratory parameters as well as a standardized spirometry and DLCO measurement (single breath) were performed immediately before, and 2–12 months after iron substitution (mean follow-up time 175 days). Patients were grouped by early follow-up (up to 140 days after iron substitution) and late follow-up (more than 140 days after substitution).
Results: Iron substitution was well tolerated in all patients. Ferritin levels, transferrin saturation and cHb significantly increased after iron substitution. DLCO also showed a significant increase (Figure 1A). DLCO corrected for cHb increased, without reaching statistical significance.
However, the group of patients who were followed up within 140 days of iron substitution (n=23) showed significant increases in DLCO, as well as in DLCO corrected for cHb (Figure 1B). Alveolar volume and spirometry parameters did not show any significant changes. Patients who were followed up within 140 days did not show significant differences in ferritin levels and transferrin saturation, compared to those patients who received a later follow-up.
Conclusions: Patients with PH and iron deficiency show a significant DLCO im-