

GENDER DIFFERENCES IN COAGULATION PROFILE IN OBSTRUCTIVE CORONARY ARTERY DISEASE: PRELIMINARY RESULTS FROM AN ANGIOGRAPHICALLY CONTROLLED COHORT STUDY

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Background and Aims. Gender differences in ischemic heart disease are widely reported but remain still not fully understood. In the present study we aimed to assess sex-related variations in coagulation profiles among individuals with angiographically confirmed obstructive coronary artery disease (CAD).

Methods. This analysis was conducted within the framework of the Verona Heart Study - Rovereto cohort, which is an observational study enrolling clinically stable subjects scheduled for elective coronary angiography. Obstructive CAD was defined by lumen stenosis >50% in at least one epicardial vessel. Subjects who were using oral anticoagulants, had any acute illness or had experienced a myocardial infarction within the past three months were excluded from the analysis. The coagulation panel included coagulant activity of factors II, V, VII, VIII, IX, X, XI, and XII, as well as global coagulation test, like thrombin generation assay (TGA), and biomarkers of tissue factor (TF) pathway, such as tissue factor pathway inhibitor (TFPI) and activated factor VII-antithrombin (FVIIa-AT) complex.

Results. Complete coagulation profiles were obtained for 64 females and 257 males with obstructive CAD (mean age 68.9 ± 9.4 years). With respect to general clinical and laboratory characteristics, females were older, had lower body mass index (BMI), and higher LDL cholesterol plasma concentration, while no difference was found for prevalence of hypertension, diabetes, dyslipidemia and smoking habit. Compared to males, females had significantly higher levels of coagulant activity of factors V, VII, XI, and XII, as well as higher plasma concentration of FVIIa-AT (Table 1). Female sex remained associated with increased levels of both FVII coagulant activity and FVIIa-AT plasma concentration after adjustment for age, BMI, renal function, plasma lipids and coagulant activity of the other factors by linear regression models. On the other hand, there was no significant difference for TGA parameters (Table 1).

Conclusions. Women with obstructive CAD showed specific differences in their coagulation profiles and biomarkers compared to men, though there was no impact on overall TGA parameters.

Table 1: Differences in coagulation parameters according to gender

	Total (n = 321)	Males (n = 257)	Females (n = 64)	*P* *
Coagulant activity of coagulation factors				
FII:C (%)	88.9 ± 11.8	88.3 ± 11.7	91.5 ± 12.2	0.077
FV:C (%)	86.6 ± 18.1	85.1 ± 18.2	93.3 ± 16.3	**0.004**
FVII:C (%)	87.4 (84.9-89.9)	85.4 (82.8-88.1)	96.2 (89.7-103.2)	**0.001**
FVIII:C (%)	98.8 (95.2-102.7)	98.4 (94.3-102.7)	100.6 (92.5-109.5)	0.656
FIX:C (%)	116.6 ± 18.9	116.6 ± 18.4	116.6 ± 21.4	0.997
FX:C (%)	93.9 (92.0-96.0)	93.4 (91.2-95.6)	96.4 (91.6-101.4)	0.247
FXI:C (%)	102.1 ± 19.7	100.3 ± 19.0	110.0 ± 20.9	**0.001**
FXII:C (%)	98.0 ± 25.4	95.8 ± 25.1	107.1 ± 24.6	**0.004**
Thrombin generation assay				
Lag time (min)	3.70 (3.59-3.80)	3.73 (3.62-3.85)	3.55 (3.31-3.80)	0.159
Time to peak (min)	7.13 (6.96-7.32)	7.17 (6.98-7.37)	6.99 (6.54-7.46)	0.428
Peak (nM)	166 (158-174)	167 (159-176)	161 (142-174)	0.523
ETP (nM*min)	1001 (967-1036)	998 (962-1036)	1013 (924-1109)	0.746
MRI (nM/min)	49.1 (45.7-52.7)	49.5 (45.8-53.5)	47.4 (39.5-56.9)	0.633
Biomarkers of TF pathway				
FVIIa-AT (pM)	101.1 (95.7-106.8)	96.0 (90.2-102.2)	124.0 (111.9-137.3)	**<0.001**
Total TFPI (ng/mL)	65.5 ± 14.5	64.7 ± 13.7	68.7 ± 16.9	0.060

* by t-test.

ETP: Endogenous Thrombin Potential; MRI: Mean Rate Index; TF: Tissue Factor; TFPI: Tissue Factor Pathway Inhibitor