Supplementary methods.

Definitions of DCM according to etiology

Since 2005, we analyzed patients with different DCM etiology. All patients with DCM enrolled from 2005 to 2015 were classified according to the cause of the disease defined as:

Genetically determined DCM: patients with DCM and genotype positive for pathogenic or likely pathogenic variants at genetic analysis, according to American College of Medical Genetic and Genomic (ACMG) 2015 guidelines criteria [1]. The classification of variant considered data from international databases (ClinVar) and familial segregation studies.

Post-myocarditis DCM: patients with persistent LV dysfunction (i.e. LVEF <50%) 1 year after the diagnosis and subsequent therapy of active lymphocytic myocarditis at EMB according to Dallas Criteria and immunohistochemistry analysis [2,3].

Alcohol-induced DCM: patients with DCM due to excessive alcohol intake (i.e. >80 g/day for at least 5 years) [4].

Chemotherapy-induced DCM: patients underwent chemotherapy experiencing worsening LVEF >10% falling below 55% or > 5% with signs or symptoms of HF.

Tachycardia-induced DCM: patients with persistent high-rate supraventricular arrhythmias documented in the 6 months before enrolment and persistent left ventricular systolic dysfunction 6 months after the resolution of the arrhythmia.

Idiopathic DCM: patients with DCM after exclusion of other possible causes (i.e. hypertension, ischemia, valvular disease, inflammation, toxics) including a negative genetic testing.

Genetic testing

Genetic testing was done using NextGeneration DNA sequencing of multi-gene DCM panels. For this study, the DCM genes analyzed were: *ACTC1, BAG3, CTTNA3, DES, DMD, DSC2, DSG2, DSP, FLNC, JUP, LAMA4, LDB3, LMNA, MYH7, MYPN, NEBL, NEXN, OBSL1, PKP2, RBM20,*

RYR2, SCN5A, TMEM43, TNNT2, and TTN. All variants were validated with bidirectional Sanger sequencing. Gene variants were classified as pathogenic (P) or likely pathogenic (LP) using accepted algorithms including the American College of Medical Genetics and Genomics standards. (ACMGG) [1]. In order to maintain a conservative approach, all variants of uncertain significance (VUS) were excluded from the present analysis and pathogenic variants were clusterized as previously reported [5].

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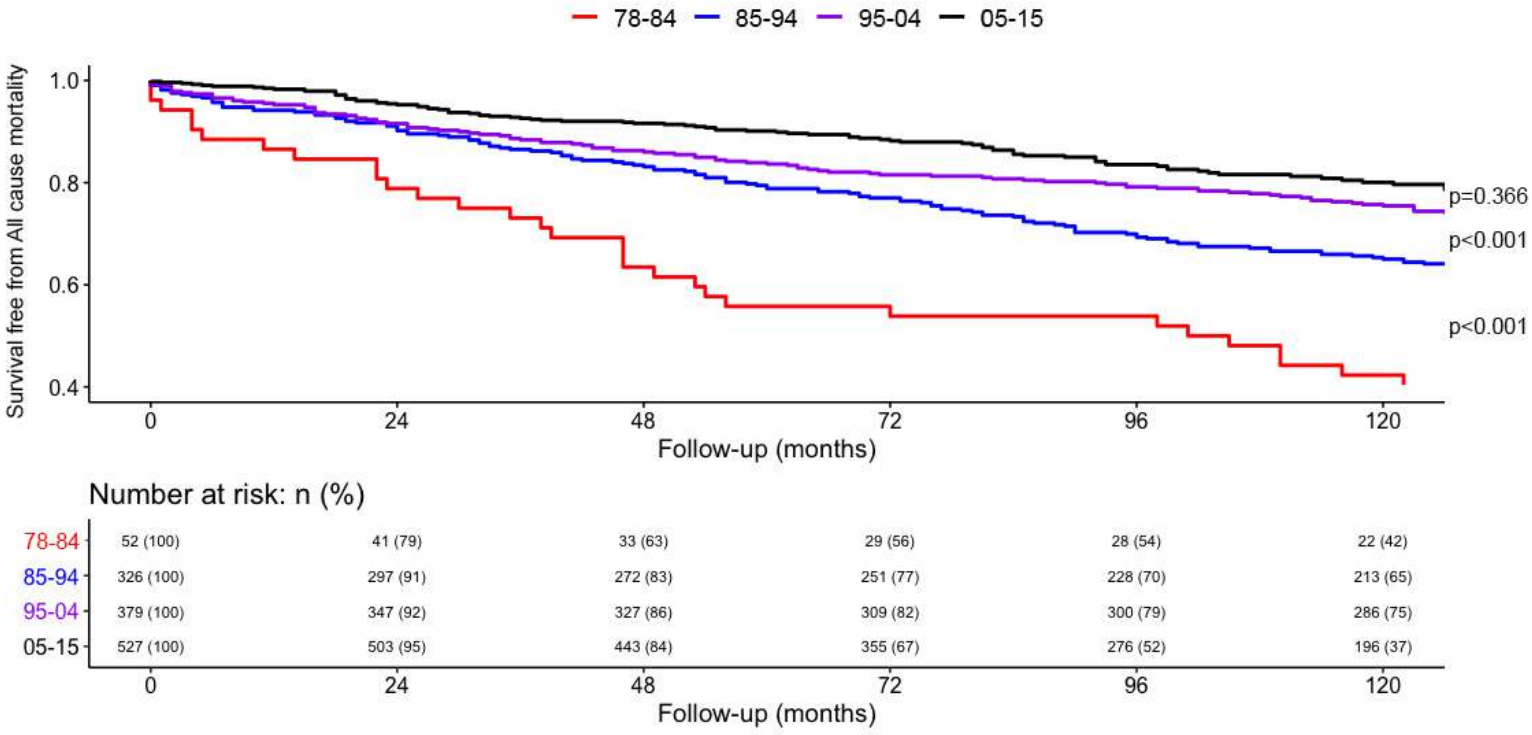
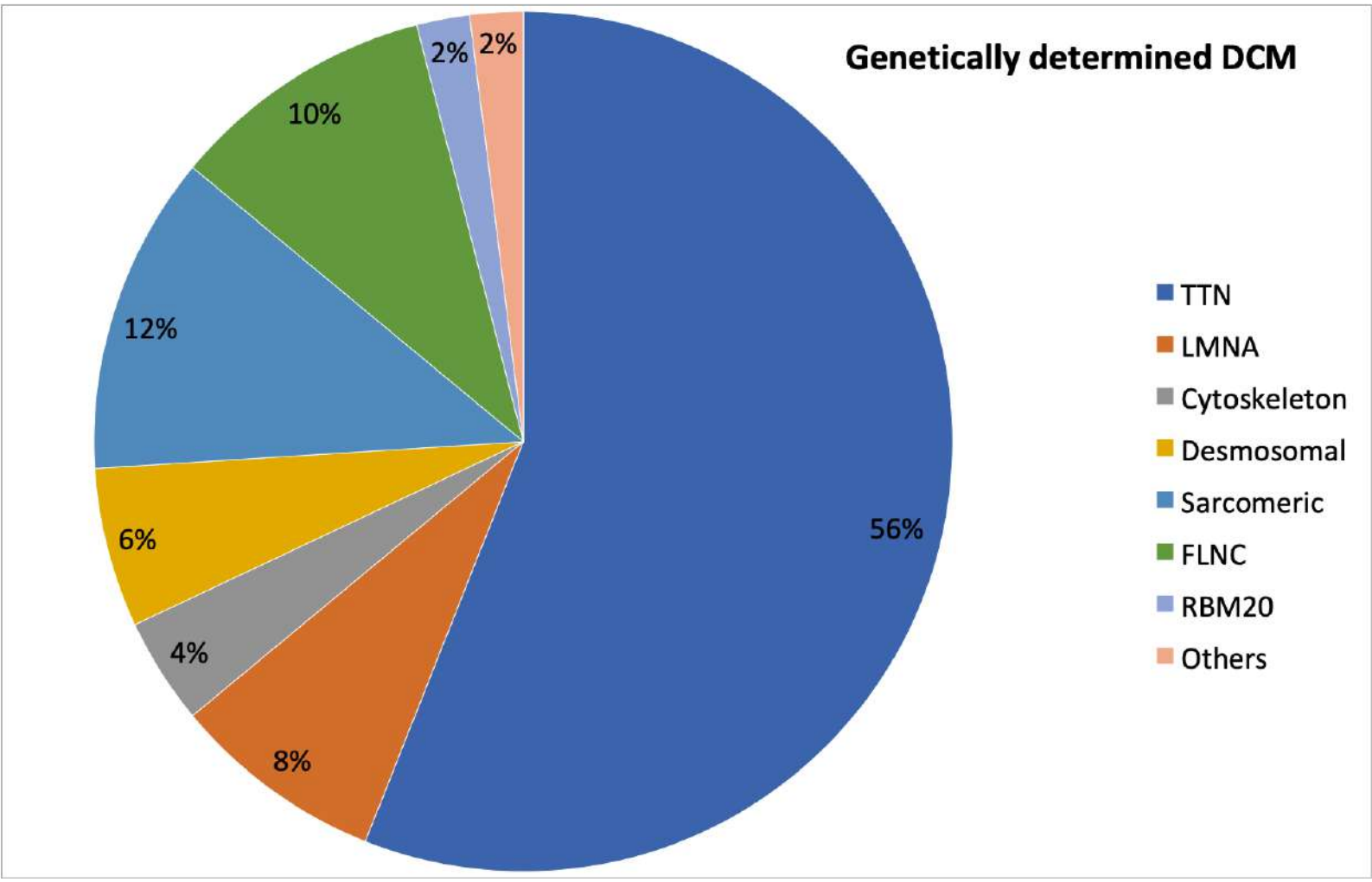


Number at risk: n (%)

78-84	52 (100)	41 (79)	33 (63)	29 (56)	28 (54)	22 (42)
85-94	326 (100)	297 (91)	272 (83)	251 (77)	228 (70)	213 (65)
95-04	379 (100)	347 (92)	327 (86)	309 (82)	300 (79)	286 (75)
05-15	527 (100)	503 (95)	443 (84)	355 (67)	276 (52)	196 (37)

0 24 48 72 96 120

Follow-up (months)


Genetically determined DCM
56%
8%
4%
6%
12%
10%
2%
2%
TTN
LMNA
Cytoskeleton
Desmosomal
Sarcomeric
FLNC
RBM20
Others