D-dimer testing during anticoagulant therapy should be used to indicate patients who need extended anticoagulant therapy

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Background

- The PROLONG study showed that patients with venous thromboembolism who had elevated D-dimer level **after discontinuation of anticoagulant therapy** benefit from resumption of anticoagulant therapy[1]
- It is not yet clear should D-dimer testing **during anticoagulant therapy** be used to indicate VTE patients who need extended anticoagulant therapy

[1]*Palareti G. et al. N Engl J Med 2006; 355: 1780-1789*

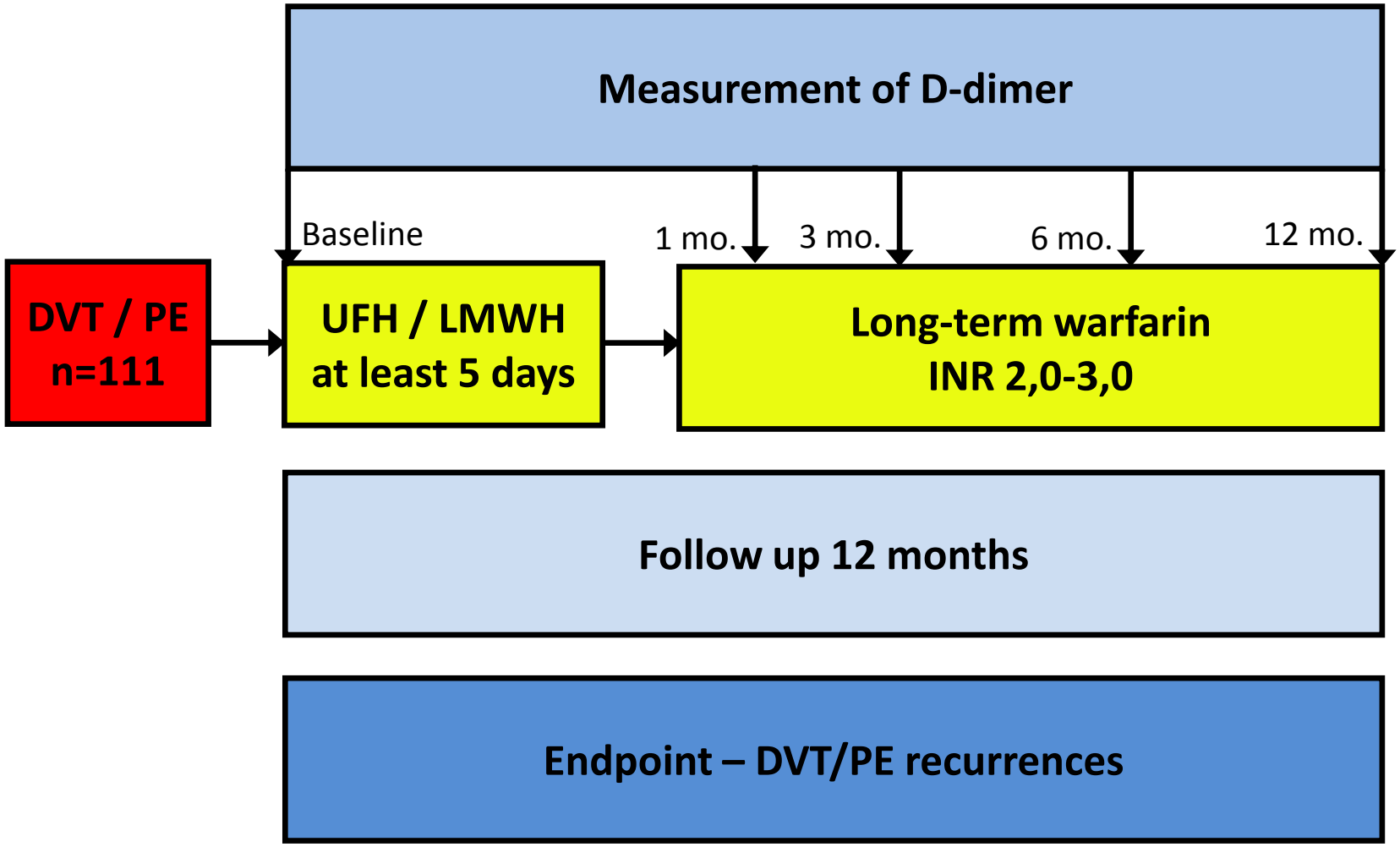
What is D-dimer?

- D-dimer is a degradation product of cross-linked fibrin that is formed immediately after thrombin-generated fibrin clots are degraded by plasmin and reflects a global activation of blood coagulation and fibrinolysis
- D-dimer level rises during acute event of venous thromboembolism
- Testing for D-dimer was explored as a tool for the diagnosis of VTE and has been integrated into diagnostic algorithms in the management of patients with suspected VTE
- A negative value of D-dimer may safely rule out both DVT and PE with high sensitivity of up to 95% and a negative predictive value of nearly 100%

Purpose

- To estimate should D-dimer testing during anticoagulant therapy be used to indicate patients with venous thromboembolism who need extended anticoagulant therapy

Study design



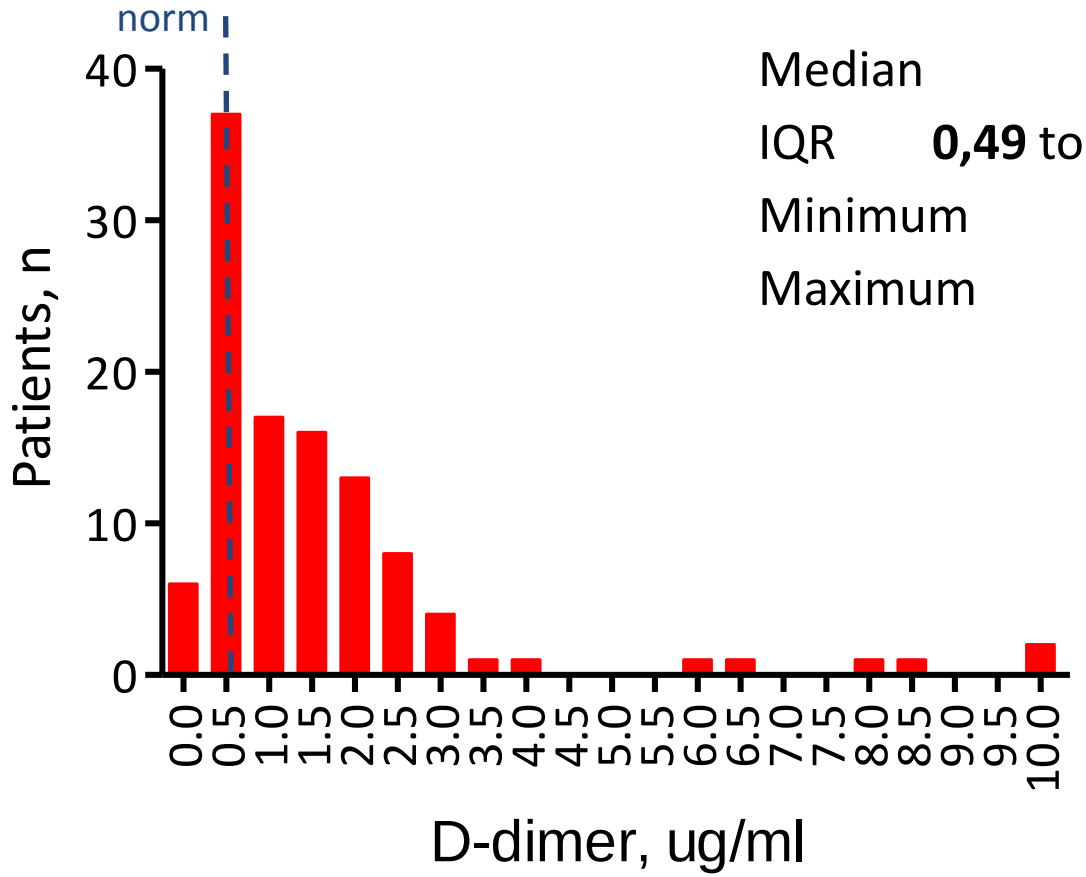
Statistical analysis

- Statistical analysis was performed using a commercially available statistical package (SPSS 17.0 for Windows, SPSS Inc., USA)
- Differences between groups were tested using two-sided Fisher's exact test and Kruskel-Wallis test
- Univariate Cox regression was used to calculate the hazard ratio and 95% confidence interval for the risk of DVT recurrences

Characteristics of VTE patients (n=111)

Characteristic	Value
Sex (male/female)	76/35
Age, years [median (range)]	54 (18 to 76)
Body mass index, kg/m^2 [median (IQR)]	28,4 (25,7 to 32,9)
Isolated DVT, n (%)	78 (70%)
Isolated PE, n (%)	2 (2%)
DVT + PE, n (%)	31 (28%)
Lower extremity DVT, n (%)	102 (92%)
• Proximal DVT, n (%)	88 (86%)
• Distal DVT, n (%)	14 (14%)
Upper extremity DVT, n (%)	7 (6%)
Previous VTE, n (%)	37 (33%)
Family history of VTE, n (%)	13 (12%)
Idiopathic VTE, n (%)	38 (34%)

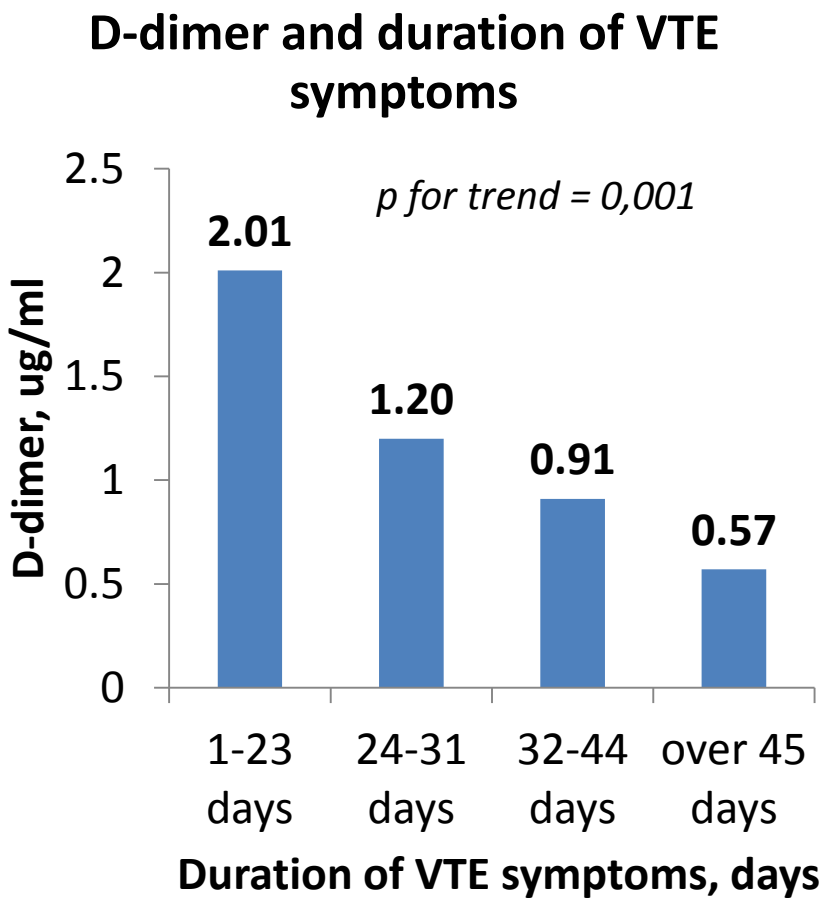
The distribution of D-dimer levels in VTE patients at baseline (~30 days after VTE symptoms onset)

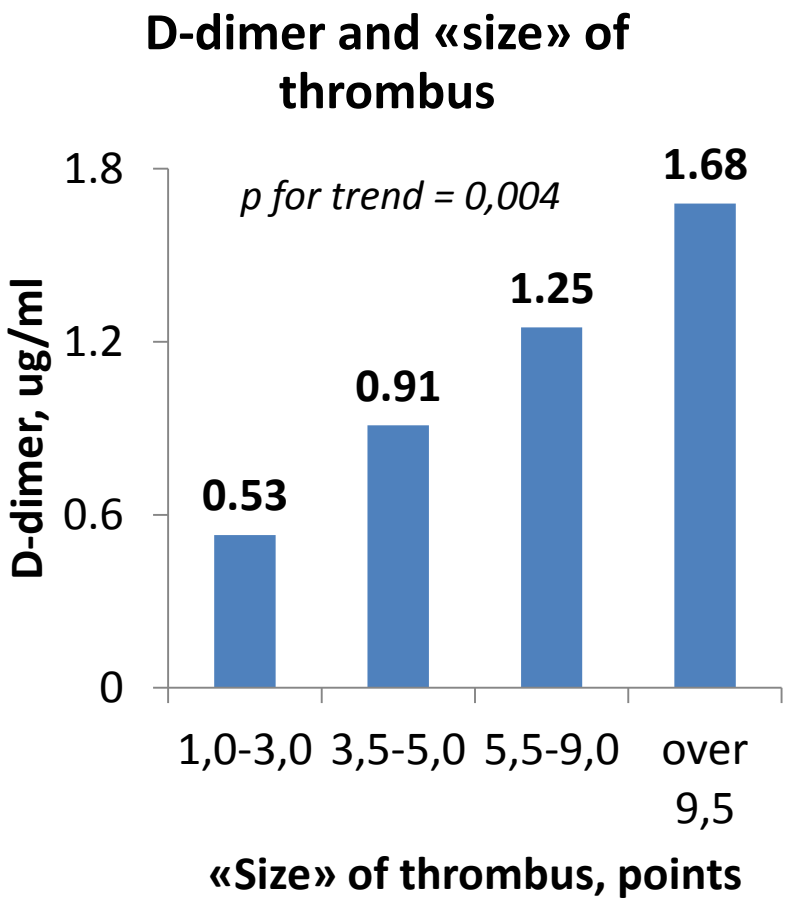


Median	**1,05** ug/ml
IQR	**0,49** to **1,99** ug/ml
Minimum	**0,02** ug/ml
Maximum	**9,92** ug/ml

Vorobyeva N. M. et al. J Thromb Haemost 2009; 7 (Suppl. 2): 1104

The distribution of D-dimer levels according «age» and «size» of thrombus





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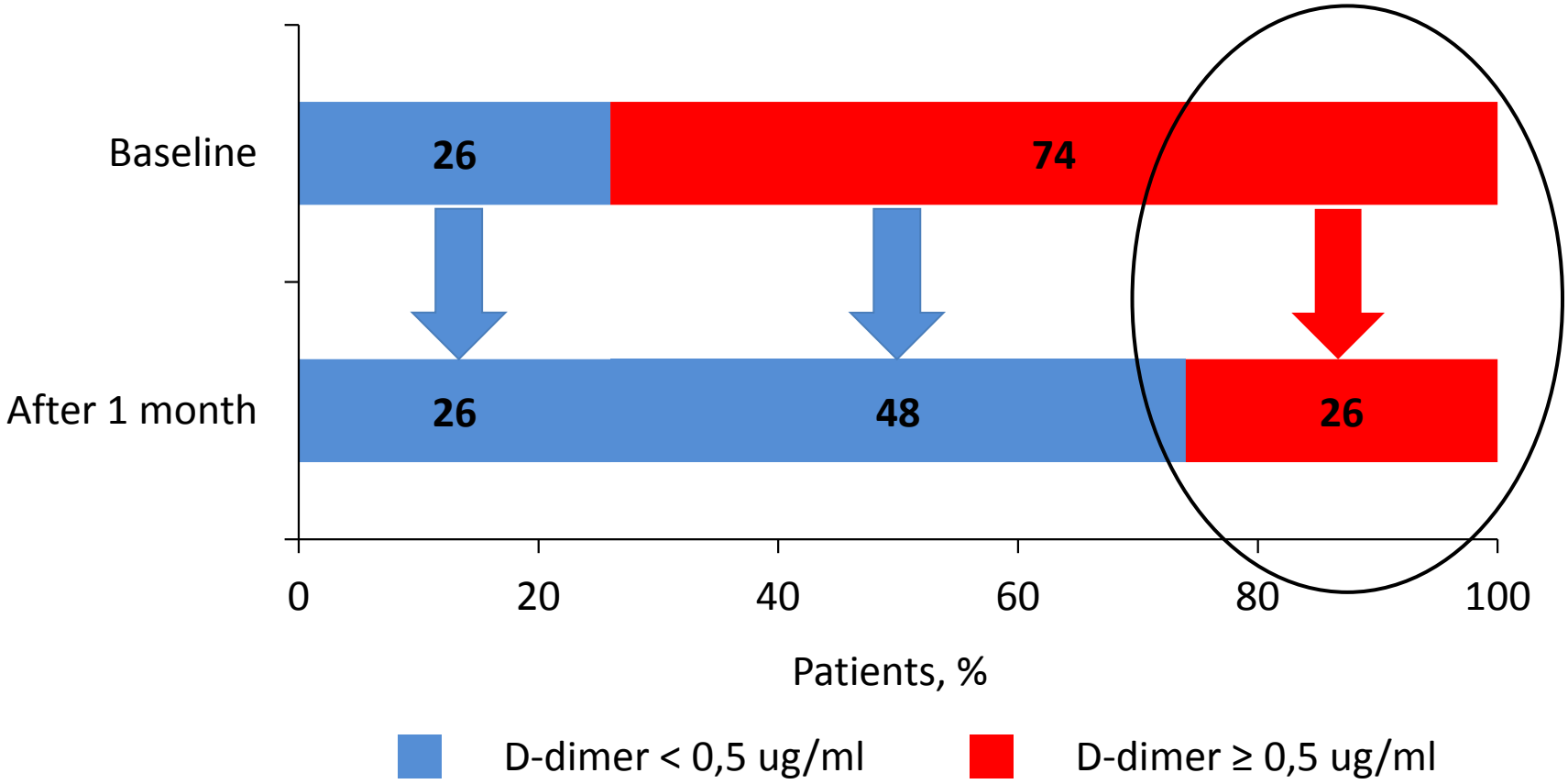
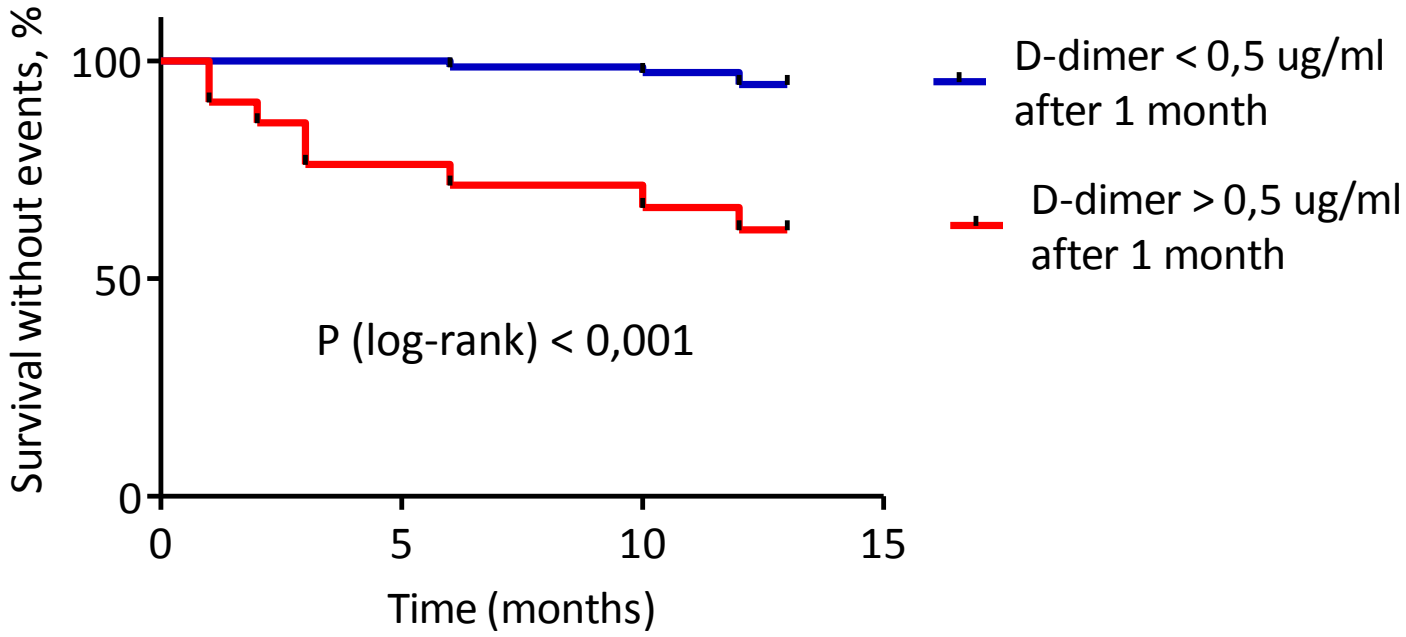
Changes of D-dimer during the first month of anticoagulant therapy



Vorobyeva N. M. et al. J Thromb Haemost 2011; 9 (Suppl. 2): 862

Prognostic value of elevated D-dimer after 1 month of anticoagulant therapy

In patients with D-dimer ≥ 0,5 ug/ml after 1 month of anticoagulant therapy, the risk of DVT recurrences is higher (HR 8,9; 95% CI 2,7 to 29,8; p<0,001)



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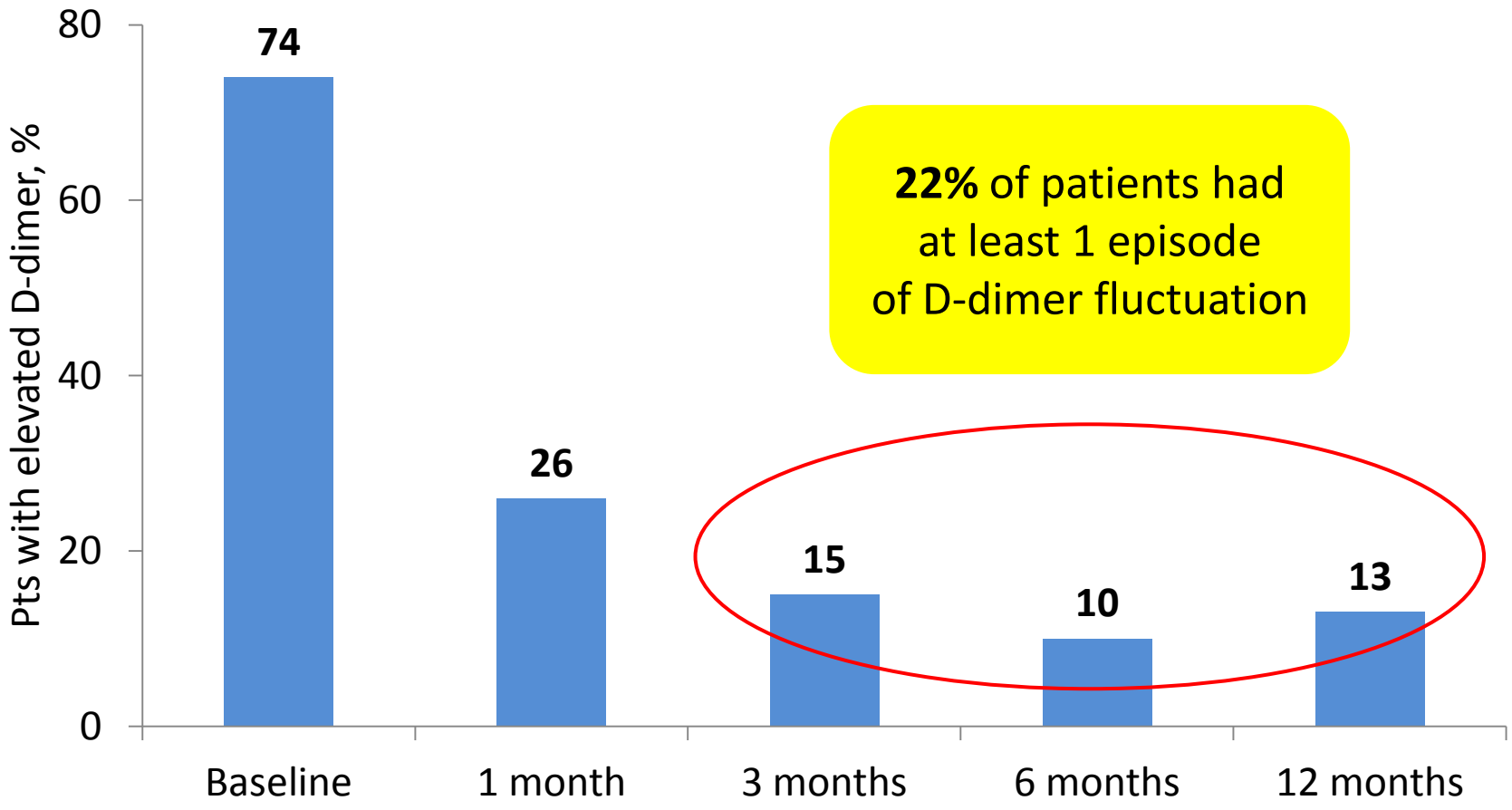
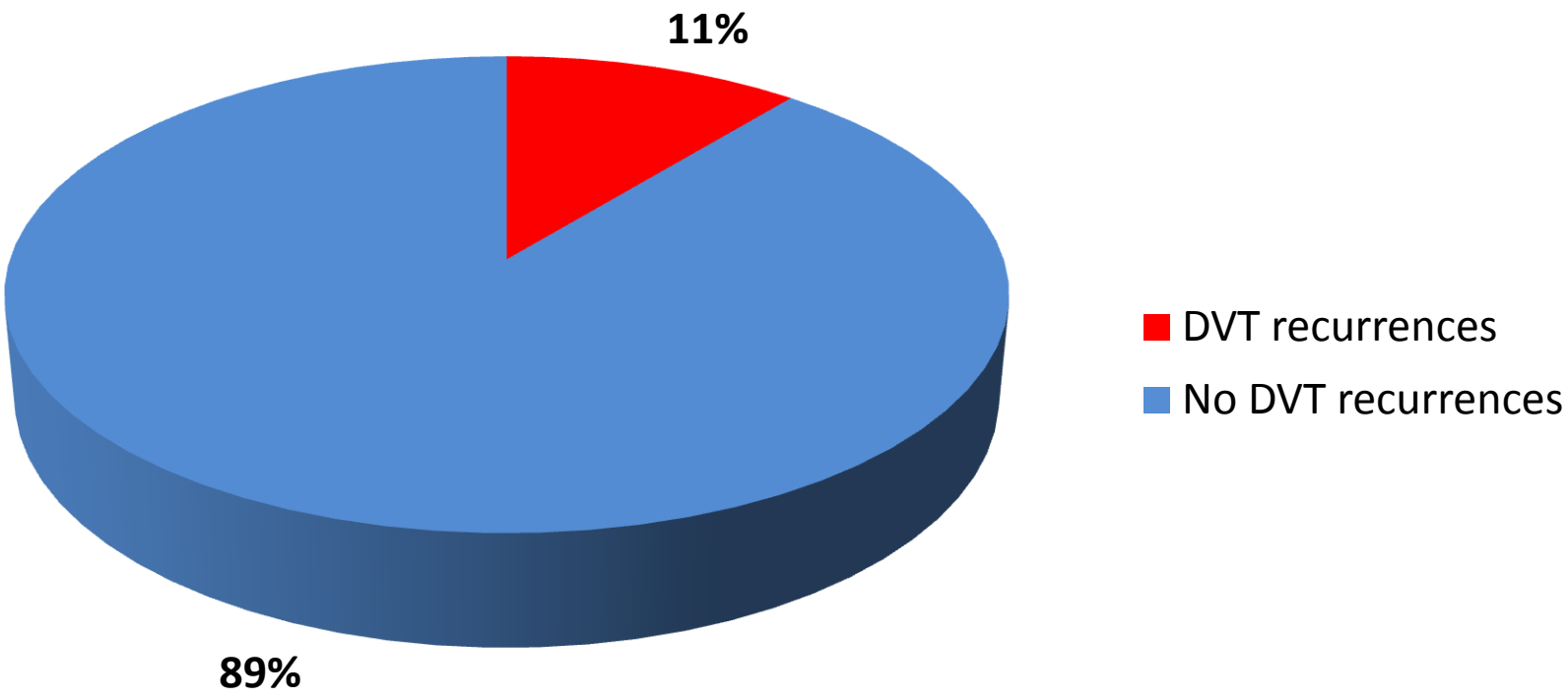
Patients with D-dimer fluctuations* during 12 months of anticoagulant therapy



22% of patients had at least 1 episode of D-dimer fluctuation

** D-dimer ≥ 0,5 ug/ml*

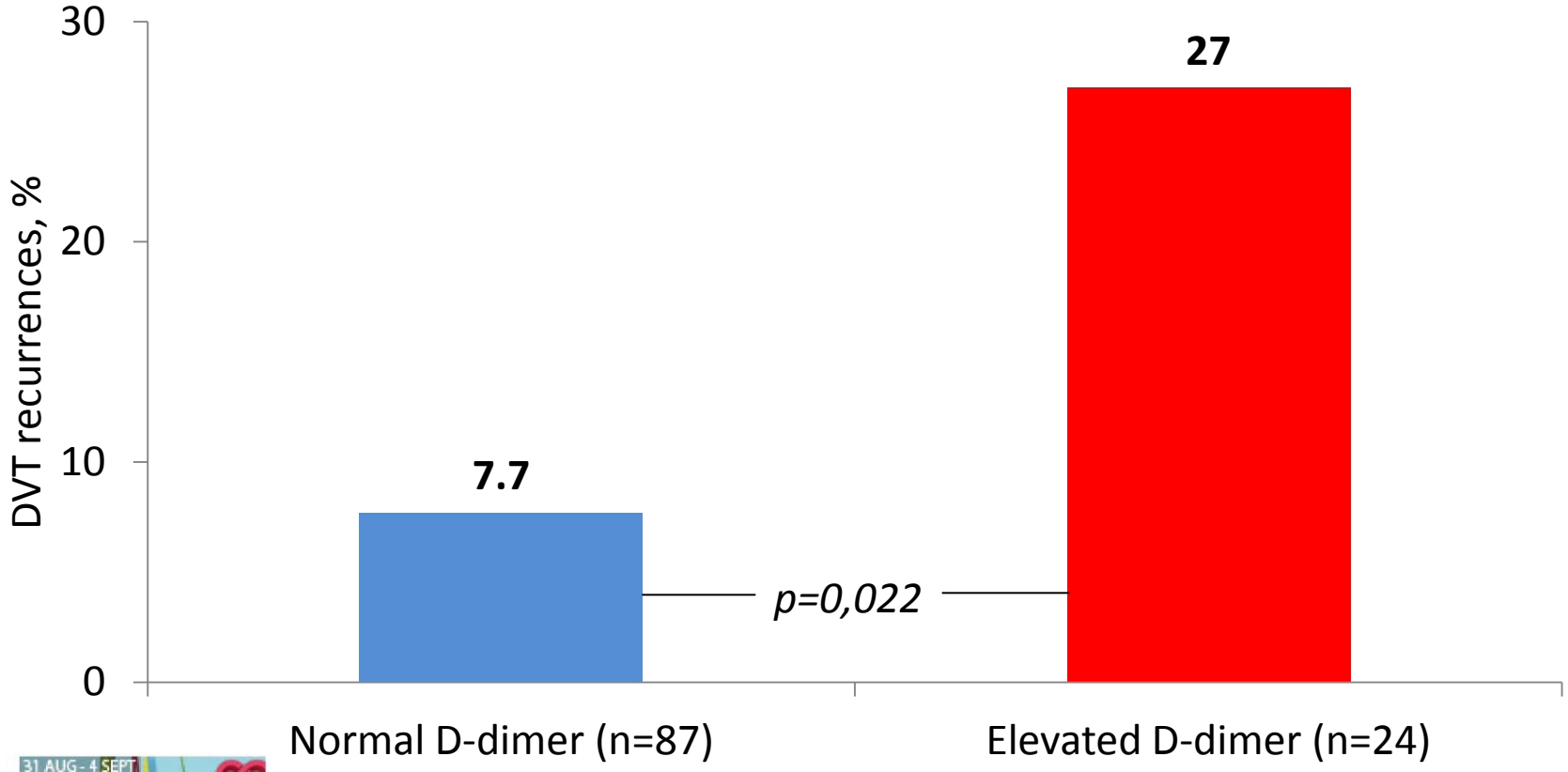
The frequency of DVT recurrences from the 2nd till the 12th months of anticoagulant therapy



There were no PE recurrences

The frequency of DVT recurrences and D-dimer levels from the 2nd till the 12th months of anticoagulant therapy

In patients with any D-dimer fluctuation ≥ 0,5 ug/ml from the 2nd till the 12th months of anticoagulant therapy, the risk of DVT recurrence is higher
HR 4,43; 95% CI 1,42 to 13,78; p=0,01



Conclusions

- Most of VTE patients (74%) have elevated D-dimer by 30th day after symptoms onset
- After 1 month of anticoagulant therapy, elevated D-dimer maintained in 26% of patients
- From the 2nd till the 12th months of anticoagulant therapy, 22% of patients had at least 1 episode of D-dimer fluctuation
- From the 2nd till the 12th months of anticoagulant therapy, the frequency of DVT recurrences was 11%
- Our pilot study showed that any D-dimer fluctuation from the 2nd till the 12th months of anticoagulant therapy is associated with a 4-fold increase of the risk of DVT recurrences
- We suggest that VTE patients who had at least 1 episode of D-dimer fluctuation during 12 months of anticoagulant therapy need extended anticoagulant therapy