ABSTRACTS - Vascular Disease, Hypertension, and Prevention  501A

Comparison Between Rescue Surgical Embolectomy and Repeat Thrombolysis After Unsuccessful Thrombolysis in Acute Pulmonary Embolism
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Background: Persistence of pulmonary hypertension (PH) or right ventricular (RV) dysfunction after thrombolytic therapy (TT) in acute pulmonary embolism (AEP) is associated with increased long-term mortality. However, management of unsuccessful TT has never been assessed in this setting. The aim of this study was to compare rescue surgical embolectomy and repeat thrombolysis in AEP pts presenting with persistent RV dysfunction and haemodynamic instability after TT.

Methods: 354 consecutive AEP pts submitted to TT were prospectively included in a monocenter registry. 37/10% had persistent haemodynamic instability (heart rate >100 bpm, systolic blood pressure <90mmHg or refractory cardiovascular shock) and residual RV dysfunction at 48th echocardiography (paradoxical septal motion, pulmonary hypertension >40 mmHg or RV/LV end diastolic diameter >1). The choice between rescue surgical embolectomy and repeat thrombolysis was left to the physician in charge. In-hospital course was assessed using a clinical composite endpoint defined as recurrent PE, bleeding complications or PE-related death.

Results: Clinical presentation and echocardiographic examination were similar in both groups before and after TT. In-hospital events are summarized in the table. Conclusion: Rescue surgical embolectomy led to better in-hospital course when compared with repeat thrombolysis in pts with persistent RV dysfunction and haemodynamic instability after TT. A randomized trial is needed in this area.

<table>
<thead>
<tr>
<th></th>
<th>Surgical embolectomy (n=12)</th>
<th>Repeat thrombolysis (n=29)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent PE</td>
<td>3 (25%)</td>
<td>15 (60%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Bleedings</td>
<td>2 (17%)</td>
<td>6 (24%)</td>
<td>0.53</td>
</tr>
<tr>
<td>PE-related death</td>
<td>0 (0%)</td>
<td>6 (24%)</td>
<td>0.002</td>
</tr>
<tr>
<td>1 or more of the above</td>
<td>4 (33%)</td>
<td>20 (80%)</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Thromboprophylaxis With Dalteparin Reduces Clinically Important Venous Thromboembolism in Patients With Congestive Heart Failure
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Background: Patients with congestive heart failure are at risk of venous thromboembolism (VTE). However, the benefit of pharmacological thromboprophylaxis in patients with congestive heart failure has not been well studied and hence is not universally accepted or adopted. We undertook a subanalysis of the recently completed Prospective Evaluation of Dalteparin Efficacy for Prevention of VTE in Immobile Patients Trial (PREVENT), which evaluated dalteparin for prevention of clinically important VTE in acutely ill medical patients, to assess the benefit of thromboprophylaxis in patients admitted with congestive heart failure.

Methods: PREVENT was a randomized, double-blind, placebo-controlled trial in 219 centers in 26 countries, which enrolled hospitalized medical patients at moderately high risk of VTE. In total, 3,706 patients were included in the study, among whom 1,595 were admitted with congestive heart failure (NYHA class III or IV). Patients received dalteparin (5,000 IU OD) or placebo for 14 days. The primary endpoint was clinically important VTE, defined as objectively verified symptomatic deep vein thrombosis, pulmonary embolism, sudden death, and objectively verified asymptomatic proximal deep vein thrombosis. Compression ultrasound was performed in all patients who had not reached an endpoint.

Results: Overall, the incidence of the composite primary outcome was 2.77% in the dalteparin group and 4.96% in the placebo group, a risk reduction of 45% (95% CI: 20%-62%) (p=0.0015). Major bleeding was reported in 9 (0.49%) patients receiving dalteparin and 8 (0.48%) receiving placebo (n.s.). Among the patients admitted with congestive heart failure, the primary endpoint incidence was 3.07% (25/814) in the dalteparin group and 4.23% (33/781) in the placebo group, a risk reduction of 27% (95% CI: -21% to 7%) (p=0.009). Conclusion: Dalteparin in a fixed dose of 5,000 IU/day reduces the rate of clinically important VTE in acutely ill medical patients, including those with congestive heart failure, with a low risk of bleeding.

Obesity Does Not Attenuate the Effectiveness of Low-Dose Dalteparin in Preventing Venous Thromboembolism in Medically Ill Patients
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Background: Dalteparin, a low-molecular-weight heparin, is used in fixed, low doses to prevent venous thromboembolism (VTE). We were concerned that a fixed rather than weight-based dosing regimen of LMWH might result in decreased efficacy in obese medically ill patients.

Methods: We analyzed data from the PREVENT trial, a study of 3,706 hospitalized, medically ill patients at least 40 years of age, with a projected hospitalization of 4 or more days, who had been randomized to receive either dalteparin 5,000 units once daily or placebo. The primary endpoint of the trial was a composite of symptomatic VTE, fatal pulmonary embolism (PE), sudden death, or asymptomatic proximal deep vein thrombosis by day 21 in the intention-to-treat population. Obesity, defined as a body mass index higher than or equal to 30 kg/m2 or greater than or equal to 28.6 kg/m2 for women, was present in 1,118 (30.2%) patients.

Results: In obese patients, the primary endpoint occurred in 2.8% and 4.3% of the dalteparin and placebo group, respectively (RR 0.64; 95% CI: 0.32-1.28). In non-obese patients, the RR was 2.8% and 5.2% for dalteparin and placebo group, respectively (RR 0.53; 95% CI: 0.34-0.82). The incidence of fatal PE or sudden death by day 21 was similar in obese (dalteparin: 0.4%; placebo: 0.4%) and non-obese patients (dalteparin: 0.2%; placebo: 0.1%). With multivariate logistic regression, the treatment effect of dalteparin remained unchanged (OR 0.55; 95% CI: 0.37-0.80) when adjusted for obesity and older age (>75 years). Data modeling using the variables of obesity, dalteparin, and interaction term indicated that the efficacy of dalteparin was not significantly altered in obese patients (p=0.63). When weight was modeled as a continuous variable, no statistically significant interaction between dalteparin and obesity was observed (p=0.97).

Conclusion: A fixed low dose of dalteparin of 5,000 units once daily reduces the risk of VTE to a similar extent in obese and non-obese medically ill patients. These results and our analysis encourage more widespread use of fixed, low-dose dalteparin to prevent VTE in hospitalized medical patients who are obese.

Sustained Hemodynamic Benefit in Patients With Pulmonary Arterial Hypertension After One-Year of Therapy With the Selective Orally-Active Endothelin-A Receptor Antagonist, Sitaxsentan
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Background: The natural history of pulmonary arterial hypertension (PAH) is one of progressive deterioration leading to death. Endothelin-1 (ET), a potent vasoconstrictor and mitogenic peptide, has been implicated in the pathogenesis of PAH, and blockade of its effects has become a therapeutic focus. We report long-term hemodynamic improvement in patients with PAH who were treated with the orally active selective ETA receptor antagonist, sitaxsentan sodium.

Methods: In a Compassionate Use protocol, 11 patients with PAH (4 idiopathic, 3 con-