Catheter ablation versus Amiodarone to prevent future shock episodes in patients with a defibrillator and a history of a myocardial infarction.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cardiac arrhythmias
Study type	Interventional

Summary

ID

NL-OMON33105

Source
ToetsingOnline

Brief title
CARFE

Condition

- Cardiac arrhythmias
- Cardiac therapeutic procedures

Synonym
Heart rythm disturbances / ICD shocks

Research involving
Human

Sponsors and support

Primary sponsor: Diagram BV
Source(s) of monetary or material Support: Investigator Initiated TRIAL

Intervention

Keyword: Ablation / ICD / Amiodaron / Myocardial Infarction

Outcome measures

Primary outcome

Primary endpoint:

• Time to reccurrence of documented ICD shock therapy for VT of VF during the follow-up period starting post ablation or after receiving amiodarone.

Secondary outcome

Secondary endpoints:

• Total number of ICD shocks during follow-up period

• Number of VT*s recorded by the ICD

• Quality of life (SF-36 score)

• Number of hospital readmissions due to a cardiovascular indication

• Number of appropriate ICD therapies (including ATP)

• Number of appropriate ICD shocks

• Number of inappropriate ICD therapies (including ATP)

• Number of inappropriate ICD shocks

• Severe clinical events (death, syncopes, electrical storm episodes (defined as > 3 VT episodes whithin 24 hours) and cessation of amiodarone due to side-effects)

Study description

Background summary

Ventricular tachycardia or fibrillation is a rhythm disturbance commonly encountered among patients with coronary artery disease. lt is the primary tachyarrhythrmia responsible for nonfatal cardiac arrest among patients with a history of myocardial infarction. VT after myocardial infarction commonly arises from a relatively discrete and heterogeneous region of left ventricular (LV) myocardium within or bordering the infarct zone (1,2). Over the past two decades, therapeutic approaches have included pharmacological suppression or surgical excision of the arrhythmogenic focus (3-5). Because of the unsatisfactory results provided by these approaches, an alternative solution in common use during the past years has been the implantable cardioverter-defibrillator (6,7). This method does not eliminate the tachyarhythmia but, instead, attempts to terminate it by delivering pacing stimuli or countershocks. Although most patients can adapt to its presence, it has both considerable cost and the potential for significant long-term psychological impact on the recipient. ICD therapy has a significant positive impact on long-term survival in patients with an impaired LV function, with or without history of (inducible) VT*s (3,8-12). Increasing numbers of patients with CAD are treated with an ICD. One of the major concerns after implantation is management and prevention of ICD shocks caused by (unstable) ventricular tachycardia (VT) or ventricular fibrillation (VF). Recurrent ICD shocks lead to a decreased quality of life and increased hospitalisation and costs (13,14). Clinically significant anxiety and depression as a result of recurrent ICD shocks may occur in more than 50% of patients (15-17). Repeated ICD shocks within a short time interval, known as an ICD *storm,* occur in 10 to 25% of patients. (18,19)
Radiofrequency ablation and/or antiarrhythmic medication are both used to prevent recurrences of shock therapy. Catheter ablation of VT requires that the reentry circuit of the VT be accurately pinpointed. This is performed using a catheter introduced into the left ventricle. Through a process known as endocardial mapping, the catheter is methodically guided throughout the left ventricular endocardial surface during tachycardia while observing the characteristics of the sequentially recorded electrograms representing local endocardial activation. Specific features of electrograms denoting the site of origin of the VT and the response to certain pacing maneuvers have been described (20-23) The delivery of radiofrequency energy at the site of origin can eliminate the VT. Catheter ablation is effective in the treatment of stable VT (24- 32) as well as unstable VT (33-36). Modern ablation techniques (substrate mapping and ablation) which use the electroanatomic mapping system CARTO (37-39) allow the ablation of hemodynamically poorly tolerated VT. Recently, prophylactic substrate-based catheter ablation was found to reduce the incidence of ICD therapy in patients with a history of myocardial

infarction who received ICDs for the secondary prevention of sudden death.(40) In a subgroup analysis of this study, revascularization of patients was correlated with increased effect of catheter ablation in comparison with placebo. This might be due to a decrease in ablation effectiveness in patients with myocardial ischemia. Long-term medical therapy with amiodarone is an effective therapy to prevent ICD shock therapy, but it is known to coincide with multiple important side effects (41). Therefore, long-term amiodarone therapy is debatable. However, no comparison between catheter ablation and medical therapy was made, and only secondary prevention and mostly non-revascularized patients were included.

Study objective

The main objective of this study is to compare the occurrence of next ICD shock therapy for VT or VF in patients with hospital presentation for an ICD shock therapy for VT or VF, with a history of a myocardial infarction, between patients randomized to substrate based ablation or amiodarone.

Study design

A prospective, randomized study will be conducted in a single center: hospital Isala Klinieken, location de Weezenlanden, Zwolle, the Netherlands. Patients with a prior myocardial infarction, and appropriate ICD therapy will be included into the study.

Intervention

1 group takes daily 200 mg amiodarone
1 group undergoes ones a catheter ablation

Study burden and risks

The ablation procedural mortality varies between 0-4.8 % in the largest reported series (25,27,31,32,33,35,46).

The most serious risks of systemic arterial embolization which can cause myocardial infarction, stroke, cardiac perforation or tamponade occurred in 3% of patients in recent series (25-28,31). Of 52 patients from one center there was one death in the perioperative period due to acute myocardial infarction (25). Damage to cardiac valves, damage to the normal cardiac conducting system requiring a permanent pacemaker, damage to vasculature, and deep venous thrombosis can also occur, but are infrequent. Initiation of ventricular tachycardia is required. This can produce hypotension and may require electrical cardioversion with attendant musculoskeletal discomfort. Procedures are performed under sedation or general anesthesia. The risks of sedation include hypoventilation, hypotension, and allergic reactions to the

medications. Fluoroscopy will be used for initial catheter positioning. Precise identification of mapping catheter position with the CARTO system is expected to help locate and repeatedly position the catheter at desirable target sites for ablation. The systems allows identification of catheter position without fluoroscopy and will probably reduce fluoroscopy exposure in this study. Mapping during hemodynamically stable sinus rhythm is performed routinely during catheter ablation procedure.

Radiofrequency current may cause occlusion of a coronary artery, either by direct thermal damage, spasm, or thrombosis. Experience at numerous centers suggests that the risk of coronary occlusion is less than 0.5%. Coronary arterial occlusion could produce myocardial infarction, angina or death. Should occlusion of a coronary artery occur for any reason, the physician will attempt to restore coronary blood flow through pharmacological, catheter and/or surgical intervention as medically indicated.

The application of radiofrequency current close to the AV node or His bundle could damage the normal AV conduction system, producing complete heart block and requiring permanent ventricular pacing. If this should become necessary, it is possible to incorporate this function into the ICD which is to be implanted.

A thrombus may form on the ablation electrode during the application of radiofrequency current usually indicated by an impedance rise. The thrombus might become dislodged and embolize to produce a stroke, myocardial infarction, or other ischemic injury. The risk of an embolus is reduced by quickly terminating the application of current after an impedance rise, which limits the size of the coagulum on the electrode.

Thrombus formation on the endocardium following ablation may produce an arterial or pulmonary embolus, This risk may be reduced by the use of aspirin or other anticoagulant therapy, at the discretion of the investigator.

Cardiac perforation may result from catheter manipulation or application of radiofrequency current (risk is <1%). This may result in cardiac tamponade and may require percutaneous pericardial drainage or surgical repair. Significant hemodynamic compromise can result in neurologic injury or death.

lnjury to a cardiac valve may result from catheter manipulation or the application of radiofrequency current (risk < 1 %). This may produce valvular insufficiency and possibly require surgical valve replacement.

Radiation exposure during the fluoroscopic imaging of the catheters may result in an increase in the lifetime risk of developing a fatal malignancy (0. 1 %) or a genetic defect in offspring (0.002%).

Other potential complications that may result from catheter insertion and manipulation as part of the prerequisite electrophysiology study and mapping

procedure include:

Allergic reaction to the local anesthetic, sedatives, x-ray dye, heparin, protamine, or other agents administered during the procedure (risk < 1 %).

Arterial or venous injury, including arterial dissection, thrombosis, occlusion or hemorrhage at the catheter insertion sites or at other sites along the vessels (risk < 1 %). This may produce hemorrhage, hematoma or ischemic injury to an extremity or major organ.

Hemorrhage as a result of anticoagulation (risk <0.5%) which may require transfusion.

Infection, either at the catheter insertion site or systemically, including endocarditis and septic emboli (risk < 0.5 %). This risk can be minimized by using standard aseptic technique and, when indicated, by the use of antibiotic agents.

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

Inclusion criteria:
1. prior myocardial infarction, at least 3 months ago
2. ICD implantation for any cause except for: Brugada sy, ARVC, HCM, LQTS, SQTS, cathecholaminergic polymorphic VT, other channelopathies
3. ICD shock for VT of VF without a reversible cause
reversible causes (must be checked):
a. Acute myocardial ischemia in the following circumstances:
i. Acute coronary syndrome
ii. Myocardial ischemia as documented by non-invasive myocardial ischemia testing
b. Whenever VT or VF occurs in the setting of antiarrhythmic medication intake (class I or III Vaughn-William) with increased QTc
c. High fever (T>39 degrees Celcius) and signs of infection/sepsis at presentation
d. Lead dislocation on X-ray plus signs of mechanical VT induction
e. Other reversible causes as significant hypoxaemia not caused by cardiac failure or known hyperthyroidism. Judgement whether this will be possible cause of VT/VF will be at discretion of the attending physician
4. Optimal revascularization before ICD implantation performed
5. Written informed consent

Exclusion criteria

Exclusion criteria
1. Age < 18 years
2. use of amiodarone more than 7 days before randomization within the period of 3 months before randomization
3. unability to use amiodarone due to past side effects
4. Class I antiarrythmic drugs not stopped <= 5 times *T prior to randomization
5. Protruding LV thrombus or cardiac tumor on pre-ablation echocardiogram
6. Acute myocardial infarction within the preceding 3 months
7. non-reversible Class IV NYHA heart failure
8. Valvular heart disease or mechanical heart valve precluding access to the LV.
9. Unstable coronary artery syndrome or active myocardial infarction
10. Cardiac surgery within the past 2 months
11. mechanical mitral or tricuspid valve prothesis
12. Serum creatinine > 220 mmol/L (2.5 mg/dL)
13. Thrombocytopenia or coagulopathy

14. Contraindication to anticoagulation
15. stroke within past 30 days
16. Pregnancy
17. Acute illness or serious active systemic infection

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	14-01-2010
Enrollment:	238
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Amiodaron
Generic name:	Cordarone
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	09-07-2009

Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	18-03-2010
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)

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
EudraCT	EUCTR2009-011790-32-NL
CCMO	NL26795.075.09