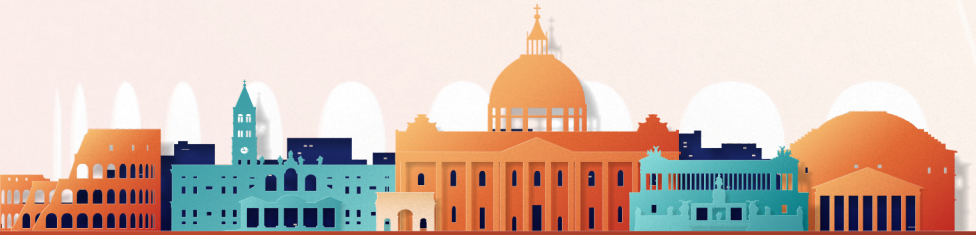
PLACE 2026
PLATFORM OF LABORATORIES FOR ADVANCES IN CARDIAC EXPERIENCE

CONGRESSO
ROMA, 25 - 27 Giugno 2026

MORTE CARDIACA IMPROVVISA, CANALOPATIE E CARDIOMIOPATIE GENETICHE

A recurrent *LMNA*:c.949G>A variant associated with shared cardiomyopathic and arrhythmic features in a series of unrelated affected patients

Valerio Caputo, PhD
Università degli Studi di Roma Tor Vergata



AIM OF THE STUDY

***LMNA* pathogenic variants**
Lamin A/C protein

- **Dilated / arrhythmogenic cardiomyopathy**
- **Conduction disease**
- **Malignant ventricular arrhythmias**

Unmet need

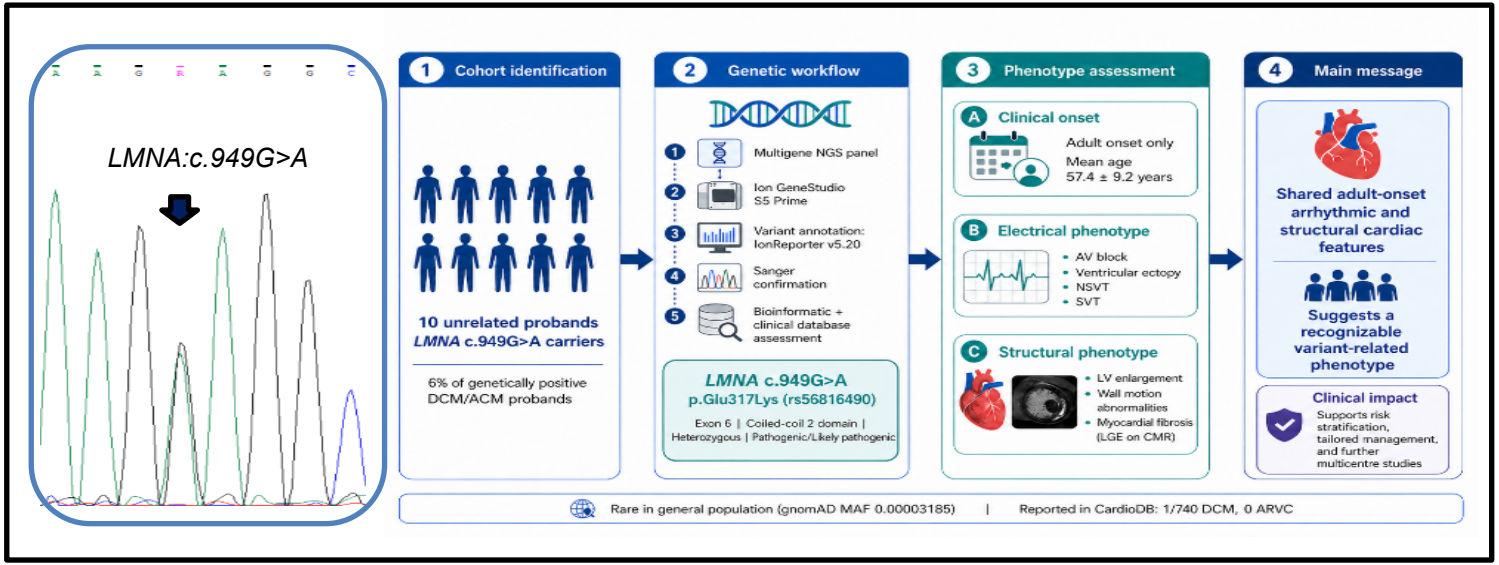
To determine whether a recurrent variant identified in apparently unrelated families gives rise to a recognizable clinical profile that may be useful for risk stratification, follow-up, and family screening.

AIM OF THE STUDY

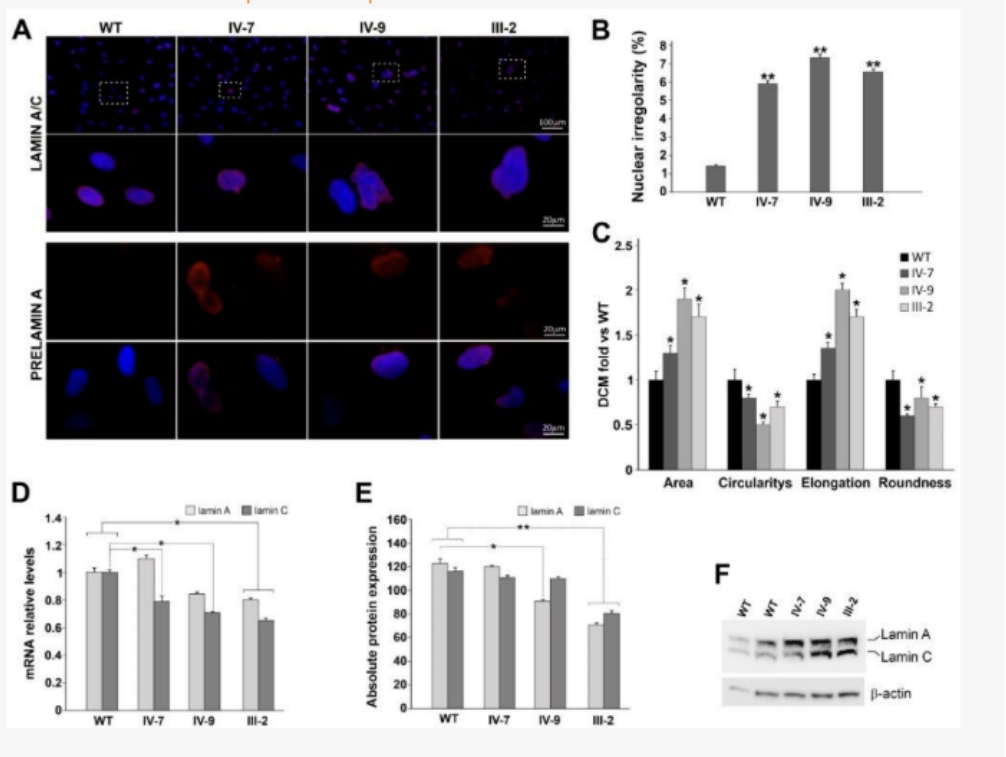
to characterize the phenotypic spectrum of unrelated probands carrying the pathogenic *LMNA:*c.949G>A, p.(Glu317Lys) variant (rs56816490) and to identify potential shared clinical features.

Key hypothesis

The recurrence of the same rare variant in a geographically defined population may reflect a founder effect or a specific clinical profile.



LMNA:c.949G>A



Journal of *Clinical Medicine*
MDPI

Article

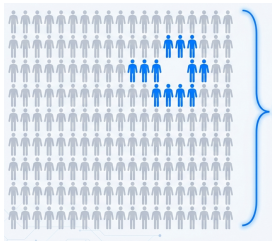
Clinical Features of LMNA-Related Cardiomyopathy in 18 Patients and Characterization of Two Novel Variants

Valentina Ferradini [1], Joseph Cosma [2], Fabiana Romeo [2], Claudia De Masi [1], Michela Murdocca [1], Paola Spitalieri [1], Sara Mannucci [1], Giovanni Parlapiano [1], Francesca Di Lorenzo [1], Annamaria Martino [3], Francesco Fedele [4], Leonardo Calò [3], Giuseppe Novelli [1,5,6], Federica Sangiuolo [1,*] and Ruggiero Mango [2]

- Increased percentage of abnormal nuclei, irrespective of the type of nuclear malformation correlating with nuclear architecture instability
- Lamin C expression is statistically significantly reduced if compared to WT ones

STUDY COHORT

11 Unrelated patients



6% of unrelated probands with DCM/ACM-like features who tested positive for genetic variants

***LMNA*:c.949G>A, p.(Glu317Lys) · rs56816490**

Rare in public databases

Classified as pathogenic

Geographic clustering

METHODS

1 → 2 → 3 → 4 → 5

Genetic testing
Multigene NGS panel

Variant annotation
IonReporter v5.20

Confirmation
Sanger sequencing

Pathogenicity support
Bioinformatic tools + clinical databases

Phenotype analysis
Clinical, ECG, imaging, genetic data

Integrated retrospective analysis

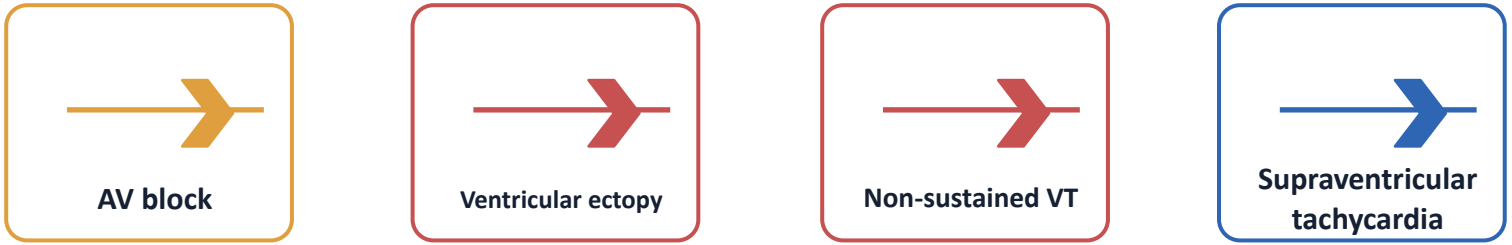
Combination of molecular confirmation and multidomain phenotypic reconstruction

RESULTS

Shared prominent electrical involvement....

Clinical onset (mean + ds)

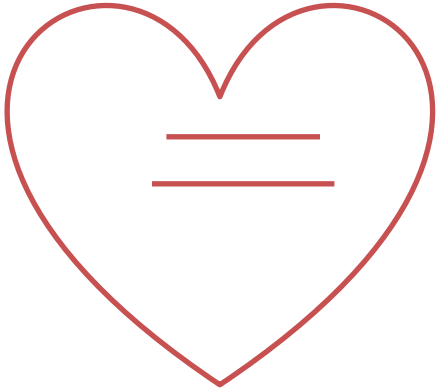
55.5 ± 8.9 years



Adult-onset disease with conduction abnormalities and both ventricular and supraventricular arrhythmias.

RESULTS

….and shared structural involvement



> 50%

Altered imaging

Left ventricular enlargement	LV remodeling
Wall motion abnormalities	regional dysfunction
Myocardial fibrosis	tissue injury substrate

The phenotype is not confined to arrhythmias, but also includes morpho-functional and tissue abnormalities consistent with LMNA-related cardiomyopathy.

CONCLUSIONS

- *LMNA*:c.949G>A, although rare in public databases, is a recurrent variant in the observed cohort.
- The variant appears to be associated with a homogenous phenotype
- Recurrence in unrelated probands supports founder-effect assessment and multicentre expansion

A rare variant, a shared geography, and a recurrent cardiac signature.

PERSPECTIVES

Follow-up of genotype-positive relatives	To define penetrance, age at onset, and disease progression.
Founder-effect assessment	To determine whether recurrence reflects a common ancestor.
Multicentre expansion	To increase sample size and strengthen phenotypic robustness.
Clinical refinement	Arrhythmic surveillance, serial imaging, family screening.

THANK YOU FOR YOUR ATTENTION!

U.O.C Genetica Medica, Policlinico Tor Vergata
Prof. Giuseppe Novelli
Prof.ssa Federica Carla Sangiuolo
Dr.ssa Enrica Marchionni
Dr.ssa Giorgia D'Ortenzi
Dr. Alessio Ludovico Del Popolo
Dr.ssa Eleonora Ziantoni
Dr.ssa Ylenia Aura Minafò
Dr. Ruggiero Mango