Does inherited thrombophilia contributes thrombosis in microvascular free flap surgery: a pilot study.

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Background and Goal of study:

The role of microvascular surgery as a part of reconstructive surgery is enhancing and has been technically improved, nevertheless mishap due to thrombosis still occurs delaying restitution, thus bearing detrimental effect for patient, medical team and expenses.

Hereditary thrombophilia is a well known factor possessing increased risk for vascular events, however still beyond the scope of microvascular surgery. The goal of the study is to educe whether link between genetic factors and likelihood of thrombosis in microvascular free flap surgery exists.

Material and Methods:

60 patients undergone free flap microvascular surgery were enrolled in the cohort study.

Table 1. Phenotypic characteristics of the study group

	n= 60	(%)
Age, years (M; ±SD)	39.35	
	±12.74	
Sex, males	53	88
Risk factors, n		
Recent trauma	19	32
Metabolic disturbances (DM, obesity)	6	10
Cardiovascular disease*	3	5
Other factors**	6	10
Smoking	28	47

*Cardiovascular pathology- MI, PAH, DVT

**Other factors- paraparesis, tetraparesis, spina bifida, epilepsy, neurofibroma

We selected nine single nucleotide polymorphisms (SNPs) reported to be associated with vascular thrombosis (Table 2).

Results and Discussion:

In 10/60 (17 %) patients free flap failure due to thrombosis occurred.

We found SNP rs2289252 in *F11* and rs13146272 in *CYP4V2* in 7 and 5 patients in thrombosis group, respectively. Occurrence in non- thrombotic group of same SNPs is common either, both indicating high prevalence in observed population. (Table 3.)

rs6025 *FV Leiden* and rs1799963 *FII* were found in non-thrombotic group but none in thrombotic group.

rs2227589 in *SERPINC1* were identified in 4 patients with flap thrombosis and in 10 patients with non-thrombosis, including those (6) having perioperative thromboprophylaxis due to co-morbidities.

rs1613662 in *GP6* along with history of myocardial infarction prior age of 45 were identified in 3 patients in non- thrombosis group with thromboprophylaxis.

Several SPNs combinations in thrombotic patients group were detected however no correlation was defined yet.

Table 3. Analysed SNPs

SNP (Gene)	Genotype	Thrombosis	Non- thrombosis	OR (95% CI)	p value
1. rs5361 (<i>SELE</i>)	GG/GT/TT	0/3/7	1/7/42	2.25 (0.47-10.59)	0.305
2. rs2227589 (<i>SERPINC1</i>)	TT/CT/CC	0/4/6	0/10/40	2.66 (0.63-11.28)	0.182
3. rs2066865 (<i>FGG</i>)	AA/AG/GG	0/3/7	1/10/39	1.51 (0.33- 6.87)	0.587
4. rs13146272 (<i>CYP4V2</i>)	CC/AC/AA	1/4/5	2/26/22	0.78 (0.20- 3.06)	0.728
5. rs2289252 (<i>F11</i>)	TT/CT/CC	1/6/3	4/21/25	2.33 (0.54- 10.06)	0.256
6. rs1613662 (<i>GP6</i>)	GG/AG/AA	0/3/7	1/8/41	1.95 (0.42- 9.04)	0.392
7. rs1801133 (<i>MTHFR</i>)	AA/AG/GG	0/4/6	1/16/33	1.29 (0.32-5.21)	0.717
8. rs6025 (<i>FV Leiden</i>)	TT/CT/CC	0/0/0	0/2/58	-	-
9. rs1799963 (<i>FII</i>)	AA/AG/GG	0/0/0	0/1/59	-	-

Conclusion: Several gene polymorphisms are found in patients with thrombotic complications indicating a potential cause of microvascular free flap thrombosis likely synergistic with other well known thrombophilia contributing factors. Further data are mandatory and greater sample size is needed to set relationship between gene mutation and thrombosis in free flap surgery.

Table 2. Summary of selected SNPs

SNP (Gene)	Encoded proteins and their defects
1. rs5361 (<i>SELE</i>)	Alteration of leukocyte- endothelial interaction due to E- selectine enhanced adhesion to leukocytes
2. rs2227589 (<i>SERPINC1</i>)	Antithrombin (AT) deficiency- decreased antigen level and functional activity (type I)
3. rs2066865 (<i>FGG</i>)	Increased level of fibrinogen
4. rs13146272 (<i>CYP4V2</i>)	Metabolic disorder of fatty acids
5. s2289252 (<i>F11</i>)	Increased level of coagulation factor F11 (XI)
6. rs1613662 (<i>GP6</i>)	Glycoprotein VI- the platelet receptor for collagen-increased aggregation potency
7. rs1801133 (<i>MTHFR</i>)	Increased level of homocysteine (inhibits activation of protein C)
8. rs6025 (<i>FV Leiden</i>)	Activated protein C resistance (APC), inability to form protein C-FVa complex due to defective FV
9. rs1799963 (<i>FII</i>)	Increased prothrombin level

Figure 1. SNPs found in thrombosis group

Figure 2. SNPs found in non-thrombosis group

α -0.005