# Uncontrolled psoriasis is an independent risk factor for a hypercoagulable state

T Hillary[1], T Vanhoutvin[1], M Peeters[2], M Imbrechts[2], T Vanassche[3], M Garmyn[1], S Vermeire[4]

[1]Dermatology department, University Hospitals Leuven Belgium; [2] KU Leuven, Laboratory for Therapeutic and Diagnostic Antibodies, Department of Pharmaceutical and Pharmacological Sciences, Leuven Belgium; [3]Department of Cardiovascular Diseases, University Hospitals Leuven Belgium; [4] Department of Gastroenterology & Hepatology, University Hospitals Leuven and Translational Research in Gastrointestinal Disorders (TARGID) KU Leuven

## Background & Hypothesis

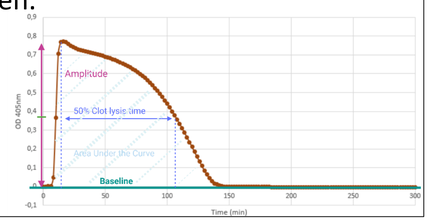
- Chronic inflammatory diseases, including psoriasis, are associated with development of venous thromboembolism (VTE).
- The clot lysis profile (CLP) provides information on both the clotting tendency as well as the fibrinolysis activity.
- It is unclear whether the increased risk of VTE in psoriasis is attributed to increased clotting tendency, decreased lysis activity, or both.
- **We hypothesized that the CLP in uncontrolled psoriasis patients is disturbed towards more clotting/less lysis compared to healthy controls (HC) and that successful psoriasis-treatment could normalize the CLP towards that of HC.**

## Objectives

- To compare the CLP in patients with uncontrolled moderate to severe psoriasis with age- and sex-matched HC.
- To investigate how anti-inflammatory treatment for psoriasis affects the CLP.

## Materials & Methods

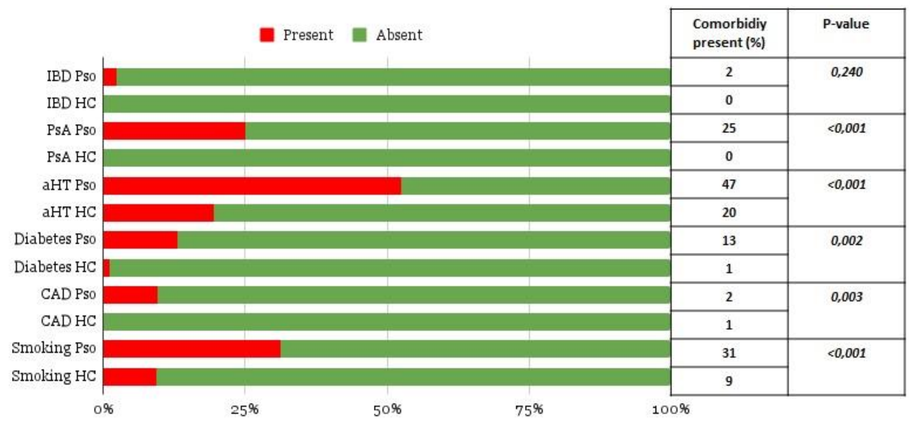
- Patients with active uncontrolled psoriasis (PASI or BSA > 10)(n=87) and HC (n=87) recruited at the dermatology department of the University Hospital Leuven.
- Samples from patients were obtained before treatment and at the moment of remission (PASI<3).
- Clot profile generated through a functional clot lysis assay, in which the speed of clot formation and dissolution is measured.
- By measuring the optical density at 405nm every 2 minutes for 300 minutes, the clot lysis turbidity profile is determined.
- The CLP informs about maximal clot absorbance (amplitude: indication for clot formation or coagulation tendency, the overall coagulation/fibrinolysis profile (AUC), and the timepoint between maximum turbidity and clear transition (50% CLT: indication for the fibrinolysis rate).




## Results

| | n |
|---|---|
| **Systemic** | **14** |
| **IL17-i** | **39** |
| **IL23-i** | **31** |
| **TNFα-i** | **3** |

**Figure 1**: Treatment modalities and number of patients. Systemic: methotrexate, cyclosporine A, UV-therapy. IL: interleukin; i: inhibitor; TNFα: Tumor Necrosis Factor α




| Comorbidiy present (%) | P-value |
|---|---|
| 2 | 0,240 |
| 0 | |
| 25 | <0,001 |
| 0 | |
| 47 | <0,001 |
| 20 | |
| 13 | 0,002 |
| 1 | |
| 2 | 0,003 |
| 1 | |
| 31 | <0,001 |
| 9 | |

**Figure 2**: Comorbidities were significantly more present in the psoriasis cohort compared to healthy controls. IBD: Inflammatory Bowel Disease; PsA: Psoriatic arthritis; aHT: arterial hypertension; CAD: Coronary artery disease; HC: Healthy controls; Pso: Psoriasis patients.

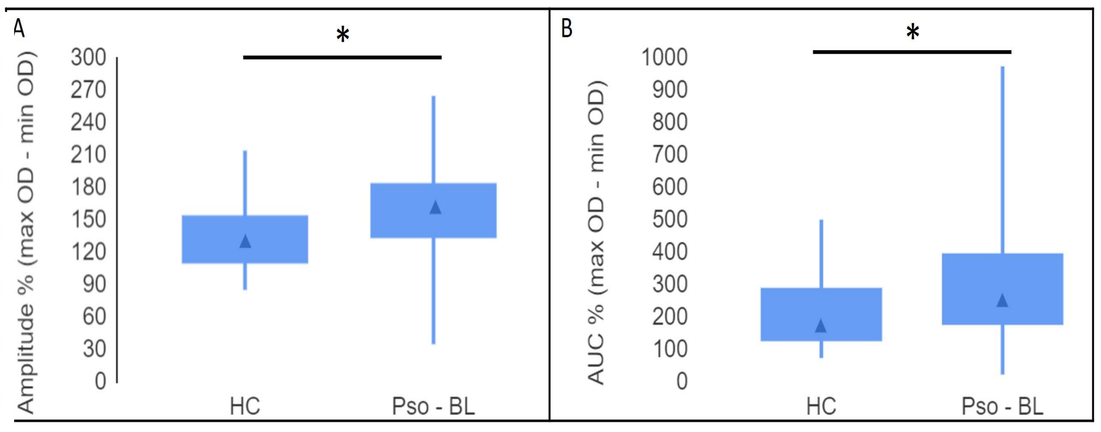



**Figure 3**: Indicators of clotting tendency derived from the clot lysis profile. Panel A: amplitude was significantly higher in psoriasis patients versus healthy controls (*p < 0.0001). Panel B: Area under the curve was significantly higher in psoriasis patients versus healthy controls (*p < 0.0001). The box represents interquartile ranges. The black triangles represent the median values. The whiskers mark minimal and maximal values. HC = 87; Pso-BL = 87

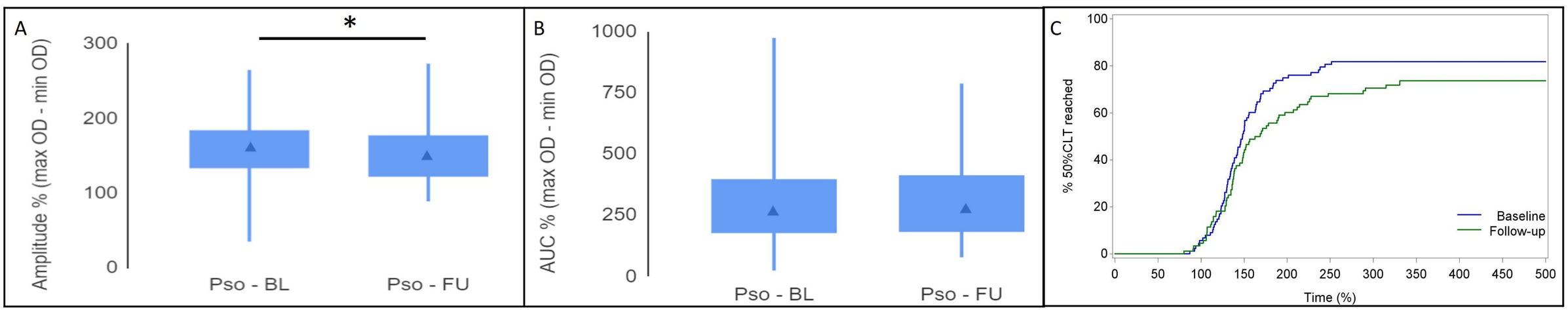



**Figure 4**: Evolution of indicators of clotting tendency derived from the clot lysis profile before and after psoriasis treatment. Panel A: amplitude significantly decreased in psoriasis patients after successful anti-inflammatory treatment (*p=0.0365). Panel B: No significant changes in AUC were observed after successful anti-inflammatory treatment. Panel C: 50%CLT significantly increased at follow up compared to baseline (p=0.0052). Panel A and B: The box represents interquartile ranges. The black triangles represent the median values. The whiskers mark minimal and maximal values. (AUC: Area under the curve; Pso-BL: Psoriasis baseline; Pso-FU: Psoriasis follow up)

## Discussion

- CLP showed hypercoagulable characteristics (high amplitude and AUC) in active psoriasis patients compared to HC.
- Successful anti-inflammatory therapy resulted in a significant tendency towards normalization of this hypercoagulable CLP.
- 50% CLT was not different between patients and controls, although an increase was observed within patients over time despite controlling for disease activity. The explanation for our finding of an increase in 50%CLT in patients treated with IL23-blockers is unclear and may be explained by low sample size and type 1 error.
- After correction for possible confounders (high BMI, smoking, concomitant psoriatic arthritis, arterial hypertension, diabetes and coronary artery disease), the CLP amplitude remained significantly higher in psoriasis patients compared to healthy controls.
- This suggests that merely the presence of active uncontrolled psoriasis – even in the absence of any comorbidity – is a risk factor for VTE.

## Conclusion

- This is the first prospective study comparing the CLP of psoriasis patients with that of HC.
- A significant increase in both amplitude and area under the curve, indicative of a hypercoagulable CLP, was observed in psoriasis patients compared to HC.
- After successful anti-inflammatory treatment, amplitude significantly decreased.