

Summary and significance of the work

In our study “*Omega-3 fatty acids predict recurrent venous thromboembolism or total mortality in elderly patients with acute venous thromboembolism*“, published in the *Journal of Thrombosis and Haemostasis* 2017; 15: 47–56 (Impact factor 2016: 5.287), we were able to prove our hypothesis of antithrombotic properties of Omega-3 fatty acids (n-3 FAs) in venous thromboembolism (VTE). Based on our previous experimental findings showing that n-3 FAs, particularly the plant-derived alpha-linolenic acid, reduces atherosclerosis¹, platelet activation and aggregation² and finally, arterial thrombus formation³, we hypothesised that the anti-inflammatory and antithrombotic properties may translate into a reduced risk of VTE. In a translational approach, we determined baseline n-3 FA levels in 826 patients aged ≥ 65 years from *The Swiss cohort of elderly patients with venous thromboembolism (SWITCO65+)*, a prospective multicentre cohort study in elderly patients with acute VTE; n-3 FA levels were categorized into low, medium and high based on the 25th and 75th percentile and the association with the primary endpoint recurrent VTE or total mortality and the individual secondary endpoints recurrent VTE and total mortality were investigated.

We found that subjects with medium and high n-3 FA levels were less likely to develop the composite primary endpoint recurrent VTE or total mortality, as compared with patients with low n-3 FAs. At 6 months patients with medium and high n-3 FA levels had a relative risk reduction of developing recurrent VTE by 61% and 83%, respectively, as compared with patients with low n-3 FAs levels. This effect seemed to have worn off after 3 years. Importantly, we could show that despite a major risk reduction of thrombotic events, the incidence of major and non-major bleeding was not higher in patients with medium or high n-3 FAs. In summary we found that n-3 FAs were associated with a lower risk of recurrent VTE or total mortality in elderly patients with VTE, but not with a greater bleeding risk.

This cohort study for the first time proves beneficial antithrombotic properties of n-3 FAs in recurrent VTE. Considering the major risk reduction for thrombotic events without an parallel increase of bleeding risk, n-3 FAs may provide a safe intervention to reduce VTE and the present study may provide the basis for a follow-up randomised controlled trial investigating a causal relationship between n-3 FAs and VTE. Despite recent advances in the standard treatment of VTE using direct oral anticoagulants, recurrent VTE remains high; Besides, anticoagulation increases the risk of bleeding complications. Therefore, prevention of recurrent VTE by life-style modifications such as healthy diet rich in n-3 FAs or n-3 FA supplements may not only be simple and cost-effective but also safe regarding bleeding complication and may provide a precious additional tool to reduce the burden of VTE.

References

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3. Holy EW, Forestier M, Richter EK, et al. Dietary alpha-linolenic acid inhibits arterial thrombus formation, tissue factor expression, and platelet activation. *Arteriosclerosis, thrombosis, and vascular biology* 2011;31(8):1772-80.