Predictores de riesgo en una cohorte española con cardiolaminopatías. Registro REDLAMINA

SUPPLEMENTARY DATA

Lista completa de investigadores y centros participantes en el registro REDLAMINA

1. Inherited Cardiac Diseases Unit, Cardiology Department, Complejo Asistencial Universitario de Salamanca, Instituto de Investigación Biomédica de Salamanca (IBSAL), Facultad de Medicina, Universidad de Salamanca, Salamanca, Spain: María Isidoro, Belén García, María Gallego-Delgado, Eduardo Villacorta.

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7. Balearic Islands Health Research Institute (iDisBA), Inherited Cardiovascular Disease Unit, Cardiology Department Son Llatzer University Hospital, Illes Balears, Spain: Jorge Álvarez-Rubio, Tomas Ripoll-Vera.

8. Área del Corazón, Complejo Hospitalario de Navarra, Spain: Mª Teresa Basurte-Elorz.

9. Cardiology Service, Hospital Universitario Miguel Servet de Zaragoza, Spain: Ainhoa Pérez-Guerrero.

10. Hereditary Cardiopathies Unit, Hospital Universitario 12 de Octubre, Madrid, Spain: Julián Palomino-Doza.

11. Inherited Cardiovascular diseases and Imaging Unit, Cardiology Service, Hospital Universitario Virgen del Rocío, Sevilla, Spain: Maria Luisa Peña-Peña.

12. Cardiology Department, University General Hospital of Alicante, Alicante, Spain, Institute of Health and Biomedical Research (ISABIAL), Alicante, Spain, Hospital General Universitario de Alicante, Alicante, Spain: Maria I. García-Álvarez, Vicente Climent-Payá.

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14. Unidad de Cardiopatías Familiares, Muerte Súbita y Mecanismos de Enfermedad (CaFaMuSMe), Instituto de Investigación Sanitaria La Fe, Cardiology Service, Hospital Universitario y Politécnico La Fe, Valencia, Spain: Jorge Sanz, Esther Zorio-Grima.

15. Unidad de Hemodinámica y Ecocardiografía, Cardiology Service, Hospital Universitario Juan Ramón Jiménez, Huelva, Spain: Ana Manovel.

16. Department of Cardiology, Hospital General Universitario Gregorio Marañón, Instituto de Investigación Sanitaria Gregorio Marañón, Madrid, Spain: María Ángeles Espinosa, Raquel Yotti.

17. Department of Cardiology, Hospital Universitario Ramón y Cajal, Madrid, Spain. Luis M. Rincón-Díaz.

18. Department of Cardiology, Biosanitary Research Institute of Granada (ibs.GRANADA), Virgen de las Nieves University Hospital, Granada, Spain: Juan Jiménez-Jáimez, Francisco J Bermúdez-Jiménez.

19. Inherited Cardiac Diseases Unit, Department of Cardiology, Hospital Clínico Universitario Virgen de la Arrixaca; European Reference Network on Rare and Complex Diseases of the Heart, Murcia,

Spain: María Carmen Olmo-Conesa, Elisa Nicolás-Rocamora, María Sabater-Molina, Juan Ramón Gimeno-Blanes.

METHODS

Dilated cardiomyopathy and hypoquinetic non-dilated cardiomyopathy were defined according to the consensus document published in 2016.[1] Heart failure was defined according to the 2013 guidelines.[2] Unexplained left ventricular dilatation was defined according to nomograms.[1] Atrial tachyarrhythmias were classified as atrial flutter or paroxysmal (duration > 30 seconds), persistent or permanent atrial fibrillation. Atrioventricular block was classified as first, second or third degree. We defined non-sustained ventricular tachycardia as the presence of ≥ 3 complexes at ≥ 120 beats per minute. The presence of at least one family member (first, second or third degree) who died suddenly aged < 50 years was considered as familial sudden cardiac death. Appropriate ICD intervention was considered one that was necessary for the termination of ventricular fibrillation. Sudden cardiac death was defined as cardiac death with or without documented ventricular fibrillation within one hour after the onset of acute symptoms or unwitnessed nocturnal death without a history of prior worsening. Myopathy was considered when the patient presented with muscle pain or weakness, with or without concomitant elevated creatine kinase, but muscle biopsy was not systematically performed. Embolic events included cerebrovascular accidents and peripheral embolisms that required admission.

Table 1 of the supplementary data. Genetic variants in *LMNA* gene included in the REDLAMINA registry final analysis

PROTEIN 733821.1)	CHROMOSOME	c.DNA (170707.3)	Variant type	Exon	Probands/ relatives	Segregation	Previously published	ClinVar	gnomAD MAF% (alleles)	Patho genicity	Rational for classification of pathogenicity
p.0?	g.156084710A > T	c.1A > T	Non-missense (initiation site)	1	1/3	Yes	No	Not reported	Not present	Pathogenic	. Null variant[1] . Absent from controls[5] . Segregation in families . Computational evidence . Phenotype highly suggestive of laminopathy[6]
p.Ser22*	g.156084774C > A	c.65C > A	Non-missense (nonsense)	1	3/0	Yes	Yes[1]	Not reported	Not present	Pathogenic	. Null variant[1] . Absent from controls[5] . Segregation in families . Computational evidence . Phenotype highly suggestive of laminopathy[6]
p.Thr27Ile	g.156084789C > T	c.80C > T	Missense	1	1/1	Yes	Yes[2,3]	Not reported	Not present	Likely pathogenic	. Missense variant[2] . Absent from controls[5] . Computational evidence . Mutational hot-spot[4]
p.Glu33Asp	g.156084808G > T	c.99G > T	Missense	1	1/0	n/a	Yes[4-7]	Uncertain significance	Not present	Pathogenic	. Missense variant[2] . Absent from controls[5] . Computational evidence[3] . Mutational hot-spot[4] . Same aminoacid change associated with disease . Another variant affecting the same residue associated with disease
p.Glu65*	g.156084902G > T	c.193G > T	Non-missense (nonsense)	1	1/0	n/a	No	Not reported	Not present	Pathogenic	. Null variant[1] . Absent from controls[5] . Computational evidence
p.Arg72Leu	g.156084924G > T	c.215G > T	Missense	1	1/0	n/a	Yes[8]	VUS	Not present	Likely pathogenic	. Missense variant[2] . Absent from controls[5] . Computational evidence . Mutational hot-spot[4]
p.Tyr81Thrfs*15	g.156084949delC	c.240delC	Non-missense (frame-shift)	1	1/11	Yes	No	Not reported	Not present	Pathogenic	. Null variant[1] . Absent from controls[5]

											. Segregation in families . Computational evidence
p.Leu85Val	g.156084962C > G	c.253C > G	Missense	1	1/0	n/a	Yes[9]	Not reported	Not present	Likely pathogenic	. Missense variant[2] . Absent from controls[5] . Computational evidence[3] . Mutational hot-spot[4] . Another variant affecting the same residue associated with disease
p.Arg89Cys	g.156084974C > T	c.265C > T	Missense	1	1/0	n/a	Yes[10]	Not reported	Not present	Likely pathogenic	. Missense variant[2] . Absent from controls[5] . Computational evidence[3] . Mutational hot-spot[4] . Another variant affecting the same residue associated with disease
p.Arg119Pro	g.156085065G > C	c.356G > C	Missense	1	1/0		Yes[11]	VUS	Not present	Likely pathogenic	. Missense variant[2] . Absent from controls[5] . Computational evidence[3] . Mutational hot-spot[4]
p.Glu124Lys	g.156100421G > A	c.370G > A	Missense	2	2/6	Yes	No	Not reported	Not present	Likely pathogenic	. Missense variant[2] . Absent from controls[5] . Computational evidence[3] . Mutational hot-spot[4] . Segregation in families
p.Glu161Lys	g.156100532G > A	c.481G > A	Missense	2	1/1		Yes[11-19]	Pathogenic	Not present	Pathogenic	. Missense variant[2] . Absent from controls[5] . Computational evidence[3] . Mutational hot-spot[4] . Segregation in families . Considered pathogenic by reputable source
P.Arg190Trp	g.156104248C > T	c.568C > T	Missense	3	5/11	Yes	Yes[13,16,19-35]	Pathogenic (DCM, CMT2)	Not present	Pathogenic	. Missense variant[2] . Absent from controls[5] . Computational evidence[3] . Mutational hot-spot[4] . Segregation in families . Considered pathogenic by reputable source . Another variant affecting

											the same residue associated with disease
p.Arg190Gln	g.156104249G > A	c.569G > A	Missense	3	2/0	Yes	Yes[15,36-39]	Conflicting pathogenicity (CMT2, Cardiomyopathy)	Not present	Pathogenic	. Missense variant[2] . Absent from controls[5] . Computational evidence[3] . Mutational hot-spot[4] . Segregation in families . Considered pathogenic by reputable source . Another variant affecting the same residue associated with disease
p.Arg225*	g.156104629C > T	c.673C > T	No-missense (nonsense)	4	2/3	Yes	Yes[11,16,40-42]	Pathogenic (DCM, LGD1B, CMT2)	Not present	Pathogenic	. Null variant[1] . Absent from controls[5] . Computational evidence[3] . Segregation in families . Considered pathogenic by reputable source
p.Phe237Ser	g.156104666T > C	c.357C > T	Missense	4	1/6	Yes	Yes[43]	Pathogenic (DCM)	Not present	Likely pathogenic	. Missense variant[2] . Absent from controls[5] . Mutational hot-spot[4] . Segregation in families . Considered pathogenic by reputable source
p.Ala242Val	g.156104681C > T	c.725C > T	Missense	4	1/2	Yes	No	Likely pathogenic (DCM, ACM)	< 0.01% (2/246,234)	Likely pathogenic	. Missense variant[2] . Absent from controls[5] . Computational evidence[3] . Mutational hot-spot[4] . Segregation in families . Considered pathogenic by reputable source
p.Arg249Leu	g.156104702G > T	c.746G > T	Missense	4	1/0	n/a	No	Not reported	Not present	Likely pathogenic	. Missense variant[2] . Absent from controls[5] . Computational evidence[3] . Mutational hot-spot[4] . Another variant affecting the same residue associated with disease . Phenotype highly suggestive of laminopathy[6]

p.Gln258Pro	g.156104729A > C	c.773A > C	Missense	4	1/0	n/a	No	Not reported	Not present	Likely pathogenic	. Missense variant[2] . Absent from controls[5] . Mutational hot-spot[4] . Phenotype highly suggestive of laminopathy[6]
Asp272Glnfs*7	g.156104981_156104982del	c.814_815delGA	Non-missense	5	1/0	n/a	No	Not reported	Not present	Pathogenic	. Null variant[1] . Absent from controls[5] . Computational evidence[3]
p.Glu291Lys	g.156105038G > A	c.871G > A	Missense	5	1/2	Yes	Yes[44]	Pathogenic	Not present	Pathogenic	. Missense variant[2] . Absent from controls[5] . Computational evidence[3] . Mutational hot-spot[4] . Segregation in family . Phenotype highly suggestive of laminopathy[6]
p.Arg321*	g.156105716C > T	c.961C > T	No-missense (nonsense)	6	2/5		Yes[11,45-48]	Pathogenic (DCM)	< 0.01% (1/30,936)	Pathogenic	. Null variant[1] . Absent from controls[5] . Computational evidence[3] . Segregation in families . Considered pathogenic by reputable source
p.Arg331Gln	g.156105747G > A	c.992G > A	Missense	6	1/0		Yes[11,46,49,50]	Conflicting pathogenicity (Pathogenic, likely pathogenic, VUS)	< 0.01% (3/245,554)	Likely pathogenic	. Missense variant[2] . Absent from controls[5] . Computational evidence[3] . Mutational hot-spot[4] . Considered pathogenic by reputable source
p.Arg335Trp	g.156105758C > T	c.1003C > T	Missense	6	1/1		Yes[8,11,16,51, 52]	Pathogenic, Likely pathogenic (DCM, HGS, LGD1B, CMT2 EDMD3)	Not present	Likely pathogenic	. Missense variant[2] . Absent from controls[5] . Computational evidence[3] . Mutational hot-spot[4] . Considered pathogenic by reputable source
p.Arg335Glyfs*145	g.156105758delC	c.1003delC	Non-missense (frame-shift)	6	1/0		No	Pathogenic (CMT2)	Not present	Pathogenic	. Null variant[1] . Absent from controls[5] . Computational evidence[3] . Considered pathogenic by reputable source
p.Arg349Leu	g.156105801_156105802delGGinsT	c.1046_1047delGGinsTT	Missense	6	2/2	Yes	No	Not reported	Not present	Likely pathogenic	. Missense variant[2] . Absent from controls[5]

	T										. Mutational hot-spot[4] . Considered pathogenic by reputable source
p.Glu372Asp	g.156105871G > C	c.1116G > C	Missense	6	1/0	n/a	No	Likely pathogenic (DCM, de novo)	Not present	Likely pathogenic	. Missense variant[2] . Absent from controls[5] . Mutational hot-spot[4] . Considered pathogenic by reputable source
p.Arg377Cys	g.156105884C > T	c.1129C > T	Missense	6	3/6	Yes	Yes[11,54-56]	Pathogenic, Likely pathogenic (DCM, LGD, CMT2)	Not present	Pathogenic	. Missense variant[2] . Absent from controls[5] . Computational evidence[3] . Mutational hot-spot[4] . Segregation in families . Considered pathogenic by reputable source . Another variant affecting the same residue associated with disease
p.Arg377His	g.156105885G > A	c.1130G > A	Missense	6	4/3	Yes	Yes[16,30, 40,57-64]	Pathogenic (DCM, LGD1B, CMT2)	Not present	Pathogenic	. Missense variant[2] . Absent from controls[5] . Computational evidence[3] . Mutational hot-spot[4] . Segregation in families . Considered pathogenic by reputable source . Another variant affecting the same residue associated with disease
p.Gly382=	g.156105901C > T	c.1146C > T	Non-missense (synonymous; splicing)	6	1/1		Yes[11,65]	Pathogenic, Likely pathogenic (LGD1B, DCM, CMT2)	Not present	Pathogenic	. Null variant[1] . Absent from controls[5] . Computational evidence (splicing affected) . Considered pathogenic by reputable source
n/a (intronic variant)	g.156106004G > A	c.1158-1G > A	Non-missense	In 6	2/6	Yes	No	Not reported	Not present	Pathogenic	. Null variant[1] . Absent from controls[5] . Computational evidence (splicing affected) . Considered pathogenic by reputable source

											. Segregation in families
p.Gln410*	g.156106075C > T	c.1228C > T	Non-missense (nonsense)	7	1/1		No	Pathogenic (DCM)	Not present	Pathogenic	. Null variant[1] . Absent from controls[5] . Computational evidence
p.Ser437Hisfs*2	g.156106154_156106155insGCAC	c.1307_1308insGCAC	Non-missense (frame-shift)	7	1/11	Yes	Yes[37]	Pathogenic (Cardiomyopathy)	Not present	Pathogenic	. Null variant[1] . Absent from controls[5] . Segregation in families . Computational evidence
p.Glu444*	g.156106177G > T	c.1330G > T	Non-missense (nonsense)	7	1/1	Yes	No	Not reported	Not present	Pathogenic	. Null variant[1] . Absent from controls[5] . Segregation in families . Computational evidence
p.Trp514*	g.156106956G > A	c.1541G > A	Non-missense (nonsense)	9	2/3	Yes	No	Not reported	Not present	Pathogenic	. Null variant[1] . Absent from controls[5] . Segregation in families . Computational evidence
p.Arg541Ser	g.156107457C > A	c.1621C > A	Missense	10	1/0		Yes[27,53,70,71]	Not reported	Not present	Pathogenic	. Missense variant[2] . Absent from controls[5] . Computational evidence[3] . Considered pathogenic by reputable source . Another variant affecting the same residue associated with disease

1. Null variant (nonsense, frameshift, canonical ±1 or 2 splice sites, initiation codon, single or multiexon deletion) in a gene where loss of function is a known mechanism of disease.
2. Missense variant in a gene that has a low rate of benign missense variation and in which missense variants are a common mechanism of disease.
3. Multiple lines of computational evidence support a deleterious effect on the gene or gene product (conservation, evolutionary, splicing impact, etc.).
4. Located in a mutational hot spot and/or critical and well-established functional domain (e.g., active site of an enzyme) without benign variation.

5. Absent from controls (or at extremely low frequency if recessive) in Exome Sequencing Project, 1000 Genomes Project, or Exome Aggregation Consortium
6. Patient's phenotype or family history is highly specific for a disease with a single genetic etiology (in this paper, suggestive of laminopathy: DCM plus another specific finding such as cardiac conduction disease, miopathy, family history of SCD, etc.)

n/a, not available; DCM, dilated cardiomyopathy; GnomAD, Genome Aggregation Database; MAF, Minor allele frequency; SCD, sudden cardiac death;

Table 2 of the supplementary data. Genetic variants in *LMNA* gene excluded from the REDLAMINA registry analysis

PROTEIN NP_733821.1)	CHROMOSOME (NC_000001.10)	c.DNA (NM_170707.3)	Variant Type	Exon	Probands/relatives	Pathogenicity	gnomAD MAF% (alleles)	Comments
p.Glu112Val	g.156085044A > T	c.335A > T	Missense	1	1/0	VUS	No	
p.Arg119=	g.156100408C > T	c.357C > T	Missense	2	1/0	Likely benign	0,33% (922/277,140)	
p.Arg220His	g.156104615G > A	c.659G > A	Missense	4	1/3	VUS	< 0.01% (4/246,242)	
p.Arg298Cys	g.156105059C > T	c.892C > T	Missense	5	1/3	VUS	< 0.01% (7/245400)	
Intronic variant	g.156105928G > A	c.1157+16G > A	Non-missense (splicing)	In 6	1/0	Benign	10.79% (29807/276196)	Splicing not affected according bioinformatic predictors
p.Glu361Lys	g.156105836G > A	c.1081G > A	Missense	6	1/0	VUS	Not present	
p.Arg419His	g.156106103G > A	c.1256G > A	Missense	7	1/1	Likely benign	< 0.01% (13/276450)	
p.Arg439Cys	g.156106162C > T	c.1315C > T	Missense	7	1/1	Likely benign	< 0.01% (7/275204)	
p.Arg455His	g.156106211G > A	c.1364G > A	Missense	7	3/5	Likely benign	0% (0/196288)	
p.Arg482Trp	g.156106775C > T	c.1444C > T	Missense	8	1/0	Pathogenic	< 0.01% (1/246108)	Associated with partial familial lipodystrophy; not clear its association with DCM
p.His506Pro	g.156106932A > C	c.1517A > C	Missense	9	1/2	VUS	< 0.01% (8/275106)	
p.Gly523Arg	g.156106982G > A	c.1567G > A	Missense	9	3/3	VUS	0,01% (20/260172)	
p.Thr528Met	g.156106998C > T	c.1583C > T	Missense	9	3/9	Likely pathogenic	< 0.01% (2/210140)	Associated with lipodystrophy; not clear its association with DCM
p.Arg545His	g.156107470G > A	c.1634G > A	Missense	10	1/2	VUS	0,02% (43/186,044)	
p.Ser573Leu	g.156108298C > T	c.1718C > T	Missense	11	2/2	Likely benign	0,01% (37/26,6974)	

p.Arg624His	g.156108451G > A	c.1871G > A	Missense	11	1/0	Likely benign	< 0.01% (6/243,434)	
p.Arg627Cys	g.156108459C > T	c.1879C > T	Missense	11	1/1	Likely benign	< 0.01% (9/274,666)	
p.Arg644Cys	g.156108510C > T	c.1930C > T	Missense	11	3/1	Likely benign	0,12% (326/274,458)	

DCM, dilated cardiomyopathy; MAF, minor allele frequency; GnomAD, Genome Aggregation Database; VUS, variant of uncertain significance.

Table 3 of the supplementary data. Clinical data of the 140 *LMNA* carriers included in the REDLAMINA registry analysis

Family ID	Patient ID	Genetic variant	Index case	Age at first visit (years)	Age at last follow-up (years)	Gender	LVEDD	LVEF	CCD	NSVT	ICD	Appropiate ICD discharge	SCD	Heart trasplant	ESC 2015[3] RF ≥ 2	Wahbi et al. *LMNA* score[4]
I	1	p.0?	Yes	50	70	F	52	20%	3rd AVB, LBBB	No	Yes	Yes	No	Yes	Yes	33.1%
	2	p.0?	No	49	49	M	63	17%	1st AVB	No	No	-	No	Yes	Yes	44.4%
	3	p.0?	No	32	48	F	59	38%	LBBB	Yes	Yes	Yes	No	No	Yes	19.2%
	4	p.0?	No	35	37	F	46	57%	No	No	Yes	No	No	No	No	6.6%
II	5	p.Ser22*	Yes	60	70	F	61	38%	3rd AVB, LBBB	No	Yes	No	No	No	Yes	24.7%
III	6	p.Ser22*	Yes	45	49	M	58	48%	3rd AVB	No	Yes	No	No	No	Yes	32.3%
IV	7	p.Ser22*	Yes	46	46	F	47	53%	No	No	No	-	No	No	No	7.1%
V	8	p.Thr27Ile	Yes	45	60	M	58	50%	1stAVB, LBBB	No	No	-	No	No	No	16.1%
	9	p.Thr27Ile	No	39	55	F	46	60%	No	Yes	No	-	No	No	No	7.6%
VI	10	p.Glu33Asp	Yes	48	51	F	45	50%	1stAVB	No	No	-	No	No	No	10.0%
VII	11	p.Glu65*	Yes	53	63	M	60	41%	3rdAVB	No	No	-	No	No	Yes	36.1%
VIII	12	p.Arg72Leu	Yes	48	64	M	54	25%	2nd AVB, RBBB	No	Yes	No	No	No	Yes	29.4%
IX	13	p.Tyr81Thrfs*15	Yes	45	59	M	48	55%	3rdAVB	Yes	Yes	No	No	No	Yes	52.0%
	14	p.Tyr81Thrfs*15	No	21	23	M	47	60%	No	No	No	-	No	No	Yes	10.2%
	15	p.Tyr81Thrfs*15	No	49	51	M	52	39%	3rd AVB	No	Yes	No	No	No	Yes	37.2%
	16	p.Tyr81Thrfs*15	No	21	23	M	53	60%	No	Yes	No	-	No	No	Yes	20.8%

	17	p.Tyr81Thrfs*15	No	18	23	M	56	46%	No	Yes	Yes	No	No	No	Yes	26.3%
	18	p.Tyr81Thrfs*15	No	23	29	F	46	65%	No	No	No	-	No	No	No	5.7%
	19	p.Tyr81Thrfs*15	No	53	57	F	44	60%	1stAVB	No	No	-	No	No	No	14.1%
	20	p.Tyr81Thrfs*15	No	49	54	F	43	52%	2ndAVB	Yes	Yes	Yes	No	No	Yes	37.2%
	21	p.Tyr81Thrfs*15	No	41	52	M	51	35%	3rd AVB	Yes	Yes	Yes	No	Yes	Yes	66.2%
	22	p.Tyr81Thrfs*15	No	44	46	M	57	54%	1stAVB	No	Yes	No	No	No	Yes	24.8%
	23	p.Tyr81Thrfs*15	No	49	50	F	45	60%	1stAVB	No	Yes	No	No	No	No	14.1%
	24	p.Tyr81Thrfs*15	No	48	49	M	51	55%	3rd AVB	No	Yes	No	No	No	Yes	28.9%
X	25	p.Leu85Val	Yes	52	62	M	52	38%	3rd AVB	No	Yes	No	No	No	Yes	23.7%
XI	26	p.Arg89Cys	Yes	31	39	F	47	47%	LBBB	Yes	No	-	No	Yes	No	9.7%
XII	27	p.Arg119Pro	Yes	34	40	F	39	70%	No	No	Yes	No.	No	No	No	3.0%
XIII	28	p.Glu124Lys	Yes	55	64	M	72	21%	LBBB	Yes	Yes	Yes	No	Yes	Yes	24.7%
	29	p.Glu124Lys	No	60	61	F	60	50%	1stAVB	No	No	-	No	No	No	10.0%
	30	p.Glu124Lys	No	32	33	F	42	69%	No	No	No	-	No	No	No	3.0%
	31	p.Glu124Lys	No	35	36	F	51	65%	No	No	No	-	No	No	No	3.3%
XIV	32	p.Glu124Lys	Yes	46	65	M	57	22%	RBBB	No	No	-	No	Yes	Yes	12.1%
	33	p.Glu124Lys	No	23	24	M	58	61%	No	No	No	-	No	No	No	5.9%
	34	p.Glu124Lys	No	22	40	M	52	53%	No	No	No	-	No	No	No	6.8%
	35	p.Glu124Lys	No	55	56	F	48	61%	No	No	No	-	No	No	No	3.5%

XV	36	p.Glu161Lys	Yes	56	61	M	61	45%	2nd AVB, RBBB	Yes	Yes	Yes	No	No (WL)	Yes	39.8%
	37	p.Glu161Lys	No	25	28	M	50	65%	No	No	No	-	No	No	No	5.4%
XVI	38	p.Arg190Trp	Yes	42	51	M	66	25%	RBBB	No	Yes	No	No	Yes	Yes	11.5%
	39	p.Arg190Trp	No	39	50	M	69	24%	RBBB	No	Yes	No	No	Yes	Yes	11.7%
	40	p.Arg190Trp	No	43	53	M	68	25%	No	Yes	No	-	No	Yes	Yes	23.1%
	41	p.Arg190Trp	No	28	29	F	52	65%	No	No	No	-	No	No	No	3.3%
	42	p.Arg190Trp	No	24	25	F	42	63%	No	No	No	-	No	No	No	3.4%
XVII	43	p.Arg190Trp	Yes	43	45	F	53	40%	No	No	No	-	Yes	No	No	5.3%
	44	p.Arg190Trp	No	23	28	M	54	61%	No	No	No	-	Yes	No	No	5.8%
	45	p.Arg190Trp	No	19	35	M	46	58%	No	No	Yes	No	No	No	No	6.2%
	46	p.Arg190Trp	No	41	45	M	58	32%	RBBB	No	No	-	No	Yes	Yes	10.1%
XVIII	47	p.Arg190Trp	No	20	22	F	48	55%	No	No	No	-	No	No	No	4.0%
	48	p.Arg190Trp	Yes	51	55	M	65	30%	No	Yes	Yes	No	No	Yes	Yes	21.2%
XIX	49	p.Arg190Trp	No	54	62	M	60	38%	No	No	No	-	No	Yes	Yes	9.0%
	50	p.Arg190Trp	Yes	50	59	F	60	38%	No	No	No	-	No	Yes	No	5.5%
	51	p.Arg190Trp	No	37	40	M	60	60%	No	No	No	-	No	No	No	6.0%
XX	52	p.Arg190Trp	No	21	21	F	52	65%	No	No	No	-	No	No	No	3.3%
	53	p.Arg190Trp	Yes	32	35	M	51	56%	No	Yes	No	-	No	No	Yes	13.3%
XXI	54	p.Arg190Gln	Yes	37	49	F	43	18%	No	No	No	-	No	Yes	No	8.0%

XXII	55	p.Arg190Gln	Yes	60	69	F	58	23%	3rd AVB	No	Yes	No	No	No (WL)	No	19.4%
XXIII	56	p.Arg225*	Yes	44	48	F	62	30%	2nd AVB, LBBB	No	Yes	No	No	No	Yes	28.2%
XXIV	57	p.Arg225*	Yes	40	50	F	53	32%	LBBB	Yes	Yes	Yes	No	No	Yes	21.3%
	58	p.Arg225*	No	38	43	F	55	53%	1st AVB, LBBB	No	No	-	No	No	No	16.0%
	59	p.Arg225*	No	42	47	F	46	29%	1st AVB, LBBB	Yes	No	-	Yes	No	Yes	45.0%
	60	p.Arg225*	No	59	64	F	54	51%	No	Yes	Yes	No	Yes	No	Yes	15.3%
XXV	61	p. Phe237Ser	No	27	32	M	50	65%	No	No	No	-	No	No	No	5.4%
	62	p. Phe237Ser	No	48	54	F	47	65%	2nd AVB	Yes	Yes	No	No	No	No	18.6%
	63	p. Phe237Ser	Yes	44	48	M	55	36%	1st AVB, LBBB	Yes	Yes	Yes	No	No (1)	Yes	39.2%
	64	p. Phe237Ser	No	52	57	M	53	65%	RBBB	Yes	Yes	Yes	No	No	Yes	11.3%
	65	p. Phe237Ser	No	35	40	F	42	64%	No	No	No	-	No	No	No	3.3%
	66	p. Phe237Ser	No	36	42	F	50	66%	No	Yes	No	-	No	No	No	6.9%
	67	p. Phe237Ser	No	20	25	M	46	65%	No	No	No	-	No	No	No	5.4%
XXVI	68	p. Ala242Val	Yes	47	53	M	49	18%	LBBB	Yes	Yes	Yes	No	No	Yes	25.9%
	69	p. Ala242Val	No	48	56	F	45	65%	No	No	No	-	No	No	No	3.3%
	70	p. Ala242Val	No	20	21	M	40	56%	No	No	No	-	No	No	No	6.4%
XXVII	71	p.Arg249Leu	Yes	35	42	F	45	33%	3rd AVB	Yes	No	-	No	Yes	Yes	31.8%
XXVIII	72	p.Gln258Pro	Yes	47	61	M	54	41%	3rd AVB, RBBB	Yes	Yes	No	No	No	Yes	42.2%
XXIX	73	p.Asp272Glnfs*7	Yes	53	54	M	51	40%	3rd AVB	Yes	Yes	No	Yes	No	Yes	62.3%

XXX	74	p.Glu291Lys	No	28	30	F	56	47%	LBBB	No	Yes	No	No	No	No	4.6%
	75	p.Glu291Lys	No	35	40	M	55	43%	1stAVB, LBBB	No	Yes	No	No	No	Yes	18.3%
	76	p.Glu291Lys	Yes	36	39	F	56	51%	1stAVB, LBBB	No	Yes	No	No	No	No	9.8%
XXXI	77	p.Arg321*	Yes	40	59	M	68	25%	3rd AVB, LBBB	No	Yes	No	No	Yes	Yes	45.7%
	78	p.Arg321*	No	21	28	F	45	77%	No	Yes	No	-	No	No	Yes	9.5%
	79	p.Arg321*	No	21	28	F	48	64%	No	No	No	-	No	No	No	5.8%
	80	p.Arg321*	No	40	65	F	62	38%	3rd AVB, RBBB	No	No	-	No	Yes	Yes	24.7%
XXXII	81	p.Arg321*	Yes	46	51	F	52	74%	1stAVB	No	No	-	No	No	No	10.9%
	82	p.Arg321*	No	46	61	F	54	35%	3rdAVB, LBBB	Yes	Yes	No	No	No	Yes	47.6%
	83	p.Arg321*	No	29	36	M	47	61%	1stAVB	Yes	Yes	No	No	No	Yes	41.5%
XXXIII	84	p.Arg331Gln	Yes	46	48	M	51	60%	No	No	No	-	No	No	No	6.0%
XXXIV	85	p.Arg335Trp	Yes	21	24	F	63	15%	1stAVB, LBBB	Yes	Yes	Yes	No	No	Yes	36.1%
	86	p.Arg335Trp	No	46	47	F	49	64%	1stAVB	No	No	-	No	No	No	7.7%
XXXV	87	p.Arg335Glyfs*145	Yes	48	50	M	53	64%	2nd AVB	No	Yes	No	No	No	Yes	24.9%
XXXVI	88	p.Arg349Leu	Yes	36	59	F	61	10%	RBBB	No	No	-	No	Yes	No	9.3%
	89	p.Arg349Leu	No	18	38	F	54	40%	No	No	No	-	No	Yes	No	5.3%
	90	p.Arg349Leu	No	18	38	F	59	21%	No	No	No	-	No	Yes	No	7.6%
XXXVII	91	p.Arg349Leu	Yes	40	48	M	46	40%	RBBB	No	Yes	No	No	Yes	Yes	8.7%
XXXVIII	92	p.Glu372Asp	Yes	46	65	M	45	47%	3rd AVB, LBBB	No	No	-	No	Yes	No	20.3%

XXXIX	93	p.Arg377Cys	Yes	43	45	M	61	40%	No	Yes	Yes	No	No	No	Yes	17.8%
XL	94	p.Arg377Cys	Yes	41	55	M	57	45%	1st AVB	Yes	Yes	Yes	No	Yes	Yes	34.1%
	95	p.Arg377Cys	No	36	49	M	50	54%	1st AVB	Yes	Yes	Yes	No	Yes	Yes	29.6%
	96	p.Arg377Cys	No	48	54	M	48	60%	1st AVB	No	No	-	No	No	No	13.5%
	97	p.Arg377Cys	No	48	51	F	49	64%	1st AVB	No	No	-	No	No	No	7.7%
	98	p.Arg377Cys	No	65	79	F	45	65%	3rd AVB, LBBB	No	No	-	No	No	Yes	9.1%
	99	p.Arg377Cys	No	20	26	F	44	76%	No	No	No	-	No	No	No	2.7%
XLI	100	p.Arg377Cys	Yes	34	36	M	63	19%	No	Yes	Yes	Yes	No	Yes	Yes	25.5%
	101	p.Arg377Cys	No	57	59	F	45	65%	No	No	No	No	No	No	No	3.3%
XLII	102	p.Arg377His	Yes	50	53	F	52	31%	3rd AVB	No	Yes	No	No	Yes	No	16.9%
	103	p.Arg377His	No	54	55	M	53	27%	LBBB	No	No	No	No	Yes	Yes	11.0%
XLIII	104	p.Arg377His	Yes	17	21	F	48	62%	No	No	No	No	No	No	No	3.5%
	105	p.Arg377His	No	46	48	M	50	64%	1st AVB	Yes	No	No	No	No	Yes	25.0%
	106	p.Arg377His	No	50	55	M	58	32%	3rd AVB, LBBB	No	Yes	No	No	No	Yes	26.2%
XLIV	107	p.Arg377His	Yes	44	56	F	49	55%	1st AVB, LBBB	No	Yes	No	No	No	Yes	9.1%
XLV	108	p.Arg377His	Yes	47	49	F	47	43%	2nd AVB, LBBB	Yes	Yes	No	No	No	Yes	27.0%
XLVI	109	p.Gly382=	Yes	63	68	M	57	27%	3rd AVB	Yes	Yes	No	No	No	Yes	71.8%
	110	p.Gly382=	No	53	58	M	54	46%	LBBB	Yes	Yes	No	No	No	Yes	26.3%
XLVII	111	p.Gln410*	Yes	35	45	F	49	76%	No	No	Yes	No	No	No	No	4.6%

	112	p.Gln410*	No	17	20	M	50	65%	No	No	No	-	No	No	Yes	9.3%
XLVIII	113	p.Ser437Hisfs*2	Yes	54	61	M	60	24%	LBBB	Yes	Yes	Yes	No	No	Yes	37.5%
	114	p.Ser437Hisfs*2	No	39	42	F	50	58%	LBBB	No	No	-	No	No	No	6.5%
	115	p.Ser437Hisfs*2	No	40	45	F	42	73%	No	No	No	-	No	No	No	4.9%
	116	p.Ser437Hisfs*2	No	53	56	M	45	42%	1stAVB	No	No	-	No	No	Yes	30.3%
	117	p.Ser437Hisfs*2	No	47	54	F	47	58%	1stAVB	No	No	-	No	No	No	14.6%
	118	p.Ser437Hisfs*2	No	46	50	M	60	66%	No	Yes	Yes	No	No	No	Yes	18.7%
	119	p.Ser437Hisfs*2	No	43	53	M	58	39%	1stAVB	No	Yes	No	No	No	Yes	31.8%
	120	p.Ser437Hisfs*2	No	18	19	F	47	64%	No	No	No	-	No	No	No	5.8%
	121	p.Ser437Hisfs*2	No	30	31	M	40	67%	No	No	No	-	No	No	Yes	9.0%
	122	p.Ser437Hisfs*2	No	19	20	M	44	67%	No	No	No	-	No	No	Yes	9.0%
	123	p.Ser437Hisfs*2	No	25	26	F	33	65%	No	No	No	-	No	No	No	5.7%
	124	p.Ser437Hisfs*2	No	16	17	F	39	75%	No	No	No	-	No	No	No	4.7%
XLIX	125	p.Glu444*	Yes	45	49	M	63	49%	3rd AVB, RBBB	Yes	Yes	No	No	No	Yes	56.2%
	126	p.Glu444*	No	45	45	M	52	59%	No	No	No	-	No	No	Yes	12.3%
L	127	p.Trp514*	Yes	35	36	M	52	45%	No	No	Yes	No	No	No	Yes	13.5%
	128	p.Trp514*	No	52	56	F	45	53%	No	No	No	-	No	No	No	7.1%
	129	p.Trp514*	No	47	48	M	61	34%	3rd AVB	No	No	-	Yes	No	Yes	40.1%
LI	130	p.Trp514*	No	23	23	M	63	55%	No	No	No	-	No	No	Yes	11.2%

	131	p.Trp514*	Yes	39	46	M	60	39%	3rd AVB, RBBB	Yes	No	-	Yes	No	Yes	63.3%
LII	132	p.Arg541Ser	Yes	20	25	F	61	39%	LBBB	Yes	Yes	Yes	No	No	Yes	11.2%
LIII	133	c.1158-1G > A	Yes	39	48	M	60	34%	1stAVB	Yes	Yes	Yes	No	Yes	Yes	59.7%
	134	c.1158-1G > A	No	36	42	M	60	33%	2nd AVB	Yes	Yes	No	No	Yes	Yes	67.6%
	135	c.1158-1G > A	No	62	71	F	50	65%	No	No	No	-	No	No	No	5.7%
	136	c.1158-1G > A	No	33	39	F	48	64%	No	No	No	-	No	No	No	5.8%
	137	c.1158-1G > A	No	40	45	F	46	70%	1stAVB	No	No	-	No	No	No	11.7%
	138#	c.1158-1G > A	Yes	33	35	F	48	61%	No	No	Yes	No	No	No	No	6.1%
	139#	c.1158-1G > A	No	39	48	M	55	70%	3rd AVB	No	Yes	No	No	No	Yes	22.5%
	140#	c.1158-1G > A	No	26	27	F	45	70%	No	No	No	-	No	No	No	5.2%

#Previously considered a different family; AVB: Atrio-ventricular block; CCD: cardiac conduction disease; ICD: implantable cardioverter defibrillator; ID: identification; LBBB: left bundle branch block; LVEDD: left ventricle end diastolic diameter; LVEF: left ventricular ejection fraction; NSVT: non-sustained ventricular tachycardia; RBBB: right bandle branch block; RF: Risk Factors; SCD: sudden cardiac death; WL: waiting list for HTx.; (1) contraindication for HTx.

Table 4 of the supplementary data. Genetic variants included in the articles by Van Rijensen et al.[5,6] current frequency in public databases, and updated pathogenicity.

Genetic Variant (Van Rijensen et al.[5,6])	**Patients**	**gnomAD**	**ClinVar**	**Pathogenicity (ACMG based)**
p.Arg25Cys	1 index, 1 relative	0	Not provided	+?
p.Arg28Trp	1	0	Pathogenic	+++
p.Tyr45Cys	1 index	0	Uncertain significance	+?
p.Glu84Lys	1 index, 2 relatives	0	Uncertain significance	+?
p.Arg89Leu	1 index, 4 relatives	0	Pathogenic	+?
p.Lys97Glu	1 index, 2 relatives	0	Not provided	+?
p.Lys117Arg	2 index, 1 relative	0.01% (16/260,306)	Conflicting interpretations of pathogenicity	?
p.Glu161Lys	7 index, 11 relatives	0	Pathogenic	+++
p.Leu183Pro	1 index	0	Not provided	+?
p.Arg189Trp	5 index, 8 relatives	< 0.01% (4/277,176)	Uncertain significance	++
p.Arg190Gln	1 index	0	Conflicting interpretation of pathogenicity	+++
p.Arg190Trp	5 index, 4 relatives	0	Pathogenic	+++
p.Glu203Val	1 index	0	Not provided	+?
p.Leu215Val	1 index	0	Uncertain significance	+?
p.Arg216Cys	1 index	< 0.01% (2/277,170)	Conflicting interpretation of pathogenicity	+?
p.Lys219Thr	2 idex, 2 relatives	0	Uncertain significance	+++

p.Lys260Asn	2 index, 1 relative	0	Not provided	+?
p.Tyr267Cys	1 index	0	Not provided	+?
p.Glu317Lys	5 index, 3 relatives	< 0.01% (1/30,946)	Pathogenic / Likely pathogenic	+++
p.Arg331Gln	1 index	< 0.01% (3/245,554)	Conflicting interpretations of pathogenicity	++
p.Arg335Trp	1 index	0	Pathogenic, Likely pathogenic	+?
p.Glu347Lys	2 index	0	Likely pathogenic	+?
p.Arg349Trp	1 index	0	Pathogenic	+++
p.Glu358Lys	1 index	0	Pathogenic	+?
p.Arg377Cys	1 index	0	Pathogenic	+++
p.Arg377His	3 index, 9 relatives	0	Pathogenic	+++
p.Arg377Leu	2 index	0	Uncertain significance	+?
p.Arg397Cys	1 index, 2 relatives	< 0.01% (7/274,546)	Uncertain significance	?
p.Arg471His	1 index, 6 relatives	0	Conflicting interpretation of pathogenicity	++
p.Trp498Arg	1 index, 1 relative	0	Not provided	+?
p.Arg527Pro	1 index, 5 relatives	0	Pathogenic	+?
p.Arg541Cys	1 index, 2 relatives	0	Pathogenic	++
p.Arg541His	1 index	< 0.01% (3/152,824)	Pathogenic, Likely pathogenic	+?
p.Arg545His	1 index	0.02% (43/186,044)	Conflicting interpretation of pathogenicity	?
p.Ser573Leu	2 index, 10 relatives	0.01 % (37/266,974)	Conflicting interpretations of pathogenicity	-?
p.Gly638Arg	1 index, 2 relatives	0.02% (50/274,922)	Conflicting interpretation of pathogenicity	-?
p.Arg644Cys	5 index, 4 relatives	0.12 % (326/274,458)	Conflicting interpretation of pathogenicity	-?

ACMG, American College of Medical Genetics and Genomics; ClinVar, public archive of relationships between sequence variation and human phenotype; GnomAD, Genome Aggregation Database; (+++): Pathogenic or disease-causing; (++), Very likely to be pathogenic or disease-causing; (+?), Likely to be pathogenic or disease-causing; (?), Unknown clinical significance; (-?), Unlikely to be pathogenic or disease-causing; (--), Non-pathogenic (not disease-causing)

Table 5 of the supplementary data. Clinical characteristics of the p.Arg190Trp *LMNA* carriers described in the literature[7-25]

Reference	Proband	Carrier	Clinical diagnosis	Sex	Age DX	Age FU	NYHA	Ventricular arrhythmias	LV Dilatation (LVEDD)	Syst. dysf. (LVEF%)	Event (Age at event)
1	Proband	Heteroz.	DCM	Male	43	43	+ (IV)	n/a	Yes	Yes	Cardiac transplant (=43)
	Relative	Heteroz.	DCM	Male	40	40	n/a	n/a	Yes (61)	Yes (24)	
	Relative	Heteroz.	DCM	Male	37	37	n/a	n/a	Yes (66)	Yes (34)	
	Relative	Heteroz.	n/a	n/a	8	8	n/a	n/a	n/a	n/a	
	Relative	Heteroz.	n/a	Female	16	16	n/a	n/a	n/a	n/a	
	Relative	Heteroz.	n/a	Female	21	21	n/a	n/a	n/a	n/a	
	Relative	Heteroz.	n/a	Male	26	26	n/a	n/a	n/a	n/a	
	Relative	Heteroz.	DCM	Male	38	38	+ (IV)	n/a	Yes	Yes	Cardiac transplant (=38)
	Relative	Heteroz.	DCM	Female	40	40	+ (IV)	n/a	Yes	Yes	Cardiac transplant (=40)
	Relative	Heteroz.	DCM	Male	43	43	+ (IV)	n/a	Yes	Yes	Cardiac transplant (=43)
	Relative	Not genotyped	DCM?	Male	n/a	n/a	n/a	n/a	n/a	n/a	Death (unknown) (> 40)
	Relative	Not genotyped	DCM?	Male	n/a	n/a	n/a	n/a	n/a	n/a	Death (unknown) (> 40)
	Relative	Not genotyped	DCM?	Male	n/a	n/a	n/a	n/a	n/a	n/a	Death (unknown) (> 40)
	Relative	Not genotyped	DCM?	Male	n/a	n/a	n/a	n/a	n/a	n/a	Death (unknown) (> 40)
1	Proband	Heteroz.	DCM	Female	37	37	n/a	n/a	Yes (59)	Yes (27)	
	Relative	Heteroz.	DCM	Male	36	36	+ (IV)	n/a	n/a	n/a	Cardiac transplant (=36)
2, 3	Proband	Heteroz.	DCM	Female	44	47	+ (II)	n/a	Yes (59)	Yes (50)	Sudden death (=47)
	Relative	Heteroz.	LVNC	Male	21	34	- (I)	No	No (53)	No (61)	
	Relative	Heteroz.	Unaffected	Male	9	10	- (I)	n/a	No (37)	No (55)	
	Relative	Heteroz.	DCM	Male	40	45	+ (III)	No	Yes (55)	Yes (27)	Cardiac transplant (=46)
	Relative	Heteroz.	DCM	Male	24	27	- (I)	No	Yes (60)	Yes (51)	Sudden death (=28)
	Relative	Not genotyped	SCD	Female	n/a	40	n/a	n/a	n/a	n/a	Sudden death (=40)
	Relative	Not genotyped	n/a	Female	n/a	71	n/a	n/a	n/a	n/a	Heart failure death (=71)
	Relative	Not genotyped	n/a	Female	n/a	n/a	n/a	n/a	n/a	n/a	Death (unknown) (=44)
	Relative	Not genotyped	DCM	Male	n/a	< 50	n/a	n/a	n/a	n/a	Heart failure death? (< 50)
4, 5	Proband	Heteroz.	DCM + CCD	Male	41	42	n/a	n/a	Yes (60)	Yes (28)	

	Relative	Heteroz.	Unaffected	Female	39	39	n/a	PVC	No (44)	No (60)	
	Relative	Heteroz.	Unaffected	Female	12	12	n/a	n/a	No (42)	No (65)	
	Relative	Heteroz.	Unaffected	Male	n/a	13	n/a	n/a	No (42)	No (65)	
	Relative	Heteroz.	Unaffected	Male	7	7	n/a	n/a	No (38)	No (55)	
	Relative	Heteroz.	DCM + CCD	Female	n/a	47	n/a	n/a	Yes	n/a	Death (unknown) (=47)
6	Proband	Heteroz.	DCM	n/a	n/a	n/a	n/a	n/a	Yes	Yes	
	Relative	Heteroz.	Unaffected	n/a	n/a	n/a	- (I)	No	No	No	
	Relative	Heteroz.	Unaffected	n/a	n/a	n/a	- (I)	No	No	No	
	Relative	Heteroz.	Unaffected	n/a	n/a	n/a	- (I)	No	No	No	
	Relative	Heteroz.	DCM	n/a	n/a	n/a	n/a	n/a	Yes	Yes	
	Relative	Heteroz.	DCM	n/a	n/a	n/a	n/a	n/a	Yes	Yes	
7, 8	Proband	Heteroz.	DCM	Male	< 58	58	n/a	No	Yes (64)	Yes (11)	Cardiac transplant
	Relative	Heteroz.	Unaffected (?)	Male	n/a	26	n/a	No	No? (57)	No (56)	
	Relative	Heteroz.	Unaffected	Female	34	34	n/a	No	No (50)	Yes (52)	
	Relative	Heteroz.	Unaffected	Female	n/a	62	n/a	No	No (39)	No (66)	
	Relative	Heteroz.	DCM	Male	< 56	56	n/a	No	Yes (59)	Yes (41)	
	Relative	Heteroz.	DCM	Male	< 40	40	n/a	n/a	Yes (61)	Yes (20)	
	Relative	Obligated	DCM?	Female	n/a	n/a	n/a	n/a	n/a	n/a	Death of unknown cause
9	Proband	Heteroz.	DCM	n/a	35	41	+ (?)	n/a	Yes	Yes	Cardiac transplant (=41)
9	Proband	Heteroz.	DCM	Male	30	35	+ (?)	n/a	n/a	n/a	Cardiac transplant (=35)
	Relative	Heteroz.	DCM	Female	43	48	+ (?)	n/a	Yes	Yes	Cardiac transplant (=48)
10	Proband	Heteroz.	DCM + CCD	n/a	n/a	48	+ (?)	n/a	Yes (64)	Yes	Heart failure death (=48)
	Relative	Not genotyped	DCM	n/a	n/a	49	+ (?)	n/a	Yes	Yes	Heart failure death (=49)
	Relative	Not genotyped	DCM	n/a	n/a	50	+ (?)	n/a	Yes	Yes	Heart failure death (=50)
	Relative	Not genotyped	DCM	n/a	n/a	51	+ (?)	n/a	Yes	Yes	Heart failure death (=51)
	Relative	Not genotyped	DCM	n/a	n/a	52	+ (?)	n/a	Yes	Yes	Heart failure death (=52)
	Relative	Not genotyped	DCM	n/a	n/a	53	+ (?)	n/a	Yes	Yes	Heart failure death (=53)
11	Proband	Heteroz.	DCM	Male	n/a	n/a	n/a	n/a	n/a	n/a	Death (unknown)
	Relative	Heteroz.	n/a	Female	n/a	n/a	n/a	n/a	n/a	n/a	
	Relative	Heteroz.	DCM	Female	n/a	n/a	n/a	n/a	n/a	n/a	

	Relative	Heteroz.	DCM	Female	n/a	n/a	n/a	n/a	n/a	n/a	
	Relative	Heteroz.	DCM	Female	n/a	n/a	n/a	n/a	n/a	n/a	
	Relative	Heteroz.	Unaffected	Female	n/a	n/a	n/a	n/a	n/a	n/a	
	Relative	Heteroz.	Unaffected	Female	n/a	n/a	n/a	n/a	n/a	n/a	
	Relative	Heteroz.	n/a	Male	n/a	n/a	n/a	n/a	n/a	n/a	
	Relative	Heteroz.	n/a	Male	n/a	n/a	n/a	n/a	n/a	n/a	
	Relative	Heteroz.	DCM	Male	n/a	n/a	n/a	n/a	n/a	n/a	
	Relative	Heteroz.	DCM	Male	n/a	n/a	n/a	n/a	n/a	n/a	
	Relative	Heteroz.	Unaffected	Male	n/a	n/a	n/a	n/a	n/a	n/a	
	Relative	Heteroz.	Unaffected	Male	n/a	n/a	n/a	n/a	n/a	n/a	
12	Proband	Heteroz.	DCM	Male	31	n/a	+ (II)	n/a	n/a	n/a	
13	Proband	Heteroz.	ACM	Female	47	47	n/a	SVT	Yes	Yes	Sudden death (=54)
	Relative	Heteroz.	n/a	Male	25	25	n/a	NSVT	No	No	
	Relative	Not genotyped	n/a	Male	n/a	56	n/a	n/a	n/a	n/a	Sudden death (=56)
5	Proband	Heteroz.	DCM?	n/a	n/a	n/a	n/a	n/a	n/a	n/a	
5	Proband	Heteroz.	DCM?	n/a	n/a	n/a	n/a	n/a	n/a	n/a	
	Relative	Heteroz.	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	
5	Proband	Heteroz.	DCM?	n/a	n/a	n/a	n/a	n/a	n/a	n/a	
	Relative	Heteroz.	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	
5	Proband	Heteroz.	DCM?	n/a	n/a	n/a	n/a	n/a	n/a	n/a	
	Relative	Heteroz.	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	
14	Proband	Heteroz.	DCM	n/a	n/a	n/a	n/a	n/a	n/a	n/a	
15	Proband	Heteroz.	DCM	Female	n/a	n/a	n/a	n/a	n/a	n/a	
15	Proband	Heteroz.	DCM	Male	n/a	n/a	+ (III)	n/a	n/a	n/a	
	Relative	Heteroz.	DCM	Male	n/a	n/a	- (I)	n/a	n/a	n/a	
	Relative	Heteroz.	Unaffected	Male	n/a	n/a	n/a	n/a	n/a	n/a	
	Relative	Heteroz.	DCM	Male	n/a	n/a	+ (IV)	n/a	n/a	n/a	Heart failure death
16	Proband	Heteroz.	DCM	n/a	n/a	n/a	n/a	n/a	n/a	n/a	
17	Proband	Heteroz.	DCM	Male	< 43	43	n/a	n/a	Yes (78)	Yes (21)	
	Relative	Heteroz.	DCM	Female	n/a	n/a	n/a	n/a	n/a	n/a	
	Relative	Heteroz.	Unaffected	Female	n/a	n/a	n/a	n/a	n/a	n/a	

	Relative	Not genotyped	n/a	Male	n/a	n/a	n/a	n/a	n/a	n/a	Sudden death
18	Proband	Heteroz.	DCM	Female	47	64	n/a	n/a	Yes	n/a	Cardiac transplant (=51)
	Relative	Heteroz.	Unaffected	Female	n/a	n/a	n/a	n/a	n/a	n/a	
	Relative	Heteroz.	Unaffected	Female	n/a	n/a	n/a	n/a	n/a	n/a	
	Relative	Heteroz.	Unaffected	Female	n/a	n/a	n/a	n/a	n/a	n/a	
	Relative	Heteroz.	Unaffected	Male	n/a	n/a	n/a	n/a	n/a	n/a	
	Relative	Heteroz.	DCM	Male	33	> 42	n/a	NSVT	Yes	n/a	Cardiac transplant (=42)
	Relative	Heteroz.	DCM	Female	36	> 45	n/a	NSVT	Yes	Yes (42)	Cardiac transplant (=45)
19	Proband	Heteroz.	DCM	Male	39	43	+ (III)	n/a	Yes	Yes (35)	
	Relative	Heteroz.	DCM	Female	48	n/a	+ (?)	n/a	Yes (55)	Yes (35)	
	Relative	Heteroz.	DCM	Female	n/a	n/a	n/a	n/a	n/a	n/a	
	Relative	Heteroz.	DCM	Female	n/a	n/a	n/a	n/a	n/a	n/a	
	Relative	Heteroz.	DCM	Male	n/a	n/a	n/a	n/a	n/a	n/a	
	Relative	Not genotyped	DCM	Male	n/a	n/a	n/a	n/a	n/a	n/a	Sudden death

?, unknown; CCD, cardiac conduction disease; DCM, dilated cardiomyopathy; DX, diagnosis; FU, follow-up; Heteroz., heterozygosis; LVEDD, left ventricle end-diastolic diameter; LV, left ventricle; LVEF, ejection fraction; n/a, not available; NSVT, non-sustained ventricular tachycardia; NYHA, New York Heart Association.

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