



THROMBIN GENERATION PROFILES IN PATIENTS WITH WILD-TYPE TRANSTHYRETIN AMYLOIDOSIS

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Background and Aims. Thromboembolic events are frequently observed in wild-type transthyretin amyloidosis (ATTRwt), with a reported prevalence ranging from 6% to 28%. The main mechanisms contributing to thrombosis include atrial fibrillation (AF), mechanical atrial dysfunction, and myocardial involvement leading to myopathy. However, thromboembolic complications have also been described in patients who are in sinus rhythm or receiving apparently adequate anticoagulant therapy, suggesting that additional, not yet fully understood, pathophysiological factors may be involved. This study aimed to assess whether hyperactivation of the coagulation system can be detected through thrombin generation (TG) testing in patients with transthyretin amyloidosis.

Methods. A total of 24 patients with ATTRwt (median age 80 years; 17 males and 7 females), all without AF and not receiving anticoagulant therapy, were enrolled. Their results were compared with those of 50 healthy controls matched for age (± 3 years) and sex. Thrombin generation was measured in platelet-poor plasma (PPP) samples, both in the presence and absence of thrombomodulin, using the automated and standardized ST Genesia analyzer (Stago, Asnières-sur-Seine, France) and the STG-ThromboScreen kit, in accordance with the manufacturer's instructions.

Results. Thrombin generation parameters are reported in Table 1. No statistically significant differences were observed between patients and controls across all evaluated parameters. Specifically, lag time (min), endogenous throm-

bin potential (ETP, nmol/L·min), peak height (nM), time to peak (min), velocity index (nM/min), and start tail (min) were comparable between the two groups, both in assays performed with and without thrombomodulin.

Conclusions. Thrombin generation profiles in patients with ATTRwt appear to be similar to those observed in healthy individuals. These findings suggest that, under the conditions examined, there is no clear evidence of coagulation system hyperactivation detectable by TG. Further studies are warranted to better elucidate the molecular mechanisms underlying potential hypercoagulability and to determine whether TG may serve as a predictive marker of a prothrombotic clinical phenotype.

	ATTRwt patients (n. 24)	Healthy Controls (n. 24)	P value
Sex (male/female)	17/7	17/7	-
Median age (years)	80 (± 16)	78 (± 14)	-
WB-TG without TM			
Lag time, min	4.2 (3.6-5.4)	4.0 (3.3-4.5)	0.19
ETP, nmol/l*min	1232 (1067-1367)	1399 (1266-1514)	0.09
Peak-height, nM	202 (160-238)	199 (173-243)	0.57
Time-to-peak, min	7.5 (6.1-8.7)	8.3 (6.8-9.2)	0.87
Vel index, nM/min	66.0 (40.6-85.5)	49.3 (36.4-75.5)	0.55
Start tail (min)	23.9 (22.3-27.0)	26.1 (22.8-27.5)	0.70
WB-TG with TM			
Lag time, min	5.1 (4.3-6.2)	4.3 (3.8-5.0)	0.13
ETP, nmol/l*min	396 (175-578)	568 (301-743)	0.10
Peak-height, nM	85 (27-133)	113 (58-137)	0.18
Time-to-peak, min	8.3 (6.8-10.0)	7.3 (6.4-8.3)	0.06
Vel index, nM/min	29.4 (7.2-55.8)	36.9 (18.5-57.7)	0.35
Start tail (min)	22.6 (21.1-25.0)	21.8 (20.5-23.3)	0.15