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	Phospholamban	Desmosomal	Lamin A/C	Sarcomeric	Total
	n=3	n=8	n=3	n=4	n=8	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	- Predominantly circumferential trabecular and midmyocardial (inner	Minor to moderate fibrosis without increased fatty infiltration
Titin Troponin T2 Troponin I3 MHC 7	compact myocardium) - Interstitial fibrosis, no adipose tissue	
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.