PROFID EHRA
PRevention Of sudden cardiac death aFter myocardial Infarction by Defibrillator im-plantation

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To demonstrate that in post-MI patients with symptomatic heart failure who receive optimal medical therapy (OMT) for this condition, and with reduced LVEF

Ethical review	Approved WMO
Status	Pending
Health condition type	Myocardial disorders
Study type	Interventional

Summary

ID

NL-OMON57177

Source
ToetsingOnline

Brief title
PROFID EHRA

Condition

- Myocardial disorders

Synonym
heart attack, sudden cardiac death

Research involving
Human

Sponsors and support

Primary sponsor: Charité - Universitätsmedizin Berlin
Source(s) of monetary or material Support: research grant of the EU commission (Horizon 2020 program;no 847999)

Intervention

Keyword: cardiology, defibrillator, myocardial infarction, sudden cardiac death

Outcome measures

Primary outcome

O1. Time from randomisation to the occurrence of all-cause death.

Secondary outcome

O2. Time from randomisation to death from cardiovascular causes.

O3. Time from randomisation to SCD.

O4. Time from randomisation to first hospital readmissions for cardiovascular causes after date of randomisation.

O5. Average length of stay in hospital during the study period.

O6. Quality of life (EQ-5D-5L) trajectories over time at baseline and 12-month intervals thereafter.

Study description

Background summary

Patients who have survived a myocardial infarction (MI) are at increased risk for sudden cardiac death (SCD), mostly caused by life-threatening ventricular tachyarrhythmias such as ventricular tachycardia and ventricular fibrillation. A severely reduced left ventricular ejection fraction (LVEF) as a rough overall measure of impaired heart function after MI was shown to indicate a higher risk for SCD. Based on this observation, two landmark randomised trials, MADIT II and SCD-HeFT, were conducted between end of the 1990s and early 2000s. These trials compared the survival of patients with severely reduced LVEF, either

after MI or due to other causes of heart failure, who received a defibrillator with the
survival of patients being on medical therapy alone. These two trials reported a significantly better survival of patients in the defibrillator arm and led to international guideline recommendations for routine implantation of defibrillators in survivors of MI with severely impaired LVEF as a means for primary prevention of SCD. Indeed, in these trials and in other studies from this period, therapies delivered by the defibrillators were reported in a substantial portion of patients. Since then, the management of these patients has changed dramatically with the advent of a series of novel drug classes that reduce not only mortality but specifically SCD leading to a substantial decrease of the sudden death rates as
well as of the rates of appropriate defibrillator therapies implanted for primary prevention of SCD. At the same time, the complication rates associated with the defibrillator therapy remain significant without obvious decrease. Thus, there is meanwhile a whole bulk of evidence that the risk-benefit of defibrillator implantation for primary prevention of SCD in patients with severely reduced LVEF has substantially changed since the conduction of these two landmark trials 20-25 years ago.
A personalised prediction of the SCD risk would be desirable, but remains not feasible up to now and various attempts have not found their way into clinical practice. Cardiovascular imaging or genetics seem to be promising but their value has not been established mainly due to the relevant paucity of respective data.

Study objective

To demonstrate that in post-MI patients with symptomatic heart failure who receive optimal medical therapy (OMT) for this condition, and with reduced LVEF <=35%, OMT without implantable cardioverter defibrillator (ICD) implantation (index group) is not inferior to OMT with ICD implantation (control group) with respect to all-cause mortality within about 2.5 years of observation.
A secondary objective of the trial is to explore the potential of novel and promising risk markers for personalised risk prediction of SCD. For this purpose, two sub-studies will be conducted: a cardiac Magnetic Resonance Imaging (cMRI) sub-study and a genomics sub-study, each of them in a subset of participating study sites with adequate potential. In addition, an artificial intelligence-based analysis of the twelve-lead Electrocardiograms (ECGs) collected in the main study at baseline and at follow-ups will be performed.

Study design

PROFID EHRA is a non-commercial, investigator-driven, prospective, parallel-group, randomised, open-label, blinded outcome assessment (PROBE), multi-centre, non-inferiority trial without dedicated investigational medical device (Proof of Strategy Trial) with two groups with 1:1 randomisation. The

randomisation to one of the treatment strategy groups is the only study intervention, all medical treatment (drugs, devices, procedures) used within this trial is at the discretion of the treating physicians and represent clinical routine. It will be conducted in about 12 European countries with about 180 clinical sites actively participating.

Intervention

No investigational medical product is defined to be used within PROFID EHRA but only the therapeutic strategy (ICD versus no ICD) is a pre-defined study treatment and allocated by random group (Proof of Strategy Trial). The marketed devices to be implanted will be decided by the treating physician based on the clinical situation of the individual study patient and in line with local policies in routine clinical care for device implantation.

Study burden and risks

see risk- benefit assessment (study protocol, 3.3)

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

I1. Age >=18 years.
I2. Naïve to implantation of any pacemaker or defibrillator.
I3. Documented history of MI either as ST segment elevation myocardial infarction (STEMI) or as non-ST
segment elevation myocardial infarction (NSTEMI) at least 3 months prior to enrolment.
I4. Symptomatic heart failure with New York Heart Association (NYHA) class II or III.
I5. On OMT for at least 3 months prior to enrolment.
I6. LVEF <=35% (at transthoracic echocardiography (TTE) or cMRI at least 3 months after MI).
I7. Signed informed consent.

Exclusion criteria

E1. Class I or IIa indication for implantation of an ICD for secondary prevention of SCD and ventricular tachycardia.
E2. Ventricular tachycardia induced in an electrophysiologic study.
E3. Unexplained syncope when ventricular arrhythmia is suspected as the cause of syncope.
E4. Class I or IIa indication for Cardiac Resynchronization Therapy (CRT).
E5. Foreseeable violation of instruction for use (IFU) of the ICD device selected for implantation (valid for control group patients, only).
E6. Acute coronary syndrome or coronary angioplasty or coronary artery bypass grafting performed within 6 weeks prior to enrolment.
E7. Cardiac valve surgery or percutaneous cardiac valvular intervention performed within 6 weeks prior to enrolment.
E8. On the waiting list for heart transplantation.
E9. Any known disease that limits life expectancy to less than 1 year.
E10. Participation in another randomised clinical trial if study-specific treatment is still active at enrolment into PROFID EHRA.
E11. Previous participation in PROFID.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-11-2024
Enrollment:	292
Type:	Anticipated

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Date:	28-11-2024
Application type:	First submission
Review commission:	METC Amsterdam UMC

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
ClinicalTrials.gov	NCT05665608
CCMO	NL84224.018.23