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PHENOTYPE OF BLOOD BORNE MICROPARTICLES: MARKER OF PREMATURE ATHEROSCLEROSIS IN RECENTLY MENOPAUSAL WOMEN?

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Objective: Circulating microparticles are membrane fragments shed from activated cells which are characterized by surface markers consistent with their cells of origin. Alterations within the microparticle pool may indicate early pre-clinical vascular disease processes. Our study was designed to test the relationship between the phenotype of circulating microparticle and plaque formation quantified by coronary calcification scans in early menopausal women.

Methods: Blood from women being screened for the Kronos Early Estrogen Prevention Study (KEEPS) was collected into citrate-benzamidine anticoagulant. Microparticles were prepared by differential centrifugation and evaluated by flow cytometry (FACS Canto™) for expression of phosphatidylserine (PS) and platelet and endothelial antigens. Coronary artery calcification (CAC) was scored using 64 slice CT scanners (Siemens).

Results: Women averaged 53.6 ± 0.6 years of age and were 21 ± 2.9 months past menopause. Twenty three of 157 women had measurable calcium in their coronary arteries (range 0.3-315 Agatston Units). Blood samples were randomly selected from ten age-matched individuals who had negative scores. Cardiovascular risk factors for atherosclerotic disease did not differ among women with low (Agatston scores $0 < 50$; range 0.3-32), high (scores > 50 ; range 93-315) or negative scores (Table). Current smokers ($n=2$) were both in the low CAC group. Metabolic syndrome was present in negative ($n=1$), low ($n=4$) and high ($n=1$) CAC groups. Total numbers of microparticles (Table), those expressing PS and those of platelet- and endothelial-origin were elevated significantly ($p < 0.05$) in women of the high CAC group. Framingham Risk Score (FRS) was calculated by the NCEP calculator. Overall risk was low for this group of women. Total number of microparticles was positively related to FRS: 729 ± 115 ($n=25$) in women with FRS $\leq 1\%$ compared to 1767 ± 770 ($n=8$) in women with FRS of 2-3%.



KEEPS

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Conclusion: Total and phenotypic characterization of blood borne microparticles may be useful for identification of early menopausal women with premature atherosclerosis who otherwise would not be identified by the usual risk factor analysis.

	BMI (Kg/m ²)	Total Cholesterol (mg/dL)	HDL (mg/dL)	Microparticles (number / μ L plasma)			
				Total	PS positive	Platelet- derived	Endothelium -derived
Negative CAC (n=10)	26.1 \pm 1.2	208.5 \pm 11.3	62.8 \pm 3.9	584 \pm 94	286 \pm 80	131 \pm 49	11 \pm 1.3
Low 0<50 CAC Score (n=18)	27.9 \pm 1.0	213.2 \pm 9.5	57.3 \pm 4.4	810 \pm 153	263 \pm 104	169 \pm 66	9 \pm 2.7
High >50 CAC Score (n=5)	28.6 \pm 3.1	213.0 \pm 12.6	59.1 \pm 8.1	2376 \pm 1169	1731 \pm 1154	2007 \pm 1023	124 \pm 83

^aData are shown as mean \pm SEM