SUPPLEMENTARY DATA

Supplementary methods

SM1. Genetic analysis

All individuals included in the study were analyzed using a cardiomyopathy gene panel including: *ABCC9, ACTC1, ACTN2, AKAP9, ALPK3, ANK2, ANKRD1, BAG3, CACNA1C, CACNA2D1, CACNB2, CALM1, CALM2, CALM3, CALR3, CASQ2, CAV3, CRYAB, CSRP3, CTNNA3, GJA1, CTF1, DES, DMD, DMPK, DPP6, DSC2, DSG2, DSP, DTNA, ECE1, EMD, EN1, EYA4, FHL2, FHOD3, FKTN, FLNA, FLNC, GAA, GJA5, GLA, GLRA1, GPD1L, HCN2, HCN4, JPH2, JUP, KCNA5, KCND3, KCNE1, KCNE2, KCNE3, KCNE4, KCNE5, KCNH2, KCNJ2, KCNJ5, KCNJ8, KCNQ1, LAMA4, LAMP2, LDB3, LMNA, MYBPC3, MYH6, MYH7, MYL2, MYL3, MYLK2, MYOZ2, MYPN, NEBL, NEXN, NKX2-5, NOS1AP, NOTCH1, NPPA, NUP155, PDLIM3, PHOX2A, PHOX2B, PITX2, PKP2, PLN, PPP1R13L, PRKAG2, RANGRF, RBM20, RYR2, SCN1B, SCN2B, SCN3B, SCN4B, SCN5A, SCN10A, SDHA, SGCD, SLC22A5, SLC6A4, SLC8A1, SLMAP, SLN, SNTA1, TAZ, TCAP, TGFB3, TLX3, TMEM43, TMPO, TNNC1, TNNI3, TNNI3K, TNNT2, TP63, TPM1, TRDN, TRIM63, TRPM4, TTN, TTR* and *VCL*. Libraries were prepared using the SureSelectXT HS/HS2 Target Enrichment System (Agilent), and sequencing was performed on MiSeq and NextSeq 2000 platforms (Illumina). The custom panel captures all coding regions and ±25 bp of flanking intronic sequences, achieving >20× coverage across the targeted regions and >99% sensitivity for SNVs and indels. Regions with a call rate <90% at 20× were resequenced by Sanger sequencing (ABI3500). Bioinformatic analysis was performed using a validated in-house pipeline, including preprocessing with FastQC and fastp, alignment with BWA-MEM (hg19), duplicate marking with Picard, and variant detection with GATK HaplotypeCaller, Manta, GRAPES, and DECoN, followed by annotation using gnomAD, ClinVar, and internal databases. Analysis of copy number variations was performed using Gendical Software. All genes currently associated with CM were included in the panel.

Table S1. Clinical and genetic data of patients with early onset nonsyndromic cardiomyopathies included in the cohort

Patient	Sex	Clinical diagnosis ESC 2023	Age at onset, y	Cardiac events	Genetic diagnosis #OMIM	Disease causing gene/potential disease causing gene	Disease causing variant (c.)/potential disease causing variant (c.)	Disease causing variant (p)/potential disease-causing variant (p.)	ACMG classification	Zygosity (inheritance)	Segregation	Previously reported	Usefulness of genetic diagnosis	Uncertain or additional gene Variants	Fibrosis	IVS (z-score)	LVPW (z-score)	LVEDD (z-score)	LVEF (Simpson; %)	BSA
P1	Male	HCM	13		# 115197 cardiomyopathy, familial hypertrophic, 4; CMH4	*MYBPC3*	c.2149-1G>A	p.(?)	P	Heterozygous	Inherited from affected father	PMIDs: 27532257, 30393631, 23782526, 37652022, 36129056, 34588271	Diagnosis confirmed		Present	24.86	0.51	−2.33	73	1.37
P2	Female	HCM	11	ICD appropriate shock, HTx	cardiomyopathy, familial hypertrophic, 4; CMH4	*MYH7*	c.2156G>A	p.(Arg719Gln)	P	Heterozygous	Unknown	PMIDs:21896538, 23140321, 23711808.	Diagnosis confirmed		Present	20.50	0.40	−2.25	71	1.43
P3	Male	HCM	12		Potential # 613765 cardiomyopathy, familial hypertrophic, 9; CMH9	*TTN*	c.7021G>T	p.(Asp2341Tyr)	VUS*	Heterozygous	No	Novel	Potential associated gene-variant identified		Absent	11.24	9.49	−1.36	75	1.56
P4	Male	DCM	18		Potential # 604145 cardiomyopathy, dilated, 1G; CMD1G	*TTN*	c.34449A>C	p.(Glu11483Asp)	VUS*	Heterozygous	No	Novel	Potential associated gene-variant identified	*TTN*: c.89827G>A; p.(Val29943Ile) (VUS) heterozygous	Absent	2.47	1.69	2.64	52	1.73
P5	Male	ACM/NDLVC	15	SCA	# 617047 arrhythmogenic right ventricular dysplasia, familial, 15, included; ARVD15, includeD	*FLNC*	c.1414del	p.(Cys472Valfs*20)	LP	Heterozygous	Inherited from affected father	PMID:38612618	Diagnosis confirmed	*TTN*: c.24617A>G; p.(Asn8206Ser) (VUS) heterozygous	Present	0.34	−0.52	−0.10	64	1.41
P6	Male	HCM	7	SCA	# 115196 cardiomyopathy, familial hypertrophic, 3; CMH3	*TPM1*	c.248C>A	p.(Ala83Asp)	LP	Heterozygous	Inherited from affected father	PMID:28771489	High risk diagnosis confirmed	*KCNH2*: c.2531T>C; p.(Met844Thr) (VUS) heterozygous	Present	6.10	3.93	2.88	63	0.94
						MYBPC3	c.1808T>C	p.(Ile603Thr)	LP	Heterozygous	Unknown	PMIDs: 30919572, 33782553								
P7	Male	ACM	18										Inconclusive	*JPH2:* c.1357C>T; p.(Pro453Ser) (VUS) heterozygous *SCN5A*: c.3751G>A; p.(Val1251Met) (VUS) heterozygous	Present	0.84	0.95	0.31	51	2.21
P8	Male	HCM	13		# 192600 cardiomyopathy, familial hypertrophic, 1; CMH1	*MYH7*	c.1357C>T	p.(Arg453Cys)	P	Heterozygous	Inherited from affected father	PMIDs:8655135, 10662815	Diagnosis confirmed		Present	14.51	3.69	−0.88	70	1.64
P9	Male	ACM	17		# 609040 arrhythmogenic right ventricular dysplasia,	*PKP2*	c.275T>A	p.(Leu92Ter)	P	Heterozygous	Inherited from affected father	PMIDs:27532257, 24967631, 24832006	Diagnosis confirmed	*TRPM4*: c.1212C>A; p.(Asn404Lys) (VUS) heterozygous	Present	1.46	1.58	1.01	52	1.80

					familial, 9; ARVD9															
P10	Male	HCM	17	SCA									Inconclusive	RYR2: c.1154G>C; p.(Gly385Ala) (VUS) heterozygous	Absent	16.66	1.37	−2.50	71	1.43
P11	Male	DCM	15		# 613426 cardiomyopathy, dilated, 1S; CMD1S	*MYH7*	c.541G>A	p.(Gly181Arg)	LP	Heterozygous	Inherited from unnaffected father	PMIDs: 34935411, 33500567	Diagnosis confirmed	*DSP*: c.1297C>T; p.(Arg433Cys) (VUS) Heterozygouz *DMD*: c.8110T>C; p.(Trp2704Arg (VUS) heterozygous	Absent	−0.30	−1.94	0.08	74	1.80
P12	Male	DCM	15		# 617047 cardiomyopathy, dilated, 1pp, included; CMD1PP	*FLNC*	c.1414del	p.(Cys472Valfs*20)	LP	Heterozygous	Inherited from affected mother	PMID: 38612618	Diagnosis confirmed		Absent	1.34	0.58	1.47	71	1.87
P13	Male	HCM	16		# 192600 cardiomyopathy, familial hypertrophic, 1; CMH1	*MYH7*	c.4259G>A	p.(Arg1420Gln)	P	Heterozygous	Inherited from unnaffected father	PMID: 21817903, 25132132, 25351510	Diagnosis confirmed		Absent	5.82	5.06	−2.04	73	1.81
P14	Male	DCM	0.1	HF	# 613426 cardiomyopathy, dilated, 1S; CMD1S	*MYH7*	c.602T>A	p.(Ile201Thr)	P	Heterozygous	*De Novo*	PMID: 24714796	Diagnosis confirmed	*CAV3*: c.244G>A; p.(Val82Ile) (VUS) heterozygous	Absent	−0.37	−0.25	1.91	45	0.22
P15	Male	HCM	1	ICD appropriate shock	# 115197 cardiomyopathy, familial hypertrophic, 4; CMH4	*MYBPC3*	c.1484G>A	p.(Arg495Gln)	P	Heterozygous	Inherited from affected mother	PMIDs: 11499718, 20019025, 22857948, 23396983, 24093860.	Diagnosis confirmed	*SCN5A*: c.3841G>T; p.(Val1281Phe) (VUS) heterozygous *ACTN2*:c.2552G>A; p.(Arg851His) (VUS) heterozygous *DSG2*:c.2800A>G; (p.lle934Val) (VUS) heterozygous	Present	10.11	−0.31	−0.28	77	0.47
P16	Male	HCM	13		# 192600 cardiomyopathy, familial hypertrophic, 1; CMH1	*MYH7*	c.2167C>G	p.(Arg723Gly)	P	Heterozygous	Inherited from affected father	PMIDs: 11113006, 17097032, 19150014, 20865685, 24093860.	Diagnosis confirmed	*KCNH2*: c.607G>A; p.(Ala203Thr) (VUS) heterozygous *FKTN* c.703C>A; p.(Pro235Thr) (VUS) heterozygous *CACNA1C*: c.898A>G; p.(Asn300Asp) (VUS) heterozygous	Absent	5.11	1.37	0.34	68	1.43
P17	Female	HCM	13		# 192600 cardiomyopathy, familial hypertrophic, 1; CMH1	*MYH7*	c.1207C>G	p.(Arg403Gly)	LP	Heterozygous	Inherited from affected father	PMIDs: 32344918, 30950055	Diagnosis confirmed		Present	14.38	2.19	0.36	70	1.49
P18	Male	HCM	7	SCA	# 115197 cardiomyopathy, familial hypertrophic, 4; CMH4	*MYBPC3*	c.1483C>G	p.(Arg495Gly)	P	Heterozygous	Inherited from affected mother	PMIDs: 18403758, 19659763, 20624503, 22574137	Diagnosis confirmed	*TTN*: c.43359T>A; p.(Asp14453Glu) (VUS) heterozygous	Present	8.92	7.49	−2.19	74	0.44
P19	Male	HCM	4		Potential # 617047 cardiomyopathy, familial hypertrophic, 26; CMH26	*FLNC*	c.676G>A	p.(Asp226Asn)	VUS*	Heterozygous	Inherited from affected mother	Novel	Potential associated gene-variant identified	*DMD*: c.1375G>A; p.(Glu459Lys) (VUS) hemizygous	Absent	6.56	1.47	0.15	78	0.67

P20	Female	HCM	17		Potential # 612158 cardiomyopathy, dilated, 1AA, with or without left ventricular noncompaction; CMD1AA	*ACTN2*	c.1748A>C	p.(Glu583Ala)	VUS*	Heterozygous	No	PMIDs: 28790153	Potential associated gene-variant identified	*MYBPC3*: c.976C>G; p.(Arg326Gly) (VUS) heterozygous	Present	17.01	3.05	−0.52	68	1.53
P21	Male	HCM	13		# 192600 cardiomyopathy, familial hypertrophic, 1; CMH1	*MYH7*	c.2167C>T	p.(Arg723Cys)	P	Heterozygous	No	PMIDs: 1430197, 9829907, 12117842, 16199542, 25935763, 29709087	Diagnosis confirmed	*BAG3*: c.452G>A; p.(Cys151Tyr) (VUS) heterozygous *KCNQ1*: c.136G>A; p.(Ala46Thr) (VUS) heterozygous	Absent	11.83	2.32	−0.97	69	1.44
P22	Female	ACM	14		# 607450 arrhythmogenic right ventricular dysplasia, familial, 8; ARVD8	*DSP*	c.868G>A	p.(Glu290Lys)	LP	Heterozygous	Inherited from affected mother	PMID:39288222	Diagnosis confirmed	*TTN*: c.91423A>G p.(Ser30475Gly) (VUS) heterozygous *PITX2* :c.503A>G p.(Asn168Ser) (VUS) heterozygous	Present	1.28	1.39	1.92	52	1.42
P23	Male	HCM	14	SCA	# 115195 cardiomyopathy, familial hypertrophic, 2; CMH2	*TNNT2*	c.860G>A	p.(Trp287Ter)	P	Heterozygous	Unknown	PMIDs: 12707239, 20439259	Diagnosis confirmed	*DSP*: c.1618C>A; p.(Leu540Ile) (VUS) heterozygous *SCN5A*: c.1398G>T; p.(Leu466Phe) (VUS) heterozygous	Present	19.48	2.00	−1.91	71	1.58
P24	Male	HCM	2										Inconclusive	*AKAP9*: c.11077T>C; p.(Ser3693Pro) (VUS) heterozygous	Present	20.00	1.60	−2.57	68	0.65
P25	Male	ACM	5		# 609040 arrhythmogenic right ventricular dysplasia, familial, 9; ARVD9	*PKP2*	c.1297C>T	p.(Arg413Ter)	P	Heterozygous	Inherited from affected mother	PMIDs:24967631, 31156706	Diagnosis confirmed	*TTN*: c.95984T>C; p.(Val31995Ala) (VUS) heterozygous	Absent	1.06	1.18	0.68	65	0.74
P26	Female	HCM	7		cardiomyopathy, familial hypertrophic, 7; CMH7	*TNNI3*	c.433C>T	p.(Arg145Trp)	P	Heterozygous	Inherited from affected father	PMIDs: 12531876, 15607392, 15992656, 16288990	Diagnosis confirmed	*PKP2: c.1468C>T; p.(Arg490Trp) (VUS) heterozygous*	Present	8.09	1.49	2.25	69	0.98
P27	Female	ACM	14		# 607450 arrhythmogenic right ventricular dysplasia, familial, 8; ARVD8	*DSP*	c.3337C>T	p.(Arg1113Ter)	P	Heterozygous	Inherited from affected mother	PMIDs:28527814, 30382575, 31386562, 31402444	Diagnosis confirmed		Present	1.40	1.52	−1.17	51	1.83
P28	Male	HCM	1.5										Inconclusive	*GLRA1*: c.92C>T; p.(Ser31Phe) (VUS) heterozygous	Absent	4.52	6.00	−1.81	68	0.59
P29	Male	HCM	7	SCA	# 115196 cardiomyopathy, familial hypertrophic, 3; CMH3	*TPM1*	c.248C>A	p.(Ala83Asp)	LP	Heterozygous	Inherited from affected mother	PMID: 28771489	Diagnosis confirmed	*RYR2*: c.14102T>C; p.(Ile4701Thr) (VUS) heterozygous	Present	0.34	0.45	−1.59	66	0.96
P30	Male	HCM	11		# 115195 cardiomyopathy, familial hypertrophic, 2; CMH2	*TNNT2*	c.305G>A	p.(Arg102Gln)	P	Heterozygous	Unknown	PMID: 7898523, 8205619, 8951566	Diagnosis confirmed		Present	1.39	1.50	−1.53	69	1.37

P31		HCM	0.9		# 192600 cardiomyopathy, familial hypertrophic, 1; CMH1	*MYH7*	c.2156G>A	p.(Arg719Gln)	P	Heterozygous	Unknown	PMID: 32403337, 31513939	Diagnosis confirmed		Absent	6.40	6.51	−0.54	67	0.53
P32	Female	DCM	0.5	HF	# 601494 cardiomyopathy, dilated, 1D; CMD1D	*TNNT2*	c.421C>T	p.(Arg141Trp)	P	Heterozygous	Inherited from affected father	PMID:34540771, 33906374, 32746448, 32758068, 34076677	Diagnosis confirmed	*NEXN*: c.1739G>A; p.Gly(580Glu) (VUS) heterozygous	Absent	−1.38	−1.27	3.73	33	0.35
P33	Female	HCM	0.4		# 115195 cardiomyopathy, familial hypertrophic, 2; CMH2	*TNNT2*	c.817A>C	p.(Lys273Gln)	LP	Heterozygous	Inherited from affected mother	PMID:34137518	Diagnosis confirmed	*NOTCH1*: c.2675G>A; p.(Arg892His) (VUS) heterozygous *ANK2*: c.4835C>T; p.(Thr1612Ile) (VUS) heterozygous	Present	23.24	0.26	−4.30	80	1.03
P34	Male	HCM	1.5		# 192600 cardiomyopathy, familial hypertrophic, 1; CMH1	*MYH7*	c.2146G>A	p.(Gly716Arg)	P	Heterozygous	*De Novo*	PMID:23283745, 24093860, 25935763, 27161882	Diagnosis confirmed		Absent	10.14	2.72	1.46	66	0.47
P35	Male	DCM	17	VF/VT	# 604145 cardiomyopathy, dilated, 1G; CMD1G	*TTN*	c.95655del	p.(Glu31886Asnfs*3)	LP	Heterozygous	Inherited from affected father	PMID:38438525	Diagnosis confirmed	*KCNJ5*: c.409G>A; p.(Val137Met) (VUS) heterozygous	Present	−0.25	−0.14	1.36	42	1.76
P36	Female	HCM/RCM	1	ICD appropriate shock	# 115197 cardiomyopathy, familial hypertrophic, 4; CMH4	*MYBPC3*	c.[2670dup]+[c.2274C>T]	p.[(Arg891Alafs*160)+p.(?)]	P	Compound Heterozygous	First inherited from the affected father and the second from the unaffected mother	PMIDs: 24093860, 22765922, 37821546	High risk diagnosis confirmed		Absent	13.69	12.26	−1.66	70	0.44
P37	Female	DCM	0.5	HF/Tx	Potential # 192600 cardiomyopathy, familial hypertrophic, 1; CMH1	*MYH7*	c.5519T>C	p.(Met1840Thr)	VUS*	Heterozygous	No	PMID:27247418	Potential associated gene-variant identified	*TNNC1*: c.376G>A; p.(Glu126Lys) (VUS) heterozygous *KCNJ5*: c.674G>A; p.Arg225His (VUS) heterozygous	Present	−1.21	0.65	14.89	30	0.32
P38	Male	DCM	0.1		Potential # 613424 cardiomyopathy, dilated, 1R; CMD1R	*ACTC1*	c.778C>T	p.(Pro260Ser)	VUS*	Heterozygous	Inherited from unnaffected mother	Novel	Potential associated gene-variant identified	*MYH6*: c.1753G>A; p.(Gly585Ser) (VUS) heterozygous *PRKAG2*: c.428C>T; p.(Ser143Leu) (VUS) heterozygous	Absent	−0.95	−0.84	7.36	45	0.29
P39	Female	ACM	13	SCA	# 607450 arrhythmogenic right ventricular dysplasia, familial, 8; ARVD8	*DSP*	c.3337C>T	p.(Arg1113Ter)	P	Heterozygous	Inherited from affected mother	PMIDs: 28527814, 30382575, 31386562, 31402444	Diagnosis confirmed	*LAMA4*: c.1256T>C; p.(Met419Thr) (VUS) heterozygous *AKAP9*: c.6742G>C; p.(Glu2248Gln) (VUS) heterozygous	Present	1.19	1.30	−0.04	54	1.46
P40	Female	HCM	0.1		Potential # 617047 cardiomyopathy, familial hypertrophic, 26; CMH26	*FLNC*	c.2842G>A	p.(Gly948Arg)	VUS*	Heterozygous	Inherited from unnaffected mother	Novel	Potential associated gene-variant identified	*TLX3*: c.194G>T; p.Gly65Val (VUS) heterozygous	Absent	7.74	3.80	−5.24	71	0.22

P41	Male	HCM	4	ICD appropriate shock	# 115197 cardiomyopathy, familial hypertrophic, 4; CMH4	*MYBPC3*	c.2149-1G>A	p.(?)	P	Heterozygous	Inherited from affected father	PMIDs: 27532257, 30393631, 23782526, 37652022, 36129056, 34588271	High risk diagnosis confirmed		Present	17.58	1.67	−0.24	72	0.63
					# 192600 cardiomyopathy, familial hypertrophic, 1; CMH1	*MYH7*	c.2782G>A	p.(Asp928Asn)	P	Heterozygous	Inherited from unnaffected mother (affected grandfather)	PMIDs: 30972196, 19666645							
P42	Female	HCM	8	SCA	# 115197 cardiomyopathy, familial hypertrophic, 4; CMH4	*MYBPC3*	c.2149-1G>A	p.(?)	P	Heterozygous	Inherited from affected father	PMIDs: 27532257, 30393631, 23782526, 37652022, 36129056, 34588271	High risk diagnosis confirmed		Present	18.70	2.81	−2.72	55	0.93
					# 192600 cardiomyopathy, familial hypertrophic, 1; CMH1	*MYH7*	c.2782G>A	p.(Asp928Asn)	P	Heterozygous	Inherited from unnaffected mother (affected grandfather)	PMIDs: 30972196, 19666645							
P43	Female	HCM/RCM	2	SCD	# 115197 cardiomyopathy, familial hypertrophic, 4; CMH4	*MYBPC3*	c.[2670dup]+[c.2274C>T]	p.[(Arg891Alafs*160)+p.(?)]	P	Compound Heterozygous	The first inherited from the affected father and the second from the unaffected mother	PMIDs: 24093860, 22765922+PMID: 37821546	High risk diagnosis confirmed		Absent	10.19	10.30	−1.30	66	0.58
P44	Male	HCM	5		# 115197 cardiomyopathy, familial hypertrophic, 4; CMH4	*MYBPC3*	c.3627+1G>A	p.(?)	P	Heterozygous	*De Novo*	PMIDs: 9562578, 20031602, 25351510, 27532257	Diagnosis confirmed	*MYBPC3*: c.41A>G; p.(Lys14Arg) (VUS) heterozygous *SCN5A*: c.5692C>T; p.(Arg1898Cys) (VUS) heterozygous	Present	10.86	1.08	−0.86	76	0.77
P45	Male	HCM	8		# 115196 cardiomyopathy, familial hypertrophic, 3; CMH3	*TPM1*	c.523G>A	p.(Asp175Asn)	P	Heterozygous	Inherited from unnaffected mother	PMIDs: 32217077, 15000344, 8523464, 16504640	Diagnosis confirmed		Absent	27.05	8.80	−3.27	75	1.07
P46	Female	DCM	1	HF/Tx	# 611880 cardiomyopathy, dilated, 2A; CMD2A	*TNNI3*	c.204del	p.(Arg69Alafs*8)	P	Homozygous	Inherited from both unnaffected parents	PMIDs: 31568572	High risk diagnosis confirmed		Absent	−0.99	−0.88	2.33	30	0.60
P47	Male	HCM	12		Potential # 192600 cardiomyopathy, familial hypertrophic, 1; CMH1	*MYLK2*	c.869C>T	p.(Ala290Val)	VUS*	Heterozygous	No	Novel	Potential associated gene-variant identified	*TTN*: c.46211G>C; p.(Arg15404Pro) (VUS) heterozygous *TTN*: c.16638T>G; p.(Phe5546Leu) (VUS) heterozygous *AKAP9* : c.4175C>T; p.(Thr1392Ile) (VUS) heterozygous	Absent	7.71	−0.67	0.32	72	1.50

P48	Male	HCM	17		# 115197 cardiomyopathy, familial hypertrophic, 4; CMH4	*MYBPC3*	c.2539_2544del	p.(Tyr847_Ala848del)	LP	Heterozygous	Inherited from affected mother	Novel	Diagnosis confirmed		Absent	10.23	2.44	−1.80	77	1.80
P49	Male	ACM	15	SCD	# 607450 arrhythmogenic right ventricular dysplasia, familial, 8; ARVD8	*DSP*	c.868G>A	p.(Glu290Lys)	LP	Heterozygous	Inherited from affected mother	PMIDs: 39288222	Diagnosis confirmed	*PKP2*: c.184C>A; p.(Gln62Lys) (VUS) heterozygous	Absent	1.45	1.56	1.45	55	1.81
P50	Female	HCM	14		# 192600 cardiomyopathy, familial hypertrophic, 1; CMH1	*MYH7*	c.2167C>G	p.(Arg723Gly)	P	Heterozygous	Inherited from affected father	PMID: 11113006, 17097032, 19150014, 20865685, 24093860.	Diagnosis confirmed		Present	4.92	1.24	−0.90	68	1.49
P51	Female	HCM	18		# 192600 cardiomyopathy, familial hypertrophic, 1; CMH1	*MYH7*	c.2167C>G	p.(Arg723Gly)	P	Heterozygous	Inherited from affected father	PMID: 11113006, 17097032, 19150014, 20865685, 24093860.	Diagnosis confirmed		Absent	4.95	−0.20	−1.11	67	1.81
P52	Male	DCM	13										Inconclusive	*MYL2*: c.89A>C; p.(Lys30Thr) (VUS) heterozygous	Absent	0.92	1.03	−1.00	62	1.60
P53	Female	HCM	13		# 115197 cardiomyopathy, familial hypertrophic, 4; CMH4	*MYBPC3*	c.3234G>A	p.(Trp1078)	P	Heterozygous	Inherited from affected father	PMIDs: 25740977, 25740977	Diagnosis confirmed	*TPM1*: c.841A>G; p.(Met281Val) (VUS) heterozygous *TTN*: c.79919A>T; p.(Tyr2664Phe (VUS) heterozygous *PKP2*: c.2204G>A; p.(Arg735Gln) (VUS) heterozygous	Absent	14.43	0.02	−1.17	74	1.66
P54	Male	HCM	0.3		# 115197 cardiomyopathy, familial hypertrophic, 4; CMH4	*MYBPC3*	c.2308+1G>A	p.(?)	P	Heterozygous	Inherited from affected father	PMIDs: 9048664, 18957093, 21088121, 9048664, 18957093, 21088121.	Diagnosis confirmed		Absent	5.49	−1.22	−1.00	75	0.34
P55	Female	HCM	18		# 192600 cardiomyopathy, familial hypertrophic, 1; CMH1	*MYH7*	c.1357C>T	p.(Arg453Cys)	P	Heterozygous	Inherited from affected father	PMIDs:8655135 , PMID:10662815	Diagnosis confirmed		Absent	−0.29	0.69	−1.55	64	1.80
P56	Male	HCM	14		Potential # 613690 cardiomyopathy, familial hypertrophic, 7; CMH7	*TNNI3*	c.244C>A	p.(Pro82Thr)	VUS*	Heterozygous	No	PMIDs: 28166811	Potential associated gene-variant identified		Absent	4.11	1.35	−1.76	75	1.44
P57	Male	HCM	15		Potential # 613690 cardiomyopathy, familial hypertrophic, 7; CMH7	*TNNI3*	c.244C>A	p.(Pro82Thr)	VUS*	Heterozygous	No	PMIDs: 28166811	Potential associated gene-variant identified	*FLNC*: c.1568T>C; p.(Val523Ala) (VUS) heterozygous	Absent	4.40	1.55	−1.46	67	1.35

P58	Female	HCM	0										Inconclusive	*HCN4:* c.3187C>T; p.(Pro1063Ser) (VUS) heterozygous *TTN*: c.53992G>A; p.(Val17998Ile) (VUS) heterozygous *SLC22A5*: c.605T>C; p.Leu202Pro (VUS) heterozygous	Absent	1.90	4.10	4.22	68	0.21
P59	Female	HCM	0		# 192600 cardiomyopathy, familial hypertrophic, 1; CMH1	*MYH7*	c.2674C>A	p.(Gln892Lys)	LP	Heterozygous	Inherited from affected mother	PMIDs: 28840316, 23283745	Diagnosis confirmed		Absent	2.73	−0.22	−2.19	71	0.22
P60	Female	ACM	17										Inconclusive	*DSP*: c.4775A>G; p.(Lys1592Arg) (VUS) heterozygous *LMNA*: c.1364G>A; p.(Arg455His) VUS heterozygous *TP63*: c.2005C>T; p.(Arg669Cys) VUS heterozygous	Present	1.62	1.73	0.34	61	1.71
P61	Female	HCM	10		# 192600 cardiomyopathy, familial hypertrophic, 1; CMH1	*MYH7*	c.1750G>T	p.(Gly584Cys)	P	Heterozygous	Inherited from affected mother	PMIDs: 39605252, 31308319	Diagnosis confirmed	*SCN10A*: c.3417G>C; p.(Trp1139Cys) (VUS) heterozygous	Absent	6.32	0.05	−0.54	80	1.12
P62	Male	DCM	18		# 604145 cardiomyopathy, dilated, 1G; CMD1G	*TTN*	c.41467C>T	p.(Arg13823Ter)	P	Heterozygous	Inherited from unnaffected mother (affected uncle)	PMIDs: 30471092, 31737537, 34088380.	Diagnosis confirmed	*TRPM4*: c.472C>G; p.(Leu158Val) (VUS) heterozygous *SCN5A*: c.5333C>T; p.(Thr1778Met) (VUS) heterozygous *EYA4*: c.252T>A; p.(Ser84Arg) (VUS) heterozygous	Absent	1.82	1.01	1.17	56	1.61
P63	Male	DCM	14										Inconclusive	*TTN:* c.74152G>A; p.(Val24718Ile) (VUS) heterozygous *TTN*: c.73760T>C; p.(Ile24587Thr) (VUS) heterozygous *SCN4B*: c.542T>C; p.(Leu181Pro) (VUS) heterozygous	Absent	2.88	1.29	0.95	60	1.97

P64	Male	DCM	12	VF/VT	Potential # 616117 cardiac conduction disease with or without dilated cardiomyopathy; CCDD	*TNNI3K*	c.2099G>C	p.(Arg700Pro)	VUS*	Heterozygous	Inherited from unnaffected mother	Novel	Potential associated gene-variant identified	*PPP1R13L*: c.1294C>G; p.(Pro432Ala) (VUS) heterozygous *MYH6*: c.3872G>A; p.(Arg1291Gln) (VUS) heterozygous *DSG2*: c.1820A>G; p.(Tyr607Cys) (VUS) heterozygous *DMD*: c.4170C>G; p.(Asp1390Glu) (VUS) heterozygous	Absent	1.39	0.52	1.36	53	1.37
P65	Male	HCM	13	SCA	# 115195 cardiomyopathy, familial hypertrophic, 2; CMH2	*TNNT2*	c.890G>A	p.(Trp287Ter)	P	Compound Heterozygous	Inherited from affected mother	PMIDs: 20439259, 22857948	High risk diagnosis confirmed		Present	21.53	3.31	−1.45	72	1.42
					# 192600 cardiomyopathy, familial hypertrophic, 1; CMH1	*MYH7*	c.2273T>C	p.(Phe758Ser)	LP	Compound Heterozygous	Inherited from unnaffected father	PMID: 32880476								
P66	Female	DCM	0.5	HF	Potential # 613424 cardiomyopathy, dilated, 1R; CMD1R	*DES*	c.326A>G	p.(Lys109Arg)	VUS*	Heterozygous	Inherited from unnaffected father	PMID: 32403337	Potential associated gene-variant identified	*TNNT2*: c.529G>T; p.(Ala177Ser) (VUS) heterozygous *NKX2-5*: c.890_891dupTC; p.(Gly298Serfs*4) (VUS) heterozygous	Absent	0.41	0.52	11.40	25	0.34
P67	Male	HCM	17		# 619402 cardiomyopathy, familial hypertrophic, 28; CMH28	*FHOD3*	c.1583A>G	p.(Tyr528Cys)	LP	Heterozygous	Inherited from unnaffected father	PMID: 30442288	Diagnosis confirmed	*ALPK3*: c.2054A>G; p.(Lys685Arg) (VUS) heterozygous	Present	15.75	3.43	−1.90	80	1.75
P68	Female	DCM	0		# 613426 cardiomyopathy, dilated, 1S; CMD1S	*MYH7*	c.5186_5188del	p.(Lys1729del)	P	Heterozygous	Inherited from affected mother	PMID: 12975303, 15322983, 20733148	Diagnosis confirmed		Absent	3.12	−0.59	0.50	53	0.26
P69	Male	DCM	15		Potential * 191040 troponin c, slow; TNNC1	*TNNC1*	c.121C>A	p.(Leu41Met)	VUS*	Heterozygous	Inherited from unnaffected mother	Novel	Potential associated gene-variant identified		Absent	1.59	1.70	0.52	61	1.73
P70	Female	HCM	13		# 115197 cardiomyopathy, familial hypertrophic, 4; CMH4	*MYBPC3*	c.2149-1G>A	p.(?)	P	Heterozygous	Inherited from affected father	PMIDs: 27532257, 30393631, 23782526, 37652022, 36129056, 34588271	Diagnosis confirmed		Absent	4.34	3.55	−3.19	75	1.70
P71	Female	HCM	14		# 115197 cardiomyopathy, familial hypertrophic, 4; CMH4	*MYBPC3*	c.2401C>T	p.(Gln801Ter)	LP	Heterozygous	No	Novel	Diagnosis confirmed		Absent	12.07	3.41	−1.59	76	1.39
P72	Male	HCM	12		Potential # 115197 cardiomyopathy, familial hypertrophic, 4; CMH4	*MYBPC3*	c.3779G>T	p.(Gly1260Val)	VUS*	Heterozygous	Unknown	Novel	Potential associated gene-variant identified		Absent	13.10		−4.62	76	1.96

P73	Female	DCM	12		Potential # 163800 sick sinus syndrome 2 with or without cardiac noncompaction and/or ascending aorta dilation	*HCN4*	c.1454C>T	p.(Ala485Val)	VUS*	Heterozygous	Inherited from affected mother	PMID: 28254188, 34540771	Potential associated gene-variant identified		Absent	−0.82	−1.65	0.72	65	1.53
P74	Male	DCM	18		Potential # 615396 cardiomyopathy, dilated, 1mm, included; CMD1MM, included	*MYBPC3*	c.1321G>A	p.(Glu441Lys)	VUS*	Heterozygous	No	PMID: 37652022, 30972196	Potential associated gene-variant identified	*MYBPC3*: c.836G>C; p.(Gly279Ala) (VUS) heterozygous	absence	0.99	1.11	1.25	61	2.10
P75	Female	DCM	18		# 601154 cardiomyopathy, dilated, 1E; CMD1E	*SCN5A*	c.2440C>T	p.(Arg814Trp)	P	Heterozygous	Inherited from affected father	PMID 38464806	Diagnosis confirmed	*MYBPC3*: c.1010C>T; p.(Ala337Val) (VUS) heterozygous	Absent	2.91	0.21	0.20	66	1.54
P76	Male	DCM	6	SCA	# 601494 cardiomyopathy, dilated, 1D; CMD1D	*TNNT2*	c.299T>A	p.(Ile100Asn)	P	Heterozygous	*De Novo*	PMID: 18612386, 32098556, 33025817	Diagnosis confirmed	*DSC2*: c.1747A>G; (p.Ile583Val) (VUS) heterozygous *JPH2*: c.692G>A; (p.Arg231Gln) (VUS) heterozygous	Absent	7.19	2.34	0.89	48	0.76
P77	Male	HCM	15										Negative		Absent	10.37	1.14	−2.07	68	1.54
P78	Male	HCM	1										Negative		Present	9.64	2.13	−1.97	81	1.98
P79	Male	HCM	18										Negative		Absent	4.62	2.18	−0.11	68	1.95
P80	Male	ACM	16										Negative		Absent	2.39	2.50	0.62	65	1.77
P81	Male	DCM	11	HF									Negative		Absent	−1.48	−1.37	1.01	25	1.33
P82	Female	HCM	1										Negative		Present	15.53	13.45	−2.21	68	1.03
P83	Male	HCM	18										Negative		Absent	3.99	4.10	−1.44	64	1.85
P84	Male	HCM	13										Negative		Absent	15.90	2.41	−2.15	78	1.40

HCM, hypertrophic cardiomyopathy; DCM, dilated cardiomyopathy; ACM, arrhythmogenic cardiomyopathy; VT/VF, ventricular tachycardia/fibrillation; HF, heart failure stages C and D; HTx, heart transplant; SCD, sudden cardiac death; SCA, sudden cardiac arrest; IVS, thickness of the interventricular septum; LVPW-score, left ventricular posterior wall, standardized for age and body size; LVEDD z-score reflects the left ventricular end-diastolic diameter adjusted for body size; LVEF (%) corresponds to left ventricular ejection fraction calculated using the Simpson biplane method; BSA, body surface area. P, pathogenic; LP, likely pathogenic; VUS, variant of uncertain significance; VUS*: applying an internal classification, these variants were reclassified as VUS-LP (with a potential deleterious role).