SUPPLEMENTAL MATERIAL

Supplemental Table 1: Genetic Polymorphisms Evaluated in the Discovery Cohort

Gene (*Symbol*)	Nucleotide Substitution	SNPid*	Minor Allele Frequency
Angiotensin Converting Enzyme (*ACE*)	2350G>A	rs4344	0.443
	-240A>T	rs4291	0.364
β1 adrenergic receptor (*ADRB1*)	1165C>G	rs1801253	0.246
	145A>G	rs1801252	0.121
β2 adrenergic receptor (*ADRB2*)	-47T>C	rs1042711	0.396
	46G>A	rs1042713	0.368
	79C>G	rs1042714	0.314
β3 adrenergic receptor (*ADRB3*)	387T>C	rs4994	0.092
Angiotensin (*AGT*)	842T>C	rs699	0.466
	-6G>A	rs5051	0.464
	659C>T	rs4762	0.103
Angiotensin receptor (*AGTR1*)	1166A>C	rs5186	0.260
Apolipoprotein E (*APOE*)	448T>C	rs429358	0.134
	586C>T	rs7412	0.085
	-219G>T	rs405509	0.450
Bactericidal/permeability-increasing protein (*BPI*)	270C>T	rs1341023	0.477
Catalase (*CAT*)	-21T>A	rs17880664	0.349
	-262G>A	rs1001179	0.204
	-844T>C	rs769214	0.348
CD14 Antigen (*CD14*)	-260G>A	rs2569190	0.476
C reactive protein (*CRP*)	3'Fl C>T	rs1205	0.314
	1059G>C	rs1800947	0.061
Cathepsin G (*CTSG*)	2108A>G	rs45567233	0.066
E-selectin (*ELAM1*)	98G>T	rs1805193	0.084
	561A>C	rs5361	0.089
Tissue factor (*F3*)	-603A>G	rs1361600	0.493
Fibrinogen beta chain (*FGB*)	-455G>A	rs1800790	0.164
	-854G>A	rs1800791	0.141
	-148C>T	rs1800787	0.176

Fibrinogen gamma chain (*FGG*)	-649A>G	rs1800792	0.389
G-protein β3 subunit (*GNB3*)	825C>T	rs5443	0.359
Glycoprotein Iba (*GP1BA*)	-5 T>C	rs2243093	0.138
	524C>T	rs6065	0.106
Glycoprotein VI (*GP6*)	13254A>G	rs1613662	0.178
Heat shock protein 70-homologous (*HSPA1L*)	1478T>C	rs2227956	0.161
Intercellular adhesion molecule-1 (*ICAM1*)	1462A>G	rs5498	0.401
	778G>A	rs1799969	0.100
Interleukin 1α (*IL1A*)	-889 C>T	rs1800587	0.323
	4844 G>T	rs17561	0.282
Interleukin 1β (*IL1B*)	-511 C>T	rs16944	0.369
	5810G>A	rs1143633	0.300
	5887C>T	rs1143634	0.224
Interleukin 1-receptor antagonist (*IL1RN*)	11100 T>C	rs315952	0.316
	8006T>C	rs419598	0.241
Interleukin 6 (*IL6*)	-174G>C	rs1800795	0.411
	-597G>A	rs1800797	0.393
	-572G>C	rs1800796	0.056
Interleukin 8 (*IL8*)	-251T>A	rs4073	0.497
Interleukin 10 (*IL10*)	-592C>A	rs1800872	0.255
	-819C>T	rs1800871	0.252
Glycoprotein IaIIa (*ITGA2*)	-52C>T	rs28095	0.345
	807C>T	rs1126643	0.353
Glycoprotein IIIa (*ITGB3*)	1565T>C	rs5918	0.152
Lipopolysaccharide-binding protein (*LBP*)	42711T>C	rs2232618	0.114
	19983T>C	rs2232582	0.192
Lipoprotein lipase (*LPL*)	1595C>G	rs328	0.096
Matrix metallopeptidase 9 (*MMP9*)	-1562C>T	rs3918242	0.127
Methylenetetrahydrofolate reductase (*MTHFR*)	677C>T	rs1801133	0.276
Endothelial nitric oxide synthase (*NOS3*)	894G>T	rs1799983	0.324
	20628G>T	rs1799985	0.315
	-786T>C	rs2070744	0.369

Plasminogen Activator Inhibitor-1 (*PAI-1*)	-844A>G	rs2227631	0.463
Platelet-endothelial cell adhesion molecule-1 (*PECAM1*)	1688A>G	rs12953	0.387
Paraoxonase 1 (*PON1*)	-108G>A	rs705379	0.444
	A>T	rs854560	0.369
	-825C>T	rs854571	0.328
	-162C>T	rs705381	0.265
	584 A>G	rs662	0.337
Paraoxonase 2 (*PON2*)	964C>G	rs7493	0.213
Peroxisome proliferator-activated receptor α (*PPARA)*	2498G>C	rs4253778	0.179
Peroxisome proliferator-activated receptor γ(*PPARG*)	Ex4-49C>G	rs1801282	0.093
Sodium channel, voltage-gated, type V, alpha subunit (*SCN5A*)	1673A>G	rs1805124	0.260
P-selectin (*SELP*)	-1969G>A	rs1800805	0.377
	1902A>G	rs6127	0.372
	2013G>T	rs6133	0.150
	2361A>C	rs6136	0.094
	1087G>A	rs6131	0.169
Tissue factor pathway inhibitor (*TFPI*)	-399C>T	rs10153820	0.122
Transforming growth factor β1 (*TGFB1*)	869T>C	rs1800470	0.336
	915G>C	rs1800471	0.079
	-800G>A	rs1800468	0.074
	-509C>T	rs1800469	0.290
Thrombomodulin (*THBD*)	1959C>T	rs1042579	0.173
Toll-like receptor 4 (*TLR4*)	1196C>T	rs4986791	0.065
	896A>G	rs4986790	0.055
Tumor necrosis factor a (*TNFA*)	-308G>A	rs1800629	0.161
	+488G>A	rs1800610	0.068
	-238G>A	rs361525	0.054
Vascular cell adhesion molecule-1 (*VCAM1*)	-1594T>C	rs1800821	0.068
Vesicular Monoamine Transporter 2 (*VMAT2*)	813+15T>C	rs2072362	0.101

* Based on Entrez SNP (http://www.ncbi.nlm.nih.gov/entrez/)

Supplemental Table 2: Genetic Polymorphisms Evaluated in the Validation Cohort

Gene (*Symbol*)	SNPid	Location	Position
Thrombomodulin (*THBD*)	rs3176123	3'UTR	1143
	rs2007363	Flanking_3'UTR	-975
	rs6048519	Flanking_5'UTR	-3973
	rs2424505	Flanking_5'UTR	-5748
	rs1318041	Flanking_5'UTR	-11065
	rs6048526	Flanking_5'UTR	-14057

*Based on Entrez SNP (http://www.ncbi.nlm.nih.gov/entrez/). UTR, untranslated region.

Supplemental Table 3: MALDI-TOF Genotyping Assay Primers

SNPid*	**P2**	**P1**	**UEP**
rs4344	ACGTTGGATGACAATGTTGTGATGGGTGCC	ACGTTGGATGATCTATGTCGGGCAAGTCAC	CAAGATTATTAACTTCTTCCCC
rs4291	ACGTTGGATGGCAGAGGAAGCTGGAGAAAG	ACGTTGGATGTCGGGTGTTCCGGCAAACTG	CTGGAGAAAGGGCCTCCTCTCTTT
rs1801253	ACGTTGGATGATCATCTACTGCCGCAGCCC	ACGTTGGATGTCTCCGTGGGTCGCGTGGC	CGACTTCCGCAAGGCCTTCCAG
rs1801252	ACGTTGGATGCTCGTTGCTGCCTCCCGCC	ACGTTGGATGATGAGCGCCATCAGCAGACC	CTGCCTCCCGCCAGCGAA
rs1042711	ACGTTGGATGAATGAGGCTTCCAGGCGTCC	ACGTTGGATGTCTGGCAGGTAAGCGCACTG	CCCGCCGTGGGTCCGCC
rs1042713	ACGTTGGATGAACGGCAGCGCCTTCTTGCT	ACGTTGGATGCACACCTCGTCCCTTTGCTG	CGCCTTCTTGCTGGCACCCAAT
rs1042714	ACGTTGGATGAGACATGACGATGCCCATGC	ACGTTGGATGTTGCTGGCACCCAATGGAAG	ACCCACACCTCGTCCCTTT
rs4994	ACGTTGGATGGAGGCAACCTGCTGGTCATC	ACGTTGGATGGCGAAGTCACGAACACGTTG	CTGGTCATCGTGGCCATCGCC
rs699	ACGTTGGATGTGTGACAGGATGGAAGACTG	ACGTTGGATGGTGGACGTAGGTGTTGAAAG	AAGACTGGCTGCTCCCTGA
rs5051	ACGTTGGATGTACCTTCTGCTGTAGTACCC	ACGTTGGATGCCCCTCAGCTATAAATAGGG	AACAACGGCAGCTTCTTCCCC
rs4762	ACGTTGGATGACAAACGGCTGCTTCAGGTG	ACGTTGGATGTGTACAGGGCCTGCTAGTGG	CTGTGAACACGCCCACCACC
rs5186	ACGTTGGATGATTCCTCTGCAGCACTTCAC	ACGTTGGATGCGGTTCAGTCCACATAATGC	GCACTTCACTACCAAATGAGC
rs429358	ACGTTGGATGTGTCCAAGGAGCTGCAGGC	ACGTTGGATGTCGGTGCTCTGGCCGAGCAT	GCGGACATGGAGGACGTG
rs405509	ACGTTGGATGACATTCCCCTTCCACGCTTG	ACGTTGGATGTAGAGGTCTTTTGACCACCC	GAATGGAGGAGGGTGTCTG
rs1341023	ACGTTGGATGGGAGGATGAGAGAGAACATG	ACGTTGGATGTATGGCGACCAGCACCATCA	TTGCAACGCGCCGAGATGGG
rs17880664	ACGTTGGATGACCCTCAGCAGGCAAATCTG	ACGTTGGATGCTGATTGGCTGAGCCTGAAG	ATCTGCCTGTTGCCCCGAG
rs1001179	ACGTTGGATGAGGATGCTGATAACCGGGAG	ACGTTGGATGTCTGGCCCAGCAATTGGAGAG	CGCCCTGGGTTCGGCTAT
rs2569190	ACGTTGGATGGAGACACAGAACCCTAGATG	ACGTTGGATGGCAATGAAGGATGTTTCAGG	GCAGAATCCTTCCTGTTACGG
rs1205	ACGTTGGATGGCCATCTTGTTTGCCACATG	ACGTTGGATGGTTTGTCAATCCCTTGGCTC	TTGTTTGCCACATGGAGAGAGACT
rs1800947	ACGTTGGATGGAAATGTGAACATGTGGGAC	ACGTTGGATGAGGACATTAGGACTGAAGGG	TGTGAACATGTGGGACTTTGTGCT
rs1805193	ACGTTGGATGCTGCTTCCCAAAACGGAAAG	ACGTTGGATGGCTGAGAGAAACTGTGAAGC	TATTTCAAGCCTAAACCTTTGGGT
rs5361	ACGTTGGATGGTCCTCCTCATCATGCTTTG	ACGTTGGATGTGGTCTCTACACATTCACCG	GCCTGTACCAATACATCCTGC
rs1361600	ACGTTGGATGTCTTCTACCCCACGAAGGTC	ACGTTGGATGATTCCCACCGCCTTTCTCCTG	CTACCCCACGAAGGTCAAGAATAC
rs1800790	ACGTTGGATGGCTTATGTTTTCTGACAATG	ACGTTGGATGTCATAGAATAGGGTATGAAT	CATAATTCTATTTCAAAAGGGGC
rs1800791	ACGTTGGATGCTCACAGACTAAATGAGGCC	ACGTTGGATGCACACAAGTGAACAGACAAG	GAGGCCCATTTTCCTTCATTT
rs1800787	ACGTTGGATGCATTTAAGCAACATCTTCCC	ACGTTGGATGAACTTCCCATCATTTTGTCC	AAGCAACATCTTCCCAGCAAA
rs1800792	ACGTTGGATGATGCCCACCTTCAGACAAAG	ACGTTGGATGCCTCTGTGTCAACCATGTTC	GAGCTCAAAAGCTCCCTGAG
rs5443	ACGTTGGATGTCTCCCACGAGAGCATCATC	ACGTTGGATGTCGTAGCCAGCGAATAGTAG	ATCATCTGCGGCATCACGTC

rs2243093	ACGTTGGATGATCCACTCAAGGCTCCCTTG	ACGTTGGATGTTGGCAGCAGGAGCAGCAAG	GGCTCCCTTGCCCACAGG
rs6065	ACGTTGGATGTGTTGTTAGCCAGACTGAGC	ACGTTGGATGAAGGCAATGAGCTGAAGACC	TCCAGCTTGGGTGTGGGC
rs1613662	ACGTTGGATGATTTCCCAGGAACCTCTGTG	ACGTTGGATGATACGCTGTGCACCAGAATG	TACCAACAGAACCACCTTCC
rs2227956	ACGTTGGATGTGTCATTGGTGATGGTGATC	ACGTTGGATGGCCAATGGTATTCTCAATGTC	TTCACCTTGCCGGTGCTCTTGTCC
rs5498	ACGTTGGATGGATGACAATCTCATACCGGG	ACGTTGGATGAGGAGCACTCAAGGGGAGGT	GGAGAGCACATTCACGGTCACCT
rs1799969	ACGTTGGATGTTGCCATAGGTGACTGTGGG	ACGTTGGATGTCCTAGAGGTGGACACGCAG	CCGAGACTGGGAACAGCC
rs1800587	ACGTTGGATGTTGGGAGAAAGGAAGGCATG	ACGTTGGATGTTCTACCACCTGAACTAGGC	TTTTTACATATGAGCCTTCAATG
rs17561	ACGTTGGATGTTTCACATTGCTCAGGAAGC	ACGTTGGATGATCTGCACTTGTGATCATGG	GCTCAGGAAGCTAAAAGGTG
rs16944	ACGTTGGATGATTTTCTCCTCAGAGGCTCC	ACGTTGGATGTGTCTGTATTGAGGGTGTGG	TGCAATTGACAGAGAGCTCC
rs1143633	ACGTTGGATGTGACCGTATATGCTCAGGTG	ACGTTGGATGTAAAATCAGAAGGGCAGGCC	CCTCCAAGAAATCAAATTTTGCC
rs1143634	ACGTTGGATGAGTGATCGTACAGGTGCATC	ACGTTGGATGGTGCTCCACATTTCAGAACC	GCCTCGTTATCCCATGTGTC
rs315952	ACGTTGGATGGAACAGAAAGCAGGACAAGC	ACGTTGGATGAGGCGGCAGACTCAAAACTG	CGCCTTCATCCGCTCAGACAG
rs419598	ACGTTGGATGTGGGATGTTAACCAGAAGAC	ACGTTGGATGAATTGACATTTGGTCCTTGC	CTGAGGAACAACCAACTAGTTGC
rs1800795	ACGTTGGATGAGCCTCAATGACGACCTAAG	ACGTTGGATGGATTGTGCAATGTGACGTCC	TTTCCCCCTAGTTGTGTCTTGC
rs1800797	ACGTTGGATGACGCCTTGAAGTAACTGCAC	ACGTTGGATGTCTTCTGTGTTCTGGCTCTC	AAGTAACTGCACGAAATTTGAGG
rs1800796	ACGTTGGATGACGCCTTGAAGTAACTGCAC	ACGTTGGATGTCTTCTGTGTTCTGGCTCTC	CAGGCAGTCTACAACAGCC
rs1800872	ACGTTGGATGTCCTCAAAGTTCCCAAGCAG	ACGTTGGATGAAAGGAGCCTGGAACACATC	CCAGAGACTGGCTTCCTACAG
rs1800871	ACGTTGGATGTAGTGAGCAAACTGAGGCAC	ACGTTGGATGATTCTCAGTTGGCACTGGTG	GCAAACTGAGGCACAGAGAT
rs28095	ACGTTGGATGGATCCGGTGTTTGCGGAATC	ACGTTGGATGAGGGAAAAGTTTCTGGGCAG	CGGAATCAGGAGGGGCGGGC
rs1126643	ACGTTGGATGTGGCCTATTAGCACCAAAAC	ACGTTGGATGAGACATCCCAATATGGTGGG	TTACCTTGCATATTGAATTGCTCC
rs5918	ACGTTGGATGCCTTCAGCAGATTCTCCTTC	ACGTTGGATGTTGCTGGACTTCTCTTTGGG	TCACAGCGAGGTGAGCCC
rs2232618	ACGTTGGATGGCTCCTCAACTATTACATCC	ACGTTGGATGCAGCAGTGTTCACTTTTGAC	CAACTATTACATCCTTAACACC
rs2232582	ACGTTGGATGTGAACATCCACAGCTGTGAG	ACGTTGGATGAGTCGGAGATGCTGAGACTC	GCGCTGAGGCCTGTCCC
rs328	ACGTTGGATGCTTTAGCCCAGAATGCTCAC	ACGTTGGATGAAAGGCACCTGCGGTATTTG	TTAGCCCAGAATGCTCACCAGCCT
rs3918242	ACGTTGGATGAAAAATTTAGCCAGGCGTGG	ACGTTGGATGGGTTCAAGCAATTCTCCTGC	CCAGGCGTGGTGGCGCA
rs1801133	ACGTTGGATGATGCCTTCACAAAGCGGAAG	ACGTTGGATGCTTGAAGGAGAAGGTGTCTG	GCTGCGTGATGATGAAATCG
rs1799983	ACGTTGGATGAAACGGTCGCTTCGACGTGC	ACGTTGGATGATCCCTTTGGTGCTCACGTG	GCTGCAGGCCCCAGATGA
rs1799985	ACGTTGGATGAGCGGCTGCATGACATTGAG	ACGTTGGATGGTCCCTAGATTGTGTGACTC	TGAGAGCAAAGGTGAGGCTG
rs2070744	ACGTTGGATGAGTTTCCCTAGTCCCCCATG	ACGTTGGATGAGTCAGCAGAGAGACTAGGG	CATCAAGCTCTTCCCTGGC
rs2227631	ACGTTGGATGAAGGAAACAGGAGACCAACG	ACGTTGGATGGAGGATAAAGGACAAGCTGC	GACCAACGTGTAAGTTTCACTTC
rs854560	ACGTTGGATGCTTTTCTGGCAGAAACTGGC	ACGTTGGATGGAGCTAATGAAAGCCAGTCC	TGGCAGAAACTGGCTCTGAAGAC

rs705381	ACGTTGGATGAGCTAGCTGGGCCGACCAG	ACGTTGGATGAAAGTGCTGAGCTCCTGCGG	ACCAGGTGCACAGAAGGCG
rs662	ACGTTGGATGACATACGACCACGCTAAACC	ACGTTGGATGCCTGAGCACTTTTATGGCAC	CCCAAATACATCTCCCAGGAT
rs4253778	ACGTTGGATGTTCTGGAGATCACAACCACC	ACGTTGGATGGGTGGAACACTTGAAGCTTG	TGGGAAATGAAGCTTTTGAATC
rs1805124	ACGTTGGATGGGGCCAGGGCACCAGCAGT	ACGTTGGATGACAGCGCGGGAGAGCGAGA	GGGCACCAGCAGTGATGTG
rs1800805	ACGTTGGATGGCCTCCATGTCTTTCTGTTC	ACGTTGGATGTCTTCATCCCCATCTGAGAC	GTTCTTACTTTCACTCACCAGC
rs6127	ACGTTGGATGTTCAATGTTGGCTCCACCTG	ACGTTGGATGGCATTCCACATTATTGGGCC	GCTCCACCTGTCATTTCTCTTGT
rs6133	ACGTTGGATGTACAGTACATGGTTCCCTGC	ACGTTGGATGACAGGCATAGCATCACTTCC	GGTGAGGGCTGGACATTGCA
rs6136	ACGTTGGATGATGCCAAGAGAATGGCCAC	ACGTTGGATGCCTGCTTGGCAGGTTGGCA	AAGAGAATGGCCACTGGTCA
rs6131	ACGTTGGATGGCAAAAGCAGTGAGCGGATG	ACGTTGGATGTCTCCAGCTGTGCAGTGTCAG	TGAACACAGTCCATGGTTCCTTCA
rs10153820	ACGTTGGATGTAAAAGTCTGAGGGCTACCG	ACGTTGGATGAAGCCTGACACCTGCAATAG	CCGTTGGAGGTCTCTCTTAGTGA
rs1800471	ACGTTGGATGTGCTGTGGCTACTGGTGCTG	ACGTTGGATGCACCAGCTCCATGTCGATAG	GGTGCTGACGCCTGGCC
rs1800468	ACGTTGGATGTTGACCACTGTGCCATCCTC	ACGTTGGATGTGGAGTGCTGAGGGACTCTG	GTCCGGGGTGTGGATGGTGGTGA
rs1800469	ACGTTGGATGTCTTACAGGTGTCTGCCTCC	ACGTTGGATGAGGGTGTCAGTGGGAGGAG	GCCTCCTGACCCTTCCATCC
rs1042579	ACGTTGGATGAGTCACAGTCGGTGCCAATG	ACGTTGGATGGGTACCTTCGAGTGCATCTG	CACAGTCGGTGCCAATGTGGCGG
rs4986791	ACGTTGGATGACACCATTGAAGCTCAGATC	ACGTTGGATGGCTTGAGTTTCAAAGGTTGC	CAGATCTAAATACTTTAGGCTG
rs4986790	ACGTTGGATGTAGAGGGCCTGTGCAATTTG	ACGTTGGATGCACACTCACCAGGGAAAATG	CATACTTAGACTACTACCTCGATG
rs1800629	ACGTTGGATGGATTTGTGTGTAGGACCCTG	ACGTTGGATGGGTCCCCAAAAGAAATGGAG	ACCCTGGAGGCTGAACCCCGTCC
rs1800610	ACGTTGGATGGAAAGATGTGCGCTGATAGG	ACGTTGGATGCTTGCCACATCTCTTTCTGC	GGGAGGGATGGAGAGAAAAAAAC
rs361525	ACGTTGGATGACACAAATCAGTCAGTGGCC	ACGTTGGATGATCAAGGATACCCCTCACAC	GAAGACCCCCCTCGGAATC
rs2072362	ACGTTGGATGACGTCATGGGAATCGCCTTG	ACGTTGGATGAGGCCCCTCTTGCCAGTTTG	CTTAGGTGGGTAAGGCCCC

Supplemental Table 4: Definition of Variables in the EuroSCORE Risk Model

	Risk factor	STS definition match
1	Age	Per 5 years or part thereof over 60 years
2	Sex	Female
3	Chronic pulmonary disease	Patient required pharmacologic therapy for the treatment of chronic pulmonary compromise, or patient has a FEV1 <75% of predicted value
4	Extracardiac arteriopathy	Patient has peripheral vascular disease as indicated by claudication either with exertion or rest; amputation for arterial insufficiency; aorto-iliac occlusive disease reconstruction; peripheral vascular bypass surgery, angioplasty or stent; documented AAA, AAA repair, or stent; positive non-invasive testing documented – or – Patient has cerebrovascular disease, documented by any one of the following: Unresponsive coma >24 h; CVA (symptoms >72 h after onset); RIND (recovery within 72 h); TIA (recovery within 24 h); or non- invasive carotid test with >75% occlusion
5	Neurological dysfunction disease	A central neurologic deficit persisting more than 24 h
6	Previous cardiac surgery	Prior cardiac surgical operation(s) with or without the use of cardiopulmonary bypass
7	Serum creatinine	>200 mmol/l preoperatively
8	Active endocarditis	Patient currently under antibiotic treatment for endocarditis at the time of surgery
9	Critical preoperative state	Any one or more of the following: sustained ventricular tachycardia or ventricular fibrillation requiring cardioversion and/or IV amiodarone, preoperative inotropic support, preoperative intra-aortic balloon pump, or patient required cardiopulmonary resuscitation within 1 h before the start of the operative procedure
10	Unstable angina	Preoperative use of iv nitrates
11	LV dysfunction	LVEF 30–50%; LVEF <30%
12	Recent myocardial infarction	<21 days
13	Pulmonary hypertension	Systolic PA pressure >30 mmHg
14	Emergency	Procedure status is emergent or salvage. *Emergent:* The patient's clinical status includes any of the following. a. Ischaemic dysfunction (any of the following): (1) ongoing ischaemia including rest angina despite maximal medical therapy (medical and/or IABP); (2) acute evolving myocardial infarction within 24 h before surgery; or (3) pulmonary oedema requiring intubation. b. Mechanical dysfunction (either of the following): (1) shock with circulatory support; or (2) shock without circulatory support. *Salvage:* The patient is undergoing CPR en route to the OR or prior to anaesthesia induction
15	Other than isolated CABG	Any valve procedure in addition to or separate from CABG
16	Surgery on thoracic aorta	Aortic aneurysm/dissection repair
17	Post-infarct septal rupture	Ventricular septal defect

Supplemental Table 5: Baseline Demographic, Clinical and Procedural Characteristics in the Combined Cohort

Characteristics	Survived (n=1664)	Died (n=282)	*P**
Demographics			
Age (years)	62 (11)	67.3 (10)	< 0.001
Gender (% female)	26	38	<0.001
Medical history			
Diabetes (%)	31	48	<0.001
Peripheral vascular disease (%)	13	24	< 0.001
Preoperative LVEF (%)	53.5 (13.9)	48.4 (16.0)	< 0.001
Procedural factors			
CBP duration (min)	112 (47)	130 (58)	< 0.001
Aortic cross-clamp duration (min)	63 (31)	70 (36)	< 0.001
Number of grafts	2.9 (1.1)	2.9 (0.9)	0.96
Intraoperative aprotinin (%)	6	13	<0.001
IMA use (%)	95	92	0.07
Logistic EuroSCORE	3.2 [1.8-6.1]	6.3 [2.9-14.7]	< 0.001
Medications at hospital discharge			
Aspirin (%)	92	92	0.75
Beta-blocker (%)	87	75	<0.001
Statin (%)	48	41	0.037
THBD rs1045279 or rs3176123, 2 copies of minor allele (%)	4	10	< 0.001#

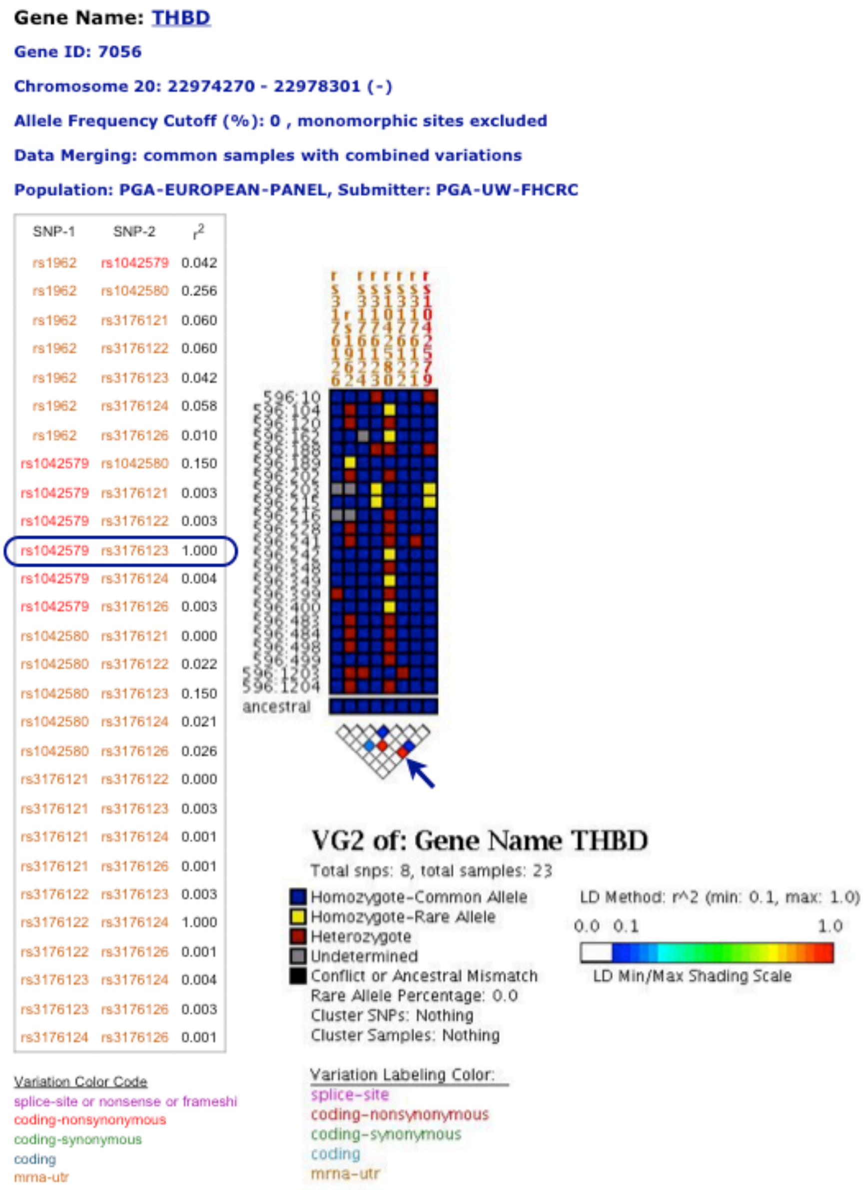
Values expressed as mean (SD), median [interquartile range], or as %. *Wilcoxon rank-sum (continuous variables); Pearson χ^2 (categorical variables). #Probability value refers to a univariate comparison of two copies of the minor (risk) allele to one or no copies of risk allele (recessive model). LVEF, left ventricular ejection fraction; CPB, cardiopulmonary bypass; IMA, internal mammary artery.

Supplemental Table 6: Multivariable Models of 5-year All-Cause Mortality Using Clinical, Procedural and Genotypic Information in the Combined Cohort

Model variables	HR (95% CI)	Predictor P	Model P	Model AIC	Model BIC	Model -2LL	C-statistic
Logistic EuroSCORE	2.07 (1.73-2.48)	<0.001					
Diabetes	1.87 (1.44-2.44)	<0.001					
CPB duration (min)	1.13 (1.02-1.26)	0.02					
Number of grafts	0.98 (0.76-1.26)	0.85					
Discharge beta-blocker	0.61 (0.45-0.83)	0.001					
Discharge statin	0.71 (0.54-0.94)	0.01	<0.0001	1126[a]	1162[a]	1111[a]	0.725[a]
rs1042579 or *rs 3176123* recessive (two copies of minor allele)	2.43 (1.57-3.74)	<0.001	<0.0001	1110[b]	1151[b]	1093[b]	0.74[b]

The predictive values of adding the THBD SNP rs1045279 or rs3176123 recessive genotypes (2 copies of the minor allele) to the baseline clinical model of all-cause mortality are shown for the combined cohort. P values expressed using Wald test; HR, hazard ratio; CI, confidence interval; CPB, cardiopulmonary bypass; AIC, Akaike information criterion; BIC, Bayes information criterion; -2LL, negative two log likelihood ratio; a, values based on clinical multivariable model only; b, values based on combined clinico-genetic model.

Supplemental Figure 1: Linkage Disequilibrium Pattern in Thrombomodulin (*THBD*) Gene



Gene Name: THBD

Gene ID: 7056

Chromosome 20: 22974270 - 22978301 (-)

Allele Frequency Cutoff (%): 0 , monomorphic sites excluded

Data Merging: common samples with combined variations

Population: PGA-EUROPEAN-PANEL, Submitter: PGA-UW-FHCRC

SNP-1	SNP-2	r^2
rs1962	rs1042579	0.042
rs1962	rs1042580	0.256
rs1962	rs3176121	0.060
rs1962	rs3176122	0.060
rs1962	rs3176123	0.042
rs1962	rs3176124	0.058
rs1962	rs3176126	0.010
rs1042579	rs1042580	0.150
rs1042579	rs3176121	0.003
rs1042579	rs3176122	0.003
rs1042579	rs3176123	1.000
rs1042579	rs3176124	0.004
rs1042579	rs3176126	0.003
rs1042580	rs3176121	0.000
rs1042580	rs3176122	0.022
rs1042580	rs3176123	0.150
rs1042580	rs3176124	0.021
rs1042580	rs3176126	0.026
rs3176121	rs3176122	0.000
rs3176121	rs3176123	0.003
rs3176121	rs3176124	0.001
rs3176121	rs3176126	0.001
rs3176122	rs3176123	0.003
rs3176122	rs3176124	1.000
rs3176122	rs3176126	0.001
rs3176123	rs3176124	0.004
rs3176123	rs3176126	0.003
rs3176124	rs3176126	0.001

Variation Color Code
splice-site or nonsense or frameshi
coding-nonsynonymous
coding-synonymous
coding
mrna-utr

VG2 of: Gene Name THBD

Total snps: 8, total samples: 23

- Homozygote-Common Allele
- Homozygote-Rare Allele
- Heterozygote
- Undetermined
- Conflict or Ancestral Mismatch

Rare Allele Percentage: 0.0
Cluster SNPs: Nothing
Cluster Samples: Nothing

LD Method: r^2 (min: 0.1, max: 1.0)
0.0 0.1 1.0
LD Min/Max Shading Scale

Variation Labeling Color:
splice-site
coding-nonsynonymous
coding-synonymous
coding
mrna-utr

Source: Seattle SNPs Variation Discovery Resource, Genome Variation Server (http://gvs.gs.washington.edu/GVS/), accessed on November, 10 2009.

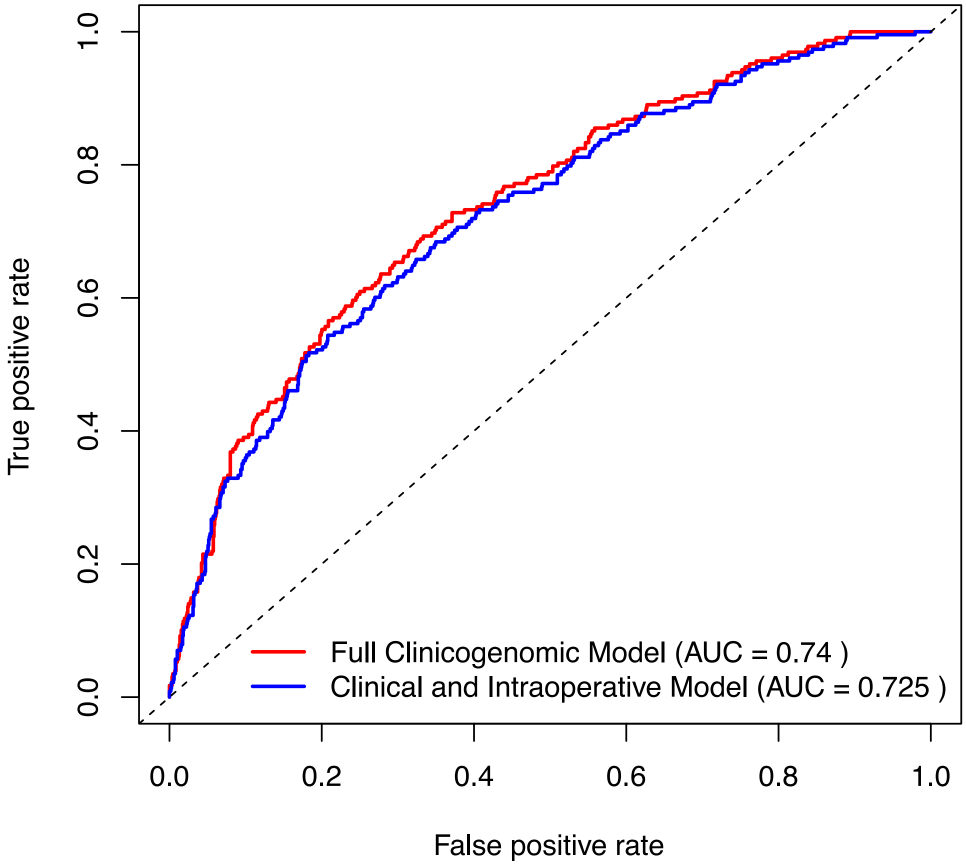
SNP	Proxy	Distance	r^2	D'	Chromosome	Coordinate_HG18	GeneVariant	GeneName	Major	Minor	MAF	NObserved
rs1042579	rs3176123	1311	1	1	chr20	22975413	3PRIME_UTR	THBD	T	G	0.133	120

Source: SNAP SNP Annotation and Proxy Search v.2.2 (http://www.broadinstitute.org/mpg/snap/), Broad Institute.

Supplemental Figure 2. Distribution of rs1042579 and rs3176123 genotypes in a cohort of N=421 patients who were jointly typed at both loci. Pairwise linkage disequilibrium estimates are D'=0.98, r^2=0.97.

```
                  | overlap$RS3176123 
overlap$RS1042579 |       A/A |       A/C |       C/C | Row Total | 
------------------|-----------|-----------|-----------|-----------|
              C/C |       263 |         3 |         0 |       266 | 
                  |     0.625 |     0.007 |     0.000 |           | 
------------------|-----------|-----------|-----------|-----------|
              C/T |         3 |       122 |         0 |       125 | 
                  |     0.007 |     0.290 |     0.000 |           | 
------------------|-----------|-----------|-----------|-----------|
              T/T |         0 |         3 |        27 |        30 | 
                  |     0.000 |     0.007 |     0.064 |           | 
------------------|-----------|-----------|-----------|-----------|
     Column Total |       266 |       128 |        27 |       421 | 
------------------|-----------|-----------|-----------|-----------|
```

Supplemental Figure 3: Receiver Operator Characteristic (ROC) curves for the clinico-genetic and clinical covariate models in the combined cohort



AUC, area under the ROC curve.

ONLINE APPENDIX

Perioperative Genetics and Safety Outcomes Study (PEGASUS) Investigative Team Members

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