International Consortium for Multimodality Phenotyping in Adults with Non-compaction

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Myocardial disorders
Study type	Observational invasive

Summary

ID

NL-OMON57174

Source
ToetsingOnline

Brief title
NONCOMPACT

Condition

- Myocardial disorders

Synonym
NCCM, Non-compaction cardiomyopathy

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: NCCM, Non-compaction cardiomyopathy

Outcome measures

Primary outcome

We hypothesize integrated analysis of clinical, genetic and imaging variables will improve outcome prediction in patients with NCCM. At 5 centers, 600 patients with suspected NCCM by joint adjudication will be comprehensively phenotyped and followed for up to 3 years. Independent core labs will perform comprehensive structural and functional evaluation of clinical echo and MRI exams. Adverse events are adjudicated by an independent event committee. Machine-learning techniques for complex multi-parameter predictions will be applied to develop predictive models for arrhythmic events, thromboembolic events and composite outcomes. Performance will be compared to currently used risk models and guideline-based criteria for ICD implantation and anticoagulation.

Secondary outcome

We hypothesize that high-resolution cardiac CT can discover structural differences between pathological non-compaction and benign hyper-trabeculation, independent of quantity. From the original cohort (Aim 1), 300 adult patients with suspected NCCM will undergo cardiac CT and advanced computational analytics including hypothesis-based features (thrombogenic cavities), measures of trabecular density and complexity, as well as hypothesis-free image interpretations of the non-compacted myocardium using artificial intelligence (radiomics), as demonstrated in our preliminary studies. Interactions between

structure and function will be investigated using regional co-registration of

CT and echo/MRI data. We will determine the incremental predictive value of the

structural CT features to the models from the primary outcome.

Study description

Background summary

Non-compaction cardiomyopathy (NCCM), also known as left ventricular non-compaction (LVNC), is a heterogeneous myocardial disorder characterized by ventricular myocardium comprising of a diminished compacted outer layer and extensive non-compacted inner muscular layer. A specific genetic mutations or histopathological substrate that defines NCCM has not yet been identified. Although the true prevalence of NCCM is unknown, non-compaction is reported in 0.05-0.24% of adult echocardiograms, and in up to 4% of patients with reduced left ventricular (LV) function. Clinically, NCCM can manifest as LV dysfunction and heart failure, and many patients ultimately require heart transplantation. Life-threatening ventricular tachyarrhythmias occur in 38-47% of NCCM patients.Stroke and other systemic emboli occur in 9-24%, which is thought to be due to deep recesses and contractile dysfunction promoting thrombus formation. Recognition and treatment of high-risk NCCM patients is important, but it is also crucial to avoid the burden, risk and cost of (indefinite) anticoagulation and ICDs in those unlikely to benefit. Increased non-compaction detection rates in adults have created an urgent unmet clinical need for better risk stratification and more effective allocation of impactful preventive therapies.

Study objective

The ultimate goal of the consortium is to use state-of-the-art imaging, genetics, and machine-learning techniques to identify NCCM patients at risk for severe arrhythmia or stroke and guide preventive therapy using personalized risk scores

Study design

This is a prospective, multicenter observational study to identify clinical, genetic and imaging predictors of clinical outcome in patients with suspected non-compaction cardiomyopathy. Written informed consent will be obtained from all study participants. The total project duration is 5 years. Patient enrollment and CT examinations will be performed in the first 4 years. CT examinations will be performed on FDA approved equipment and no investigational

drugs will be used. There is no diagnostic or therapeutic intervention that will affect standard patient management. The primary endpoints include past and prospective embolic, arrhythmic and heart failure events as assessed by an Events Adjudication Committee.

Study burden and risks

In addition to standard clinical diagnostic an therapeutic interventions, bloodsamples (incl genetic tests) will be taken, Quality of life questionnaires will be completed at baseline and follow-up and a subgroup of patients (approx. 50%) will undergo a cardiac CT scan.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• >=18 years old
• Hypertrabeculation of the left ventricle fulfilling the echo-based Jenni criteria of NCCM
• Cardiac MRI examination performed or planned for clinical purposes

Exclusion criteria

Exclusion criteria to the study (Aim 1):
• Complex congenital disease, neuromuscular disorders or isolated RV non-compaction
• Inability to provide informed consent
• Contra-indications to MRI

Exclusion criteria to the cardiac CT exam (Aim 2):
• Age <21 years
• Decompensated heart failure, or otherwise clinically unstable
• BMI>40 kg/m2
• Pregnancy (or cannot be ruled out)
• Known iodine contrast medium allergy
• Kidney dysfunction: eGFR<45 ml/min
• Thyroid disease: toxic multinodular goiter, Graves* disease, Hashimoto*s thyroiditis

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-05-2021

Enrollment:	120
Type:	Actual

Ethics review

Approved WMO Date:	05-11-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL73728.078.21