Table 1. Functional groups of mutated proteins

Functional group of mutated proteins	Mutated protein†
Desmin filament network	2 desmin, 1 alpha-B-crystallin
Calcium handling	8 phospholamban
Desmosomal	2 plakophilin-2, 1 desmoplakin
Nuclear envelope	4 lamin A/C
Sarcomeric	3 titin, 2 myosin binding protein C3,1 myosin heavy chain 7, 1 troponin T2, 1 Troponin I3

† The exact gene and protein mutations are shown in supplementary file 2.

Table 2. Patient characteristics per mutation group

	Desminopathy n=3	Phospholamban n=8	Desmosomal n=3	Lamin A/C n=4	Sarcomeric n=8	Total n=26
Age at diagnosis (yrs±SD)	40±2	36±13	34±7	48±8	27±16	36±14
Sex (m/f)	2/1	3/5	2/1	3/1	5/3	15/11
Initial clinical diagnosis	2 DCM 1 ACM	6 DCM 2 ACM	3 ACM	4 DCM	5 DCM 3 HCM	17 DCM 6 ACM 3 HCM
LVAD	2/3 (67%)	5 /8(63%)	0/3 (0%)	3/4(75%)	3 (30%)	13 (50%)
ICD/PM/CRT-D	3 /3(100%)	7/8 (88%)	3/3 (100%)	3/4 (75%)	6 (75%)	22 (85%)

DCM = dilated cardiomyopathy, HCM = hypertrophic cardiomyopathy, ACM = arrhythmogenic cardiomyopathy, LVAD = left ventricular assist device, ICD = Implantable Cardioverter Defibrillator, PM = pacemaker, CRT-D = Cardiac Resynchronization Therapy Device.

Table 3. Distribution pattern of fibrosis and adipose tissue in different mutation groups

Mutation group	**Left ventricle**	**Right ventricle**
Desminopathies	- Outer compact myocardium most affected, location varying per patient - Interstitial fibrosis, some fibrofatty replacement in 2/3 patients	- Minor to moderate fibrosis - Fibrofatty replacement in 1/3 patients
Desmosomal	- Outer compact myocardium posterolateral wall most affected - Fibrofatty replacement and interstitial fibrosis†	Fibrofatty replacement ‡
Phospholamban	- Outer compact myocardium of posterolateral wall most affected - Interstitial fibrosis and fibrofatty replacement †§	Fibrofatty replacement‡
Lamin A/C	- Predominantly circumferential trabecular and midmyocardial (inner compact myocardium) ¶ - Interstitial fibrosis, no adipose tissue	Minor to moderate fibrosis without increased fatty infiltration
Sarcomeric 1 *Titin* *Troponin T2* *Troponin I3* *MHC 7*	- Predominantly circumferential trabecular and midmyocardial (inner compact myocardium) - Interstitial fibrosis, no adipose tissue	Minor to moderate fibrosis without increased fatty infiltration
Sarcomeric 2 *MYBPC3*	- Septum, anterior and posterior wall most affected - Replacement fibrosis and interstitial fibrosis	Minor to moderate fibrosis anterior and posterior wall

MHC 7 = myosin heavy chain 7; MBPC3 = myosin binding protein C3. The schemes of the subgroups in the sarcomeric group are shown in supplementary figure 5.

† LV fibrosis was more pronounced in the PLN group (27% [22-39]) than in the desmosomal group (15% [14-17], p=0.024).

‡ A trend towards more adipose tissue in the RV in desmosomal group (46% [43-53]) compared to PLN group (28% [26-39], p=0.07) was found.

§ No difference in fibrosis and fatty replacement between patients that initially presented with ACM or DCM.

¶ In 1 patient also fibrosis in the outer part of the LV.