Supplementary Tables for the article:

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Supplementary Table S1. **Genes included in the panel for targeted resequencing.**

Supplementary Table S2. **Complete list and attributes of the variants identified in the study. The mitochondrial mutation is not included.**

Supplementary Table S3. Gene-level variant analysis, with the number (n) and the percentage (%) of variants identified in different genes [percentage is given as per class of variants (i.e. per P/LP, per VUS, per B/LB variants)]. Definitive: genes with definitive evidence for HCM association; moderate: genes with moderate evidence for HCM association; P/LP: pathogenic/likely pathogenic variant; VUS: variant of unknown significance; B/LB: benign/likely benign variant; LVH: left ventricular hypertrophy.

Supplementary Table S1. **Genes included in the panel for targeted resequencing.**

GENE SYMBOL	GENE NAME	ENSG NUMBER
Genes with definitive evidence for HCM association		
MYBPC3	myosin binding protein C3	ENSG00000134571
MYH7	myosin heavy chain 7	ENSG0000009205
TNNT2	troponin T2, cardiac type	ENSG00000118194
TNNI3	troponin I3, cardiac type	ENSG00000129991
TPM1	tropomyosin 1	ENSG00000140416
ACTC1	actin alpha cardiac muscle 1	ENSG00000159251
MYL2	myosin light chain 2	ENSG00000111245
MYL3	myosin light chain 3	ENSG00000160808
Genes with moderate evidence for HCM association		
CSRP3	cysteine and glycine rich protein 3	ENSG00000129170
JPH2	junctophilin 2	ENSG00000149596
TNNC1	troponin C1, slow skeletal and cardiac type	ENSG00000114854

Intrinsic cardiomyopathy genes		
ACTN2	actinin alpha 2	ENSG00000077522
PLN	phospholamban	ENSG00000198523
Syndromic genes, where isolated left ventricular hypertrophy (LVH) may be seen		
DES	desmin	ENSG00000175084
FHL1	four and a half LIM domains 1	ENSG00000022267
LAMP2	lysosomal associated membrane protein 2	ENSG00000005893
PRKAG2	protein kinase AMP-activated non-catalytic subunit gamma 2	ENSG00000106617
PTPN11	protein tyrosine phosphatase non-receptor type 11	ENSG00000179295
RAF1	Raf-1 proto-oncogene, serine/threonine kinase	ENSG00000132155
TTR	transthyretin	ENSG00000118271
Genes with definitive or moderate evidence for DCM or ARVC association		
BAG3	BAG cochaperone 3	ENSG00000151929
LMNA	lamin A/C	ENSG00000160789
RBM20	RNA binding motif protein 20	ENSG00000203867

TTN	titin	ENSG00000155657
DSP	desmoplakin	ENSG00000096696
PKP2	plakophilin 2	ENSG00000057294
DSG2	desmoglein 2	ENSG00000046604
DSC2	desmocollin 2	ENSG00000134755
JUP	junction plakoglobin	ENSG00000173801
TMEM43	transmembrane protein 43	ENSG00000170876
Genes with limited evidence for HCM association		
MYPN	myopalladin	ENSG00000138347
ANKRD1	ankyrin repeat domain 1	ENSG00000148677
MYLK2	myosin light chain kinase 2	ENSG00000101306
MYOZ2	myozenin 2	ENSG00000172399
NEXN	nexilin F-actin binding protein	ENSG00000162614
VCL	vinculin	ENSG00000035403
TRIM63	tripartite motif containing 63	ENSG00000158022
MYH6	myosin heavy chain 6	ENSG00000197616

PDLIM3	PDZ and LIM domain 3	ENSG00000154553
TCAP	titin-cap	ENSG00000173991
MYOM1	myomesin 1	ENSG00000101605
CALR3	calreticulin 3	ENSG00000269058
Genes with limited evidence for DCM or ARVC association		
ABCC9	ATP binding cassette subfamily C member 9	ENSG00000069431
CTF1	cardiotrophin 1	ENSG00000150281
DTNA	dystrobrevin alpha	ENSG00000134769
EYA4	EYA transcriptional coactivator and phosphatase 4	ENSG00000112319
GATAD1	GATA zinc finger domain containing 1	ENSG00000157259
ILK	integrin linked kinase	ENSG00000166333
LAMA4	laminin subunit alpha 4	ENSG00000112769
LDB3	LIM domain binding 3	ENSG00000122367
NEBL	nebulette	ENSG00000078114
PSEN2	presenilin 2	ENSG00000143801
SGCD	sarcoglycan delta	ENSG00000170624

Syndromic genes, where LVH is seen with overt syndromic features		
CAV3	caveolin 3	ENSG00000182533
CRYAB	crystallin alpha B	ENSG00000109846
FXN	frataxin	ENSG00000165060
GAA	alpha glucosidase	ENSG00000171298
Other genes		
ACADVL	acyl-CoA dehydrogenase very long chain	ENSG00000072778
AGL	amylo-alpha-1, 6-glucosidase, 4-alpha-glucanotransferase	ENSG00000162688
ATP5E	ATP synthase F1 subunit epsilon	ENSG00000124172
BRAF	B-Raf proto-oncogene, serine/threonine kinase	ENSG00000157764
CASQ2	calsequestrin 2	ENSG00000118729
CBL	Cbl proto-oncogene	ENSG00000110395
COA5	cytochrome c oxidase assembly factor 5	ENSG00000183513
CTNNA3	catenin alpha 3	ENSG00000183230
DMD	dystrophin	ENSG00000198947
DMPK	DM1 protein kinase	ENSG00000104936

DNAJC19	DnaJ heat shock protein family (Hsp40) member C19	ENSG00000205981
DNM1L	dynamin 1 like	ENSG00000087470
DOLK	dolichol kinase	ENSG00000175283
EMD	emerin	ENSG00000102119
FHL2	four and a half LIM domains 2	ENSG00000115641
FKTN	fukutin	ENSG00000106692
FOXRED1	FAD dependent oxidoreductase domain containing 1	ENSG00000110074
GUSB	glucuronidase beta	ENSG00000169919
HFE	homeostatic iron regulator	ENSG00000010704
HRAS	HRas proto-oncogene, GTPase	ENSG00000174775
KRAS	KRAS proto-oncogene, GTPase	ENSG00000133703
MAP2K1	mitogen-activated protein kinase kinase 1	ENSG00000169032
MAP2K2	mitogen-activated protein kinase kinase 2	ENSG00000126934
MIB1	MIB E3 ubiquitin protein ligase 1	ENSG00000101752
MRPL3	mitochondrial ribosomal protein L3	ENSG00000114686
NRAS	NRAS proto-oncogene, GTPase	ENSG00000213281

PSEN1	presenilin 1	ENSG00000080815
SCO2	synthesis of cytochrome C oxidase 2	ENSG00000284194
SDHA	succinate dehydrogenase complex flavoprotein subunit A	ENSG00000073578
SHOC2	SHOC2 leucine rich repeat scaffold protein	ENSG00000108061
SLC25A3	solute carrier family 25 member 3	ENSG00000075415
SOS1	SOS Ras/Rac guanine nucleotide exchange factor 1	ENSG00000115904
SPRED1	sprouty related EVH1 domain containing 1	ENSG00000166068
SYNE1	spectrin repeat containing nuclear envelope protein 1	ENSG00000131018
SYNE2	spectrin repeat containing nuclear envelope protein 2	ENSG00000054654
TAZ	ZNF561 antisense RNA 1 (head to head)	ENSG00000267106
TGFB3	transforming growth factor beta 3	ENSG00000119699
TMEM70	transmembrane protein 70	ENSG00000175606
TMPO	thymopoietin	ENSG00000120802
TSFM	Ts translation elongation factor, mitochondrial	ENSG00000123297
TXNRD2	thioredoxin reductase 2	ENSG00000184470

Supplementary Table S2. **Complete list and attributes of the variants identified in the study. The mitochondrial mutation is not included.**

Gene	Variant type	coding HGVS	protein HGVS	ENST	ENSP	Final verdict	Plus items for final verdict	Cardio Classifier	Cardio Classifier items	ClinVar max	ClinVar score	ClinVar entry, n	Novel
ACTC1													
ACTC1	missense	c.281A>T	p.Asn94Ile	ENST00000290378:c.281A>T	ENSP00000290378:p.Asn94Ile	pathogenic	PS4, PP1	VUS	PM2, PP2, PP3	4	4	1	no
ACTC1	missense	c.67T>C	p.Phe23Leu	ENST00000290378:c.67T>C	ENSP00000290378:p.Phe23Leu	VUS	-	VUS	PM2, PP2, PP3	4	3,3	3	no
ACTC1	missense	c.698C>T	p.Ala233Val	ENST00000290378:c.698C>T	ENSP00000290378:p.Ala233Val	VUS	-	VUS	PM2, PP2, PP3	-	-	-	yes
ACTN2													
ACTN2	missense	c.2677G>A	p.Asp893Asn	ENST00000366578.6:c.2677G>A	ENSP00000355537.4:p.Asp893Asn	VUS	-	-	-	3	2,67	3	no
ACTN2	missense	c.893G>A	p.Arg298His	ENST00000366578.6:c.893G>A	ENSP00000355537.4:p.Arg298His	likely benign	-	-	-	3	2,36	11	no
ACTN2	missense	c.1930G>A	p.Ala644Thr	ENST00000366578:c.1930G>A	ENSP00000355537:p.Ala644Thr	VUS	-	-	-	3	3	8	no
ACTN2	missense	c.2147C>T	p.Thr716Met	ENST00000366578:c.2147C>T	ENSP00000355537:p.Thr716Met	likely benign	-	-	-	3	2,28	14	no
CSRP3													
CSRP3	missense	c.10T>C	p.Trp4Arg	ENST00000533783:c.10T>C	ENSP00000431813:p.Trp4Arg	benign	-	benign	-	3	1,91	12	no
CSRP3	missense	c.206A>G	p.Lys69Arg	ENST00000533783:c.206A>G	ENSP00000431813:p.Lys69Arg	VUS	-	VUS	PM2, PP3	3	3	5	no
CSRP3	missense	c.136A>C	p.Ser46Arg	ENST00000533783:c.136A>C	ENSP00000431813:p.Ser46Arg	VUS	-	VUS	PM2, PP3	5	3,4	5	no
CSRP3	missense	c.208G>T	p.Gly70Trp	ENST00000533783:c.208G>T	ENSP00000431813:p.Gly70Trp	VUS	-	VUS	PP3	3	3	3	no
DES													
DES	missense	c.1216C>T	p.Arg406Trp	ENST00000373960:c.1216C>T	ENSP00000363071:p.Arg406Trp	pathogenic	-	-	-	5	4,9	10	no
DES	missense	c.1286G>A	p.Arg429Gln	ENST00000373960:c.1286G>A	ENSP00000363071:p.Arg429Gln	VUS	-	-	-	3	3	4	no
DES	missense	c.206T>C	p.Leu69Pro	ENST00000373960:c.206T>C	ENSP00000363071:p.Leu69Pro	VUS	-	-	-	-	-	-	yes
DES	missense	c.250G>A	p.Gly84Ser	ENST00000373960:c.250G>A	ENSP00000363071:p.Gly84Ser	VUS	-	-	-	3	2,89	9	no
DES	missense	c.569T>G	p.Leu190Arg	ENST00000373960:c.569T>G	ENSP00000363071:p.Leu190Arg	VUS	-	-	-	-	-	-	yes
DES	missense	c.638C>T	p.Ala213Val	ENST00000373960:c.638C>T	ENSP00000363071:p.Ala213Val	benign	-	-	-	3	1,44	16	no
DES	missense	c.728A>G	p.His243Arg	ENST00000373960:c.728A>G	ENSP00000363071:p.His243Arg	VUS	-	-	-	3	3	4	no

FHL1													
FHL1	missense	c.283C>T	p.Arg95Trp	ENST00000370674.3:c.283C>T	ENSP00000359708.1:p.Arg95Trp	VUS	-	VUS	BS1, PP3, PP2	2	1,67	3	no
FHL1	nonsense	c.286G>T	p.Glu96*	ENST00000370690:c.286G>T	ENSP00000359724:p.Glu96*	likely pathogenic	-	likely pathogenic	PVS1, PM2	-	-	-	yes
JPH2													
JPH2	missense	c.1522A>C	p.Ser508Arg	ENST00000372980:c.1522A>C	ENSP00000362071:p.Ser508Arg	VUS	-	-	-	-	-	-	yes
JPH2	missense	c.1801A>C	p.Thr601Pro	ENST00000372980:c.1801A>C	ENSP00000362071:p.Thr601Pro	VUS	-	-	-	-	-	-	yes
JPH2	missense	c.281A>G	p.Tyr94Cys	ENST00000372980:c.281A>G	ENSP00000362071:p.Tyr94Cys	VUS	-	-	-	-	-	-	yes
JPH2	missense	c.572C>G	p.Pro191Arg	ENST00000372980:c.572C>G	ENSP00000362071:p.Pro191Arg	likely benign	-	-	-	3	1,8	10	no
JPH2	missense	c.605T>G	p.Leu202Arg	ENST00000372980:c.605T>G	ENSP00000362071:p.Leu202Arg	VUS	-	-	-	-	-	-	yes
JPH2	missense	c.856A>G	p.Thr286Ala	ENST00000372980:c.856A>G	ENSP00000362071:p.Thr286Ala	likely benign	-	-	-	2	2	5	no
LAMP2													
LAMP2	intronic variant	c.1093+2514G>A	-	ENST00000200639:c.1093+2514G>A	-	benign	-	-	-	3	1,46	13	no
LAMP2	missense	c.661G>A	p.Gly221Arg	ENST00000200639:c.661G>A	ENSP00000200639:p.Gly221Arg	benign	-	benign	ExAC frequency	3	1,58	11	no
LAMP2	missense	c.755T>G	p.Ile252Ser	ENST00000200639:c.755T>G	ENSP00000200639:p.Ile252Ser	benign	-	benign	ExAC frequency	2	1,54	13	no
MYBPC3													
MYBPC3	missense	c.1483C>T	p.Arg495Trp	ENST00000545968.6:c.1483C>T	ENSP00000442795.1:p.Arg495Trp	likely pathogenic	-	likely pathogenic	PM2, PM5, PP2, PP3	5	4,5	8	no
MYBPC3	missense	c.1484G>A	p.Arg495Gln	ENST00000545968.6:c.1484G>A	ENSP00000442795:p.Arg495Gln	pathogenic	PM5	likely pathogenic	PS4, PM2, PP1, PP2	5	4,8	22	no
MYBPC3	frameshift	c.1776_1777delGT	p.Ser593ProfsTer11	ENST00000545968.6:c.1776_1777del	ENSP00000442795.1:p.Ser593ProfsTer11	pathogenic	PS4, PP1	likely pathogenic	PVS1, PM2	5	5	4	no
MYBPC3	missense	c.1855G>A	p.Glu619Lys	ENST00000545968.6:c.1855G>A	ENSP00000442795:p.Glu619Lys	benign	-	benign	ExAC frequency	3	2	16	no
MYBPC3	nonsense	c.2048G>A	p.Trp683X	ENST00000545968.6:c.2048G>A	ENSP00000442795:p.Trp683*	likely pathogenic	-	likely pathogenic	PVS1, PM2	5	4,6	3	no
MYBPC3	frameshift	c.2373dupG	p.Trp792ValfsTer41	ENST00000545968.6:c.2373dup	ENSP00000442795:p.Trp792fs	pathogenic	-	pathogenic	PVS1, PS4, PM2	5	5	24	no
MYBPC3	missense	c.2429G>A	p.Arg810His	ENST00000545968.6:c.2429G>A	ENSP00000442795:p.Arg810His	likely pathogenic	-	likely pathogenic	PS4, PM2, PP2, PP1	4	3,4	9	no
MYBPC3	missense	c.2459G>C	p.Arg820Pro	ENST00000545968.6:c.2459G>C	ENSP00000442795.1:p.Arg820Pro	VUS	-	VUS	PM2, PP2	3	3	1	no
MYBPC3	missense	c.2543C>A	p.Ala848Glu	ENST00000545968.6:c.2543C>A	ENSP00000442795.1:p.Ala848Glu	VUS	-	VUS	PM2, PP2, PP3	3	3	3	no

MYBPC3	nonsense	c.2827C>T	p.Arg943X	ENST00000545968.6:c.2827C>T	ENSP00000442795:p.Arg943*	pathogenic	-	pathogenic	PVS1, PS4, PP1, PM2	5	5	17	no
MYBPC3	frameshift	c.2864_2865delCT	p.Pro955ArgfsTer95	ENST00000545968.6:c.2864_2865del	ENSP00000442795.1:p.Pro955ArgfsTer	pathogenic	-	pathogenic	PVS1, PS3, PS4, PP1, PM2	5	4,7	18	no
MYBPC3	missense	c.2870C>G	p.Thr957Ser	ENST00000545968.6:c.2870C>G	ENSP00000442795.1:p.Thr957Ser	benign	-	benign	ExAC frequency	3	2,3	18	no
MYBPC3	missense	c.2873C>T	p.Thr958Ile	ENST00000545968.6:c.2873C>T	ENSP00000442795.1:p.Thr958Ile	VUS	-	VUS	PP2, BP4	3	2,8	13	no
MYBPC3	frameshift	c.2992_2993dupCA	p.Gln998HisfsTer9	ENST00000545968.6:c.2992_2993dupCA	ENSP00000442795:p.Gln998fs	likely pathogenic	-	likely pathogenic	PVS1, PM2	-	-	-	yes
MYBPC3	missense	c.2992C>G	p.Gln998Glu	ENST00000545968.6:c.2992C>G	ENSP00000442795.1:p.Gln998Glu	benign	-	benign	ExAC frequency	2	2,5	20	no
MYBPC3	frameshift	c.3039_3040dupCC	p.Leu1014ProfsTer7	ENST00000545968.6:c.3039_3040dupCC	ENSP00000442795:p.Leu1014fs	likely pathogenic	-	likely pathogenic	PVS1, PM2	-	-	-	yes
MYBPC3	missense	c.3065G>C	p.Arg1022Pro	ENST00000545968.6:c.3065G>C	ENSP00000442795:p.Arg1022Pro	VUS	-	VUS	PM2, PP2, PP3	5	3,6	8	no
MYBPC3	missense	c.3097C>T	p.Arg1033Trp	ENST00000545968.6:c.3097C>T	ENSP00000442795.1:p.Arg1033Trp	VUS	-	VUS	PM2, PP2, PP3	3	3	6	no
MYBPC3	missense	c.3098G>A	p.Arg1033Gln	ENST00000545968.6:c.3098G>A	ENSP00000442795.1:p.Arg1033Gln	VUS	-	VUS	PM2, PP3	3	3	5	no
MYBPC3	frameshift	c.3166dupG	p.Ala1056GlyfsTer9	ENST00000545968.6:c.3166dup	ENSP00000442795.1:p.Ala1056GlyfsTer9	pathogenic	PS4	likely pathogenic	PVS1, PM2	5	5	2	no
MYBPC3	splice donor variant	c.3190+1G>A	-	ENST00000545968.6:c.3190+1G>A	-	pathogenic	PS4	likely pathogenic	PVS1, PM2	5	5	5	no
MYBPC3	inframe indel	c.3407_3409delACT	p.Tyr1136del	ENST00000545968.6:c.3407_3409del	ENSP00000442795.1:p.Tyr1136del	likely pathogenic	PS4, PP1	VUS	PM2, PM4	5	3,8	9	no
MYBPC3	frameshift	c.3476_3477delTT	p.Phe1159TyrfsTer9	ENST00000545968.6:c.3476_3477del	ENSP00000442795.1:p.Phe1159TyrfsTer9	likely pathogenic	-	likely pathogenic	PVS1, PM2	5	5	1	no
MYBPC3	nonsense	c.3642G>A	p.Trp1214X	ENST00000545968.6:c.3642G>A	ENSP00000442795.1:p.Trp1214Ter	likely pathogenic	-	likely pathogenic	PVS1, PM2	5	4,6	7	no
MYBPC3	nonsense	c.3697C>T	p.Gln1233Ter	ENST00000545968.6:c.3697C>T	ENSP00000442795.1:p.Gln1233Ter	pathogenic	-	pathogenic	PVS1, PS4, PP1, PM2	5	4,9	12	no
MYBPC3	nonsense	c.3811C>T	p.Arg1271X	ENST00000545968.6:c.3811C>T	ENSP00000442795:p.Arg1271*	pathogenic	PS4	likely pathogenic	PVS1, PM2	5	4,9	9	no
MYBPC3	frameshift	c.431_432delGT	p.Gly144AlafsTer8	ENST00000545968.6:c.431_432del	ENSP00000442795.1:p.Gly144AlafsTer8	likely pathogenic	-	likely pathogenic	PVS1, PM2	5	5	1	no
MYBPC3	splice donor variant	c.505+1G>A	-	ENST00000545968.6:c.505+1G>A	-	likely pathogenic	-	likely pathogenic	PVS1, PM2	5	4,5	2	no
MYBPC3	missense	c.565G>A	p.Val189Ile	ENST00000545968.6:c.565G>A	ENSP00000442795.1:p.Val189Ile	benign	-	benign	ExAC frequency	2	1,6	15	no
MYBPC3	missense	c.649A>G	p.Ser217Gly	ENST00000545968.6:c.649A>G	ENSP00000442795.1:p.Ser217Gly	benign	-	benign	ExAC frequency	3	1,4	11	no
MYBPC3	splice donor variant	c.821+1G>A	-	ENST00000545968.6:c.821+1G>C	-	pathogenic	PS4, PP1	likely pathogenic	PVS1, PM2	5	5	1	no
MYBPC3	missense	c.977G>A	p.Arg326Gln	ENST00000545968.6:c.977G>A	ENSP00000442795.1:p.Arg326Gln	benign	-	benign	ExAC frequency	2	1,3	19	no
MYBPC3	frameshift	c.1293delC	p.Asp431GlufsTer19	ENST00000545968:c.1293delC	ENSP00000442795:p.Asp431fs	likely pathogenic	-	likely pathogenic	PVS1, PM2	-	-	-	yes

MYBPC3	missense	c.238G>A	p.Ala80Thr	ENST00000545968:c.238G>A	ENSP00000442795:p.Ala80Thr	VUS	-	VUS	PM2, PP2	3	3	2	no
MYBPC3	missense	c.3737T>C	p.Phe1246Ser	ENST00000545968:c.3737T>C	ENSP00000442795:p.Phe1246Ser	VUS	-	VUS	PM2, PP2	-	-	-	yes
MYBPC3	missense	c.506G>T	p.Gly169Val	ENST00000545968:c.506G>T	ENSP00000442795:p.Gly169Val	VUS	-	VUS	PM2, PP2, PP3	-	-	-	yes
MYBPC3	frameshift	c.73delA	p.Ser25AlafsTer14	ENST00000545968:c.73delA	ENSP00000442795:p.Ser25fs	likely pathogenic	-	likely pathogenic	PVS1, PM2	-	-	-	yes
MYH7													
MYH7	missense	c.1063G>A	p.Ala355Thr	ENST00000355349.4:c.1063G>A	ENSP00000347507:p.Ala355Thr	pathogenic	-	pathogenic	PS4, PM1, PM2, PP1, PP3	5	4,5	10	no
MYH7	missense	c.1208G>A	p.Arg403Gln	ENST00000355349.4:c.1208G>A	ENSP00000347507:p.Arg403Gln	pathogenic	-	pathogenic	PS3, PS4, PM1, PM2, PM5, PP1, PP3	5	5	13	no
MYH7	nonsense	c.1792A>T	p.Lys598X	ENST00000355349.4:c.1792A>G	ENSP00000347507:p.Lys598*	VUS	-	VUS	PM2	-	-	-	yes
MYH7	missense	c.1987C>T	p.Arg663Cys	ENST00000355349.4:c.1987C>T	ENSP00000347507.3:p.Arg663Cys	pathogenic	-	pathogenic	PS4, PP3, PM1, PM2, PM5	5	5	11	no
MYH7	missense	c.2146G>A	p.Gly716Arg	ENST00000355349.4:c.2146G>A	ENSP00000347507:p.Gly716Arg	pathogenic	-	pathogenic	PS4, PM1, PM2, PM6, PP1, PP3	5	4,9	10	no
MYH7	missense	c.2156G>A	p.Arg719Gln	ENST00000355349.4:c.2156G>A	ENSP00000347507.3:p.Arg719Gln	pathogenic	-	pathogenic	PS4, PP1, PM1, PM2, PM5, PP3	5	4,8	14	no
MYH7	missense	c.2207T>C	p.Ile736Thr	ENST00000355349.4:c.2207T>C	ENSP00000347507:p.Ile736Thr	pathogenic	-	pathogenic	PVS1, PM1, PM2, PP1	5	5	12	no
MYH7	missense	c.2348G>A	p.Arg783His	ENST00000355349.4:c.2348G>A	ENSP00000347507.3:p.Arg783His	likely pathogenic	-	likely pathogenic	PS4, PM1, PM2	4	4	6	no
MYH7	missense	c.2710C>T	p.Arg904Cys	ENST00000355349.4:c.2710C>T	ENSP00000347507:p.Arg904Cys	pathogenic	PS4_Moderate, PP1_Strong, PM6, PM5	VUS	PM1, PM2, PP3	5	4,5	6	no
MYH7	missense	c.2770G>A	p.Glu924Lys	ENST00000355349.4:c.2770G>A	ENSP00000347507.3:p.Glu924Lys	pathogenic	-	pathogenic	PS2, PS3, PS4, PM1, PM2, PP1, PP3	5	4,8	12	no
MYH7	missense	c.2785G>A	p.Glu929Lys	ENST00000355349.4:c.2785G>A	ENSP00000347507:p.Glu929Lys	likely pathogenic	PS4	VUS	PM1, PM2, PP3	4	4	2	no
MYH7	missense	c.3158G>A	p.Arg1053Gln	ENST00000355349.4:c.3158G>A	ENSP00000347507:p.Arg1053Gln	likely pathogenic	-	likely pathogenic	PS4, PM2, PP1, PP3	5	4,7	6	no
MYH7	missense	c.3346G>A	p.Glu1116Lys	ENST00000355349.4:c.3346G>A	ENSP00000347507:p.Glu1116Lys	VUS	-	VUS	PM2, PP2	5	4	3	no
MYH7	missense	c.3455A>C	p.Glu1152Ala	ENST00000355349.4:c.3455A>T	ENSP00000347507.3:p.Glu1152Val	VUS	-	VUS	PM2, PP2, PP3	3	3	3	no
MYH7	missense	c.4130C>T	p.Thr1377Met	ENST00000355349.4:c.4130C>T	ENSP00000347507.3:p.Thr1377Met	likely pathogenic	-	likely pathogenic	PS4, PM2, PP3	5	4,2	10	no
MYH7	missense	c.4348G>A	p.Asp1450Asn	ENST00000355349.4:c.4348G>A	ENSP00000347507.3:p.Asp1450Asn	VUS	-	VUS	PM2, PP3	3	3	5	no
MYH7	missense	c.4472C>G	p.Ser1491Cys	ENST00000355349.4:c.4472C>G	ENSP00000347507:p.Ser1491Cys	benign	-	benign	ExAC frequency	2	1,2	20	no
MYH7	missense	c.505A>G	p.Arg169Gly	ENST00000355349.4:c.505A>G	ENSP00000347507:p.Arg169Gly	likely pathogenic	PP1, PS4	VUS	PM2, PP2, PP3	4	4	2	no

MYH7	missense	c.5135G>A	p.Arg1712Gln	ENST00000355349.4:c.5135G>A	ENSP00000347507:p.Arg1712Gln	likely pathogenic	-	likely pathogenic	PS4, PM1, PM2, PP1, PP3	5	4	18	no
MYH7	missense	c.596C>T	p.Ala199Val	ENST00000355349.4:c.596C>T	ENSP00000347507:p.Ala199Val	likely pathogenic	PS4	VUS	PM1, PM2, PP3	5	4,3	4	no
MYH7	missense	c.715G>A	p.Asp239Asn	ENST00000355349.4:c.715G>A	ENSP00000347507:p.Asp239Asn	pathogenic	-	pathogenic	PS4, PM1, PM2, PP1	5	4,5	10	no
MYH7	missense	c.1988G>A	p.Arg663His	ENST00000355349:c.1988G>A	ENSP00000347507:p.Arg663His	pathogenic	-	pathogenic	PS4, PP1, PM2, PM1	5	4,9	28	no
MYH7	missense	c.2092G>A	p.Val698Met	ENST00000355349:c.2092G>A	ENSP00000347507:p.Val698Met	VUS	-	VUS	PM1, PM2, PP3	-	-	-	yes
MYH7	missense	c.2631G>T	p.Met877Ile	ENST00000355349:c.2631G>T	ENSP00000347507:p.Met877Ile	VUS	-	VUS	PM1, PM2	-	-	-	yes
MYH7	missense	c.3116A>G	p.Glu1039Gly	ENST00000355349:c.3116A>G	ENSP00000347507:p.Glu1039Gly	VUS	-	VUS	PP2, PP3	3	3	3	no
MYH7	missense	c.440G>T	p.Arg147Met	ENST00000355349:c.440G>T	ENSP00000347507:p.Arg147Met	VUS	-	VUS	PM2, PP2, PP3	-	-	-	yes
MYH7	missense	c.5159A>G	p.Asn1720Ser	ENST00000355349:c.5159A>G	ENSP00000347507:p.Asn1720Ser	VUS	-	VUS	PM2, PP3	-	-	-	yes
MYH7	missense	c.535G>C	p.Glu179Gln	ENST00000355349:c.535G>C	ENSP00000347507:p.Glu179Gln	VUS	-	VUS	PM2, PP2, PP3	-	-	-	yes
MYH7	missense	c.5615A>G	p.Gln1872Arg	ENST00000355349:c.5615A>G	ENSP00000347507:p.Gln1872Arg	VUS	-	VUS	PM2	-	-	-	yes
MYH7	missense	c.950A>G	p.Glu317Gly	ENST00000355349:c.950A>G	ENSP00000347507:p.Glu317Gly	VUS	-	VUS	PM1, PM2	-	-	-	yes
MYL2													
MYL2	missense	c.374C>T	p.Thr125Met	ENST00000228841.15:c.374C>T	ENSP00000228841:p.Thr125Met	VUS	-	VUS	PM2, PP2	3	3	6	no
MYL2	missense	c.401A>C	p.Glu134Ala	ENST00000228841.15:c.401A>C	ENSP00000228841.8:p.Glu134Ala	VUS	-	VUS	PP2, PP3	5	3,5	14	no
MYL2	missense	c.80A>G	p.Gln27Arg	ENST00000228841.15:c.80A>G	ENSP00000228841.8:p.Gln27Arg	VUS	-	VUS	PM2, PP2	4	4	2	no
MYL2	nonsense	c.190G>T	p.Glu64X	ENST00000228841:c.190G>T	ENSP00000228841:p.Glu64*	VUS	-	VUS	PM2	-	-	-	yes
MYL3													
MYL3	missense	c.170C>G	p.Ala57Gly	ENST00000292327.6:c.170C>G	ENSP00000292327:p.Ala57Gly	VUS	-	VUS	BS1, PP2	5	3,7	8	no
MYL3	missense	c.461G>A	p.Arg154His	ENST00000292327.6:c.461G>A	ENSP00000292327.4:p.Arg154His	VUS	-	VUS	PM2, PP2, PP3	5	3	8	no
MYL3	missense	c.530A>G	p.Glu177Gly	ENST00000292327.6:c.530A>G	ENSP00000292327.4:p.Glu177Gly	VUS	-	VUS	PP2, PP3	3	3	13	no
MYL3	missense	c.518T>C	p.Met173Thr	ENST00000292327:c.518T>C	ENSP00000292327:p.Met173Thr	VUS	-	VUS	PM2, PP2	3	3	2	no

PRKAG2													
PRKAG2	missense	c.245A>C	p.Gln82Pro	ENST00000287878:c.245A>C	ENSP00000287878:p.Gln82Pro	VUS	-	VUS	PM2	3	3	1	no
PRKAG2	missense	c.298G>A	p.Gly100Ser	ENST00000287878:c.298G>A	ENSP00000287878:p.Gly100Ser	benign	-	benign	ExAC frequency	3	1,46	13	no
PRKAG2	missense	c.698C>G	p.Ala233Gly	ENST00000287878:c.698C>G	ENSP00000287878:p.Ala233Gly	VUS	-	VUS	BS1	3	2,72	11	no
PRKAG2	missense	c.425C>T	p.Thr142Ile	ENST00000488258:c.425C>T	ENSP00000287878:p.Thr142Ile	VUS	-	VUS	BS1	3	3	11	no
PTPN11													
PTPN11	missense	c.556C>T	p.Arg186Trp	ENST00000351677:c.556C>T	ENSP00000340944.2:p.Arg186Trp	VUS	-	VUS	PM2, PP2, PP3	3	2,75	4	no
RAF1													
RAF1	missense	c.1837C>G	p.Leu633Val	ENST00000442415.7:c.1897C>G	ENSP00000401888.2:p.Leu633Val	pathogenic	PP2, PM2, PS3, PS2	VUS	PM2	5	4,8	11	no
RAF1	missense	c.770C>T	p.Ser257Leu	ENST00000442415.7:c.770C>T	ENSP00000401888.2:p.Ser257Leu	pathogenic	PP2, PM1, PM2, PS3, PM6_Strong	VUS	PM2	5	5	29	no
TNNC1													
TNNC1	missense	c.435C>A	p.Asp145Glu	ENST00000232975.8:c.435C>A	ENSP00000232975.3:p.Asp145Glu	VUS	-	VUS	PP2, BS1	5	3,42	7	no
TNNI3													
TNNI3	missense	c.485G>A	p.Arg162Gln	ENST00000344887.10:c.485G>A	ENSP00000341838:p.Arg162Gln	pathogenic	-	pathogenic	PM2, PP2, PP1, PS4	5	4,5	15	no
TNNI3	missense	c.497C>T	p.Ser166Phe	ENST00000344887.10:c.497C>T	ENSP00000341838.5:p.Ser166Phe	likely pathogenic	PS4	VUS	PM2, PP2, PP3	5	4,4	7	no
TNNI3	missense	c.557G>A	p.Arg186Gln	ENST00000344887.10:c.557G>A	ENSP00000341838.5:p.Arg186Gln	pathogenic	PS4, PP1	VUS	PM2, PP2	5	4,9	10	no
TNNI3	missense	c.248T>C	p.Leu83Pro	ENST00000344887:c.248T>C	ENSP00000341838:p.Leu83Pro	VUS	-	VUS	PM2, PP2	-	-	-	yes
TNNI3	missense	c.456T>A	p.Asp152Glu	ENST00000344887:c.456T>A	ENSP00000341838:p.Asp152Glu	VUS	-	VUS	PM2, PP2	-	-	-	yes
TNNT2													
TNNT2	missense	c.274C>T	p.Arg92Trp	ENST00000367318.10:c.274C>T	ENSP00000236918:p.Arg102Trp	pathogenic	-	pathogenic	PS4, PM2, PM5, PP1, PP2, PP3	5	5	11	no
TNNT2	missense	c.538A>T	p.Asn180Tyr	ENST00000367318:c.538A>T	ENSP00000236918:p.Asn190Tyr	VUS	-	VUS	PM2, PP2, PP1, PS4	-	-	-	yes
TNNT2	missense	c.844A>G	p.Lys282Glu	ENST00000367318:c.844A>G	ENSP00000236918:p.Lys292Glu	VUS	-	VUS	PM2, PP2	-	-	-	yes
TNNT2	missense	c.83C>T	p.Ala28Val	ENST00000367318:c.83C>T	ENSP00000236918:p.Ala38Val	VUS	-	VUS	PP2, BP4	5	2,3	16	no
TNNT2	inframe indel	c.487_489delGAG	p.Glu163del	ENST00000367318:c.487_489delGAG	ENSP00000236918:p.Glu173del	pathogenic	-	pathogenic	PS4, PM2, PM4, PP1	5	5	6	no

TNNT2	missense	c.832C>T	p.Arg278Cys	ENST00000367318:c.832C>T	ENSP00000236918:p.Arg288Cys	VUS	-	VUS	PP2	5	3,9	23	no
TPM1													
TPM1	missense	c.331C>G	p.Gln111Glu	ENST00000403994.9:c.331C>G	ENSP00000385107:p.Gln111Glu	VUS	-	VUS	PM2	-	-	-	yes
TPM1	missense	c.790A>G	p.Lys264Glu	ENST00000403994.9:c.790A>G	ENSP00000385107.4:p.Lys264Glu	VUS	-	VUS	PM2, PP2, PP3	3	3	2	no
TPM1	missense	c.842T>C	p.Met281Thr	ENST00000403994.9:c.842T>C	ENSP00000385107.4:p.Met281Thr	likely pathogenic	PS4, PP1	VUS	PM2, PP2	5	3,8	7	no
TPM1	missense	c.431A>G	p.Gln144Arg	ENST00000403994:c.431A>G	ENSP00000385107:p.Gln144Arg	VUS	-	VUS	PM2, PP2, PP3	-	-	-	yes
TPM1	missense	c.804A>C	p.Lys268Asn	ENST00000403994:c.804A>C	ENSP00000385107:p.Lys268Asn	VUS	-	VUS	PM2, PP2	-	-	-	yes
TTN													
TTN	frameshift	c.70437delG	p.Lys23480AsnfsTer30	ENST00000589042:c.70437delG	ENSP00000467141:p.Lys23480fs	likely pathogenic		likely pathogenic	PVS1, PM2	-	-	-	yes

Supplementary Table S3. Gene-level variant analysis, with the number (n) and the percentage (%) of variants identified in different genes [percentage is given as per class of variants (i.e. per P/LP, per VUS, per B/LB variants)]. Definitive: genes with definitive evidence for HCM association; moderate: genes with moderate evidence for HCM association; P/LP: pathogenic/likely pathogenic variant; VUS: variant of unknown significance; B/LB: benign/likely benign variant; LVH: left ventricular hypertrophy.

		P/LP, n (%)						VUS, n (%)				B/LB, n (%)		Total n (%)
		missense	nonsense	splice variant	frameshift	inframe del	novel	missense	nonsense	inframe del	novel	missense	intronic variant	
Definitive	***MYBPC3***	3 (14)	5 (23)	3 (14)	10 (45)	1 (5)	4 (18)	9 (100)	-	-	2 (22)	6 (100)	-	37 (100)
	MYH7	17 (100)	-	-	-	-	-	10 (83)	1 (8)	1 (8)	8 (67)	1 (100)	-	30 (100)
	TNNT2	1 (50)	-	-	-	1 (50)	-	4 (100)	-	-	2 (50)	-	-	6 (100)
	TNNI3	3 (100)	-	-	-	-	-	2 (100)	-	-	2 (100)	-	-	5 (100)
	TPM1	1 (100)	-	-	-	-	-	4 (100)	-	-	3 (75)	-	-	5 (100)
	ACTC1	1 (100)	-	-	-	-	-	2 (100)	-	-	1 (50)	-	-	3 (100)
	MYL2	-	-	-	-	-	-	3 (75)	1 (25)	-	1 (25)	-	-	4 (100)
	MYL3	-	-	-	-	-	-	4 (100)	-	-	-	-	-	4 (100)
Moderate	***CSRP3***	-	-	-	-	-	-	3 (100)	-	-	-	1 (100)	-	4 (100)
	TNNC1	-	-	-	-	-	-	1 (100)	-	-	-	-	-	1 (100)
	JPH2	-	-	-	-	-	-	4 (100)	-	-	4 (100)	2 (100)	-	6 (100)
Syndromic genes with isolated LVH	***ACTN2***	-	-	-	-	-	-	2 (100)	-	-	-	2 (100)	-	4 (100)
	DES	1 (100)	-	-	-	-	-	5 (100)	-	-	2 (40)	1 (100)	-	7 (100)
	FHL1	-	1 (100)	-	-	-	1 (100)	1 (100)	-	-	-	-	-	2 (100)
	RAF1	2 (100)	-	-	-	-	-	-	-	-	-	-	-	2 (100)
	PRKAG2	-	-	-	-	-	-	3 (100)	-	-	-	1 (100)	-	4 (100)
	LAMP2	-	-	-	-	-	-	-	-	-	-	2 (67)	1 (33)	3 (100)
	PTPN11	-	-	-	-	-	-	1 (100)	-	-	-	-	-	1 (100)
Other	**mitochondrial**	1 (100)	-	-	-	-	-	-	-	-	-	-	-	1 (100)
	TTN	-	-	-	1 (100)	-	1 (100)	-	-	-	-	-	-	1 (100)