Supplemental Table S1 Association of SHTG and dose of the study SNPs

SNP	Gene	Nucleotide variation	TG-raising allele	OR	95%CI	P value
rs1367117	APOB	c.293C>T	T	1·132	0·474-2·704	0·779
rs1042031	APOB	c.12541G>A	A	0·533	0·186-1·533	0·243
rs13306194	APOB	c.1594C>T	T	0·502	0·220-1·146	0·102
rs1042034	APOB	c.13013G>A	A	1·411	0·843-2·360	0·190
rs7205804	CETP	-	A	0·790	0·484-1·289	0·346
rs5104	APOA4	c.440A>G	G	2·252	1·346-3·767	**0·002**
rs651821	APOA5	c.-3G>A	A	5·612	3·049-10·179	**<0·001**
rs2075291	APOA5	c.553G>T	T	5·866	2·045-16·825	**0·001**
rs3135507	APOA5	c.457G>A	A	2·293	1·164-4·516	**0·016**
rs5128	APOC3	c.*40G>C	C	2·173	1·270-3·718	**0·005**
rs4225	APOC3	c.*71G>T	T	3·200	1·574-6·505	**0·001**
rs4984948	LMF1	c.1685C>G	G	1·961	0·799-3·332	0·198
rs8179206	GCKR	c.230A>G	G	1·037	0·291-3·689	0·935
rs1260326	GCKR	c.1337C>T	T	1·676	1·031-2·723	**0·037**
rs7412	APOE	c.526C>T	T	3·398	1·285-8·987	**0·014**
rs440446	APOE	c.42C>G	G	2·117	1·300-3·448	**0·003**
rs327	LPL	c.1323-90T>G	G	0·634	0·322-1·247	0·186
rs328	LPL	c.1421C>G	G	0·536	0·137-2·095	0·370
rs11538389	GPHIBP1	c.41G>T	T	1·332	0·794-2·236	0·278

Supplemental Table S2 Summary of pathogenic/likely pathogenic mutations in 58 patients

Subjects	Gene_Symbol	Nucleotide_Changes	Amino_Acid	Type	SIFT_Predict	PolyPhen_2_Predict	MutationTaster_Predict	Mygeno_InterACMG	Pathogenic
Controls									
1	LMF1	c.856C>T	p.R286W	het	Damaging	Possibly_damaging	Disease_causing	PM2;BP1	Uncertain
2	APOB	c.7043A>G	p.Y2348C	het	Damaging	Benign	Disease_causing	-	Uncertain
3	GPIHBP1	c.545_546ins AGTACCATTC	p.R182fs	het	-	-	-	PVS;PM2	Likely pathogenic
3	GPIHBP1	c.547_548insGC	p.R183fs	het	-	-	-	PVS;PM2	Likely pathogenic
4	APOB	c.3850C>T	p.R1284W	het	Damaging	Probably_damaging	Polymorphism	PM2	Uncertain
5	APOB	c.3404G>A	p.S1135N	het	Damaging	Possibly_damaging	Polymorphism	PM2	Uncertain
6	APOE	c.425C>T	p.A142V	het	Tolerated	Benign	Disease_causing	PM2	Uncertain
7	LMF1	c.1223C>A	p.A408D	het	Damaging	Probably_damaging	Disease_causing	PM2;PP3;BP1	Uncertain
8	APOB	c.4013C>G	p.P1338R	het	Damaging	Probably_damaging	Disease_causing	PM2;PP3	Uncertain
9	APOB	c.3301A>G	p.I1101V	het	Tolerated	Benign	Disease_causing	-	Uncertain
10	GCKR	c.307G>A	p.V103M	het	Damaging	Probably_damaging	Disease_causing	PP3;BS1	Uncertain
11	APOA4	c.916C>T	p.R306W	het	Damaging	Possibly_damaging	Polymorphism	-	Uncertain
11	APOB	c.1433G>A	p.C478Y	het	Damaging	Probably_damaging	Disease_causing	PM2;PP3	Uncertain
11	APOB	c.11303T>C	p.I3768T	het	Damaging	Probably_damaging	Polymorphism	PS1;PM2	Likely pathogenic
11	GCKR	c.1551G>T	p.W517C	het	Tolerated	Possibly_damaging	Disease_causing	BS1	Uncertain
12	APOB	c.7115_7116insCTCT	p.E2372Dfs*15	het	-	-	-	PVS;PM2	Likely pathogenic

12	APOB	c.7114_7115insT	p.E2372Vfs*14	het	-	-	-	PVS;PM2	Likely pathogenic
12	APOB	c.4502_4503insCTCT	p.G1502Sfs*10	het	-	-	-	PVS;PM2;PM5	Pathogenic
12	APOB	c.7112_7113insT	p.K2371Nfs*15	het	-	-	-	PVS;PM2	Likely pathogenic
12	APOB	c.5576_5577ins CGAATGGTAC	p.Q1860Efs*9	het	-	-	-	PVS;PM2	Likely pathogenic
12	GPIHBP1	c.530_531ins AAGAGTACCATTCGAC	p.G177fs	het	-	-	-	PVS;PM2	Likely pathogenic
Cases									
1	APOA5	c.990_993delAACA	p.D332Vfs*5	het	-	-	-	PVS;PS1;PM2	Pathogenic
2	APOB	c.7223C>T	p.S2408F	het	Damaging	Possibly_damaging	Polymorphism	-	Uncertain
3	ANGPTL3	c.587T>C	p.I196T	het	Damaging	Probably_damaging	Disease_causing	-	Uncertain
3	LPL	c.347G>A	p.R116Q	het	Tolerated	Probably_damaging	Disease_causing	PS1;PM2	Likely pathogenic
3	LPL	c.348_349insAGTACCATTC GACAGTC	p.A117Sfs*61	het	#N/A	#N/A	-	PVS;PM2	Likely pathogenic
4	GPIHBP1	c.542_543del	p.A181fs	het	#N/A	#N/A	-	PVS;PM2	Likely pathogenic
5	APOB	c.6043G>A	p.A2015T	het	Tolerated	Possibly_damaging	Disease_causing	PM2	Uncertain
6	ANGPTL3	c.386_387insGTACCATTCG	p.E130Yfs*21	het	-	-	-	PVS;PM2	Likely pathogenic
6	ANGPTL3	c.801_802insAGAGTAC	p.Q268Rfs*10	het	-	-	-	PVS;PM2	Likely pathogenic
6	ANGPTL3	c.1145C>G	p.S382C	het	Damaging	Probably_damaging	Disease_causing	PM2;PP3	Uncertain
6	ANGPTL3	c.1144_1145insAGA	p.S382delinsX	het	-	-	-	PVS;PM2	Likely pathogenic
6	ANGPTL3	c.1148_1149insCA	p.W384Ifs*31	het	-	-	-	PVS;PM2	Likely pathogenic

6	ANGPTL3	c.1150_1151insC	p.W384Sfs*23	het	-	-	-	PVS;PM2	Likely pathogenic
6	ANGPTL3	c.1152G>A	p.W384X	het	-	-	Disease_causing	PVS;PM2	Likely pathogenic
6	ANGPTL3	c.1301G>A	p.W434X	het	-	-	Disease_causing	PVS;PM2	Likely pathogenic
6	APOA1	c.345_346ins CTCTCGAATGGTACTCT	p.E116Lfs*8	hom	-	-	-	PVS;PM2	Likely pathogenic
6	APOA1	c.615_616insG	p.K206Efs*57	het	-	-	-	PVS;PM2	Likely pathogenic
6	APOA1	c.617_618insTG	p.K206Nfs*20	het	-	-	-	PVS;PM2	Likely pathogenic
6	APOA1	c.94_95ins CGTGCTCTCGAAT	p.W32Sfs*31	het	-	-	-	PVS;PM2;PM5	Pathogenic
6	APOA4	c.494A>T	p.E165V	hom	Damaging	Possibly_damaging	Polymorphism	PM2	Uncertain
6	APOA4	c.492G>C	p.M164I	het	Damaging	Possibly_damaging	Disease_causing	PM2	Uncertain
6	APOB	c.10145A>T	p.E3382V	het	Damaging	Probably_damaging	Disease_causing	PM2	Uncertain
6	APOB	c.13292_13293insTGGTA	p.F4432Gfs*47	het	-	-	-	PVS;PM2	Likely pathogenic
6	APOB	c.4216_4217ins TGCTCTCGAATGGTACTC T	p.G1406Vfs*14	het	-	-	-	PVS;PM2	Likely pathogenic
6	APOB	c.4584_4585insTGGTACTCT A	p.G1529Wfs*13	het	-	-	-	PVS;PM2	Likely pathogenic
6	APOB	c.10146_10147ins CTCTCGAATGGTACTCT	p.G3383Lfs*11	het	-	-	-	PVS;PM2	Likely pathogenic

6	APOB	c.12191_12192insGTGCTCT CGAA	p.G4065Cfs*7	het	-	-	-	PVS;PM2	Likely pathogenic
6	APOB	c.2757_2758insCGTGCTCTC GAAT	p.G920Rfs*43	het	-	-	-	PVS;PM2	Likely pathogenic
6	APOB	c.13358_13359ins TGCTCTCGAATGGTACTC T	p.I4454Afs*31	het	-	-	-	PVS;PM2	Likely pathogenic
6	APOB	c.958_959insTGGT	p.K320Mfs*21	het	-	-	-	PVS;PM2	Likely pathogenic
6	APOB	c.959_960insCTCT	p.K320Nfs*21	het	-	-	-	PVS;PM2	Likely pathogenic
6	APOB	c.9941_9942insTG	p.K3314Nfs*14	het	-	-	-	PVS;PM2	Likely pathogenic
6	APOB	c.13044_13045insGTACTCT	p.K4349_E4350delins VLX	het	-	-	-	PVS;PM2	Likely pathogenic
6	APOB	c.4979T>C	p.L1660S	het	Damaging	Possibly_damaging	Polymorphism	PM2	Uncertain
6	APOB	c.4992_4993insTC	p.L1665Sfs*8	het	-	-	-	PVS;PM2	Likely pathogenic
6	APOB	c.6055_6056ins GTGCTCTCGAATGG	p.L2019Rfs*7	het	-	-	-	PVS;PM2	Likely pathogenic
6	APOB	c.10143A>C	p.L3381F	het	Damaging	Benign	Disease_causing	PM2	Uncertain
6	APOB	c.12197_12198delTG	p.L4066Sfs*17	het	-	-	-	PVS;PM2	Likely pathogenic
6	APOB	c.12194_12195insTA	p.L4066Tfs*3	het	-	-	-	PVS;PM2	Likely pathogenic
6	APOB	c.8200_8201ins	p.P2734Rfs*36	het	-	-	-	PVS;PM2	Likely pathogenic

		GTGCTCTCGAATGGTACT CT							
6	APOB	c.956C>G	p.P319R	het	Damaging	Probably_damaging	Disease_causing	PM2	Uncertain
6	APOB	c.4793_4794insCTCGAATG	p.R1599Sfs*14	het	-	-	-	PVS;PM2	Likely pathogenic
6	APOB	c.7874_7875ins CTCTCGAATGGTACTCT	p.R2625fs	het	-	-	-	PVS;PM2	Likely pathogenic
6	APOB	c.4988G>C	p.S1663T	het	Damaging	Possibly_damaging	Polymorphism	PM2	Uncertain
6	APOB	c.560_561insGTGCTCT	p.T188Cfs*21	het	-	-	-	PVS;PM2	Likely pathogenic
6	APOB	c.561_562insGAATGGT	p.T188Efs*21	het	-	-	-	PVS;PM2	Likely pathogenic
6	APOB	c.7631_7632ins TGCTCTCGAATGGTACTC T	p.T2545Afs*14	het	-	-	-	PVS;PM2	Likely pathogenic
6	APOB	c.12201_12202delAA	p.T4068Lfs*15	het	-	-	-	PVS;PM2	Likely pathogenic
6	APOB	c.2888_2889ins CTCTCGAATGGTACTCT	p.W963Cfs*17	het	-	-	-	PVS;PM2;PM5	Pathogenic
6	APOB	c.4115_4116insGTGCTCT	p.Y1373Cfs*24	het	-	-	-	PVS;PM2	Likely pathogenic
6	APOB	c.5339A>C	p.Y1780S	het	Damaging	Probably_damaging	Disease_causing	PM2	Uncertain
6	APOB	c.5340T>G	p.Y1780X	het	-	-	Disease_causing_a utomatic	PVS;PM2	Likely pathogenic
6	APOE	c.339_340insAGCAC	p.E114Sfs*139	het	-	-	-	PVS;PM2	Likely pathogenic
6	APOE	c.334_335insCAGAGTA	p.K113Efs*54	het	-	-	-	PVS;PM2	Likely pathogenic

6	APOE	c.337_338insTTCG	p.K113Ifs*53	het	-	-	-	PVS;PM2	Likely pathogenic
6	CETP	c.353_354ins CCATTCGAGAG	p.T119Hfs*32	het	-	-	-	PVS;PM2	Likely pathogenic
6	LMF1	c.1265_1266insTG	p.Q422Hfs*45	het	-	-	-	PVS;PM2	Likely pathogenic
6	LPL	c.501_502ins GAGAGTACCATTCGAGA	p.A168Efs*10	het	-	-	-	PVS;PM2	Likely pathogenic
6	LPL	c.1081_1082insAGTA	p.A361Efs*4	het	-	-	-	PVS;PM2;PM5	Pathogenic
6	LPL	c.1303_1304delGC	p.A435Rfs*12	het	-	-	-	PVS;PM2	Likely pathogenic
6	LPL	c.429_430insGAGA	p.E145Rfs*4	het	-	-	-	PVS;PM2;PM5	Pathogenic
6	LPL	c.1306_1307ins AGTACCATTC	p.G436Efs*15	het	-	-	-	PVS;PM2	Likely pathogenic
6	LPL	c.769_770insCA	p.L257Pfs*8	het	-	-	-	PVS;PM2	Likely pathogenic
6	LPL	c.377_378ins AGAGTACCATT	p.Y127Efs*49	het	-	-	-	PVS;PM2	Likely pathogenic
6	LPL	c.1009_1010ins CATTCGAGAG	p.Y338Ffs*19	het	-	-	-	PVS;PM2	Likely pathogenic
7	APOB	c.8110_8111ins TGCAGTTCGAATGGTACT CT	p.A2704Vfs*26	het	-	-	-	PVS;PM2	Likely pathogenic
7	APOB	c.9140_9141insTCTC	p.A3048Lfs*7	het	-	-	-	PVS;PM2	Likely pathogenic
7	APOB	c.8362_8363ins	p.G2788Vfs*25	het	-	-	-	PVS;PM2	Likely pathogenic

		TTCGAATGGTACTCTG							
7	APOB	c.5854_5855insGAATGGT	p.H1952Rfs*8	het	-	-	-	PVS;PM2	Likely pathogenic
7	APOB	c.5855_5856insC	p.H1953Sfs*5	het	-	-	-	PVS;PM2	Likely pathogenic
7	APOB	c.10320_10321insG	p.K3441Efs*5	het	-	-	-	PVS;PM2	Likely pathogenic
7	APOB	c.10322_10323insTG	p.K3441Nfs*82	het	-	-	-	PVS;PM2	Likely pathogenic
7	APOB	c.8080A>T	p.R2694W	het	Damaging	Possibly_damaging	Polymorphism	PM2	Uncertain
7	APOB	c.9138_9139insGAATGGT	p.T3047Efs*9	het	-	-	-	PVS;PM2	Likely pathogenic
7	GPIHBP1	c.526_527insA	p.L176fs	het	-	-	-	PVS;PM2	Likely pathogenic
8	APOB	c.5109_5110ins	p.A1704delinsX	het	-	-	-	PVS;PM2	Likely pathogenic
		TAGCGCTTCGAATGGTAC							
		TCT							
8	APOB	c.12462_12463insTGGTA	p.L4155Wfs*4	het	-	-	-	PVS;PM2	Likely pathogenic
8	APOB	c.12457C>T	p.Q4153X	het	-	-	Disease_causing	PVS;PM2	Likely pathogenic
9	APOB	c.2398C>A	p.L800M	het	Tolerated	Possibly_damaging	Disease_causing	-	Uncertain
10	APOA5	c.104G>A	p.S35N	het	Damaging	Benign	Polymorphism	BS1	Uncertain
11	LMF1	c.1184C>T	p.T395I	het	Damaging	Benign	Disease_causing	BP1	Uncertain
12	APOB	c.10579C>T	p.R3527W	het	Damaging	Probably_damaging	Disease_causing	PS1;PP3	Uncertain
13	APOE	c.403_404insAGTAG	p.Q135_Y136delinsQ	het	-	-	-	PVS;PM2	Likely pathogenic
			X						
13	APOE	c.409_410insATTCGACGTC	p.R137Hfs*32	het	-	-	-	PVS;PM2	Likely pathogenic
		ACA							

14	APOA4	c.461G>T	p.R154L	het	Damaging	Probably_damaging	Polymorphism	BS1	Uncertain
15	GCKR	c.680G>A	p.R227Q	het	Tolerated	Possibly_damaging	Polymorphism	-	Uncertain
16	APOB	c.3404G>A	p.S1135N	het	Damaging	Possibly_damaging	Polymorphism	PM2	Uncertain
17	LMF1	c.1228G>A	p.G410R	het	Damaging	Probably_damaging	Disease_causing	BP1	Uncertain
18	LPL	c.10_11insTTCG	p.K4Ifs*38	het	-	-	-	PVS;PM2	Likely pathogenic
19	LMF1	c.475A>G	p.M159V	het	Tolerated	Benign	Disease_causing	BP1	Uncertain
20	APOB	c.12581T>C	p.I4194T	het	Damaging	Benign	Polymorphism	-	Uncertain
21	TRIB1	c.418C>T	p.H140Y	het	Damaging	Probably_damaging	Disease_causing	PM2;PP3	Uncertain
22	APOA5	c.77G>T	p.G26V	het	Tolerated	Possibly_damaging	Disease_causing	PM2	Uncertain
23	LMF1	c.1228G>A	p.G410R	het	Damaging	Probably_damaging	Disease_causing	BP1	Uncertain
24	APOB	c.3404G>A	p.S1135N	het	Damaging	Possibly_damaging	Polymorphism	PM2	Uncertain
25	LPL	c.1015A>C	p.K339Q	het	Damaging	Possibly_damaging	Disease_causing	PM2;PP3	Uncertain
26	APOB	c.6551A>G	p.Y2184C	het	Damaging	Probably_damaging	Polymorphism	-	Uncertain
27	GCKR	c.230A>G	p.E77G	het	Damaging	Benign	Polymorphism	BS1	Uncertain
27	APOA5	c.295G>A	p.E99K	het	Damaging	Probably_damaging	Disease_causing	PP3	Uncertain
28	APOB	c.650C>A	p.P217H	het	Damaging	Probably_damaging	Disease_causing	PM2	Uncertain
29	APOB	c.1620_1621insGCGCTCTTC GAATGGTACT	p.Q541Afs*16	het	-	-	-	PVS;PM2;PM5	Pathogenic
29	LPL	c.1119_1120insACCATTC	p.E374Tfs*11	het	-	-	-	PVS;PM2	Likely pathogenic
29	LPL	c.1121_1122insAGAGCGC	p.N375Efs*10	het	-	-	-	PVS;PM2	Likely pathogenic
29	LPL	c.1115dupA	p.S373Efs*2	het	-	-	-	PVS;PM2	Likely pathogenic

29	LPL	c.1106_1107ins CATTCGAAGAGCG	p.V370Ifs*9	het	-	-	-	PVS;PM2	Likely pathogenic
30	LPL	c.292G>A	p.A98T	het	Tolerated	Probably_damaging	Disease_causing	PS1	Uncertain
30	LPL	c.836T>G	p.L279R	het	Damaging	Probably_damaging	Disease_causing	PS1;PM2;PP3	Likely pathogenic
31	LMF1	c.41_42insTGCTACTCGAATG	p.L15Afs*18	het	-	-	-	PVS;PM2	Likely pathogenic
32	APOE	c.192G>C	p.Q64H	het	Tolerated	Possibly_damaging	Polymorphism	PS1	Uncertain
32	GCKR	c.335G>A	p.R112Q	het	Damaging	Probably_damaging	Polymorphism	-	Uncertain
32	LPL	c.338_339ins AGAGTACCATTCGATAC	p.W113_L114delinsX	het	-	-	-	PVS;PM2	Likely pathogenic
32	TRIB1	c.55C>A	p.L19I	het	Tolerated	Probably_damaging	Disease_causing	PM2	Uncertain
33	APOA5	c.659G>T	p.S220I	het	Tolerated	Probably_damaging	Disease_causing	PM2	Uncertain
34	TRIB1	c.76G>A	p.A26T	het	Tolerated	Probably_damaging	Disease_causing	-	Uncertain
35	GCKR	c.307G>A	p.V103M	het	Damaging	Probably_damaging	Disease_causing	PP3;BS1	Uncertain
35	LMF1	c.790C>T	p.R264C	het	Damaging	Probably_damaging	Disease_causing	PM2;BP1	Uncertain
36	APOA1	c.55C>T	p.R19W	het	Tolerated	Benign	Disease_causing	-	Uncertain
37	GCKR	c.307G>A	p.V103M	het	Damaging	Probably_damaging	Disease_causing	PP3;BS1	Uncertain
38	APOB	c.12581T>C	p.I4194T	het	Damaging	Benign	Polymorphism	-	Uncertain
38	GCKR	c.832C>G	p.H278D	het	Tolerated	Possibly_damaging	Disease_causing	-	Uncertain
38	LMF1	c.475A>G	p.M159V	het	Tolerated	Benign	Disease_causing	BP1	Uncertain
39	GCKR	c.307G>A	p.V103M	het	Damaging	Probably_damaging	Disease_causing	PP3;BS1	Uncertain

40	LPL	c.862G>A	p.A288T	het	Damaging	Probably_damaging	Disease_causing	PM2;PP3	Uncertain
41	LPL	c.835C>G	p.L279V	het	Damaging	Probably_damaging	Disease_causing	PS1;PP3	Uncertain
42	APOE	c.395G>T	p.R132L	het	Damaging	Probably_damaging	Disease_causing	PM2;PM5;PP3	Uncertain
43	APOB	c.3584T>C	p.V1195A	het	Damaging	Benign	Polymorphism	PM2	Uncertain
44	LMF1	c.475A>G	p.M159V	het	Tolerated	Benign	Disease_causing	BP1	Uncertain
45	APOA5	c.667C>T	p.R223C	het	Damaging	Probably_damaging	Disease_causing	PM2;PP3	Uncertain
45	GCKR	c.1607A>G	p.E536G	het	Damaging	Benign	Polymorphism	PM2	Uncertain
45	LMF1	c.575C>A	p.T192K	het	Tolerated	Benign	Disease_causing	PM2;BP1	Uncertain
46	APOA5	c.833C>A	p.S278Y	het	Damaging	Probably_damaging	Polymorphism	PM2;PP3	Uncertain
46	LMF1	c.1626_1627insGGAAGAGG ATCGGAGCC	p.Y543Gfs*16	het	-	-	-	PVS;PM2	Likely pathogenic

Supplemental Table S3 Comparison of TG in admission according to different LPL molecular regulating genetic variant status in patients with severe hypertriglyceridemia

	TG (mmol/L)		P
LPL variants vs. no LPL variants	9.5±3.7	9.6±4.0	>0.05
> 1 variant in LPL related genes vs. no variants in LPL related genes	9.9±4.6	9.5±3.7	>0.05