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Lamin and the heart.

Captur G[1,2,3], Arbustini E[4], Bonne G[5], Syrris P[6], Mills K[1,7], Wahbi K[5,8,9], Mohiddin SA[10], McKenna WJ[6], Pettit S[11], Ho CY[12], Muchir A[5], Gissen P[7,13,14], Elliott PM[2,3,6], Moon JC[2,3,6].

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Abstract

Lamins A and C are intermediate filament nuclear envelope proteins encoded by the *LMNA* gene. Mutations in *LMNA* cause autosomal dominant severe heart disease, accounting for 10% of dilated cardiomyopathy (DCM). Characterised by progressive conduction system disease, arrhythmia and systolic impairment, lamin A/C heart disease is more malignant than other common DCMs due to high event rates even when the left ventricular impairment is mild. It has several phenotypic mimics, but overall it is likely to be an under-recognised cause of DCM. In certain clinical scenarios, particularly familial DCM with early conduction disease, the pretest probability of finding an *LMNA* mutation may be quite high.Recognising lamin A/C heart disease is important because implantable cardioverter defibrillators need to be implanted early. Promising oral drug therapies are within reach thanks to research into the mitogen-activated protein kinase (MAPK) and affiliated pathways. Personalised heart failure therapy may soon become feasible for *LMNA*, alongside personalised risk stratification, as variant-related differences in phenotype severity and clinical course are being steadily elucidated.Genotyping and family screening are clinically important both to confirm and to exclude *LMNA* mutations, but it is the three-pronged integration of such genetic information with functional data from in vivo cardiomyocyte mechanics, and pathological data from microscopy of the nuclear envelope, that is properly reshaping our *LMNA* knowledge base, one variant at a time. This review explains the biology of lamin A/C heart disease (genetics, structure and function of lamins), clinical presentation (diagnostic pointers, electrocardiographic and imaging features), aspects of screening and management, including current uncertainties, and future directions.

KEYWORDS: advanced cardiac imaging; cardiac imaging and diagnostics; cardiac magnetic resonance (cmr) imaging; heart transplantation; implanted cardiac defibrillators

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Conflict of interest statement

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