Continuation of Measurements of Short-Term Variability of Activation Recovery Interval on Human Signals

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Primary objective: to explore the application of automatic STV measurements by the ICD (STV-ARI,automatic), by correlating the STV-ARI,automatic values to the STV-values derived from our clinical gold standard, i.e. STV-QT (STV values derived from...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cardiac arrhythmias
Study type	Observational non invasive

Summary

ID

NL-OMON51281

Source
ToetsingOnline

Brief title
STV-ARI 2.0

Condition

- Cardiac arrhythmias

Synonym
Sudden cardiac death, ventricular arrhythmias

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W,Medtronic Bakken Research Center, Maastricht,Research collaboration met Medtronic Bakken Research

Center;Maastricht

Intervention

Keyword: Activation-recovery interval (ARI), Electrogram (EGM), Internal cardioverter defibrillator (ICD), Short-term variability of repolarization (STV)

Outcome measures

Primary outcome

Short-term variability of repolarization (STV) of 30 consecutive beats is measured from different recording sites (ECG, RV EGM; unipolar & bipolar signals). STV is calculated with the formula * !n+1 * !n /30× 2, where *D* represents the repolarization duration and *n* the number of complexes, in this case 30 complexes. The repolarization duration is defined and measured differently per recording site. All intracardiac and ECG leads can be recorded simultaneously.

The following parameters are measured:

- STV-QT: QT-interval is defined as the interval from the beginning of the Q-wave until the end of the T-wave. Since the end of T-wave is hard to define, the method of fiducial segment averaging is used to calculate STV. All complexes are aligned around the R-wave as trigger point. Next, each fiducial point (QRS-onset, end of T- wave) was aligned separately by cross correlating the individual complex to the average of the other complexes till maximal correlation was achieved. After alignment, Q-onset and T-end were determined all at once. However, the individual intervals of every beat are preserved. the QT-interval of every complex was calculated by summation of the intervals of

the QRS-onset to trigger point and trigger point to the T-wave, respectively.

- STV-ARI,automatic: intracardiac EGM signals will be opened in a Matlab environment containing the algorithm to automatically determine STV-values. First, the QRS complex will be blanked to avoid interference in the T-wave end detection. Next, the first derivative of the resultant signal is calculated over time to detect changes in the slope. This gradient signal was then squared in order to make all data points positive and to emphasize slope changes in the signal. Finally, the T-wave end was defined as the point at 60% of the area under the curve of the resultant signal. The ARI is defined from the moment of ventricular sensing of the QRS-complex to the T-wave end, derived with this method.

The main endpoint is the p-value of the correlation coefficient between STV-EGM,automatic and STV-QT values in sinus rhythm.

Secondary outcome

- Explore the modulation of STV by pacing through different pacing modalities (atrial pacing (AAI) and dual pacing (DDD)) and different pacing frequencies (80 beats per minute and [SR+20] beats per minute). We will perform a repeated measure ANOVA, comparing the four pacing possibilities with SR, with post-hoc Tukey correction. We will do the repeated ANOVA for the STV-QT and STV-EGMautomatic values separately.

- Find the optimal ICD vector for each individual at each pacing modality, based on quality indicators of the signal, i.e. minimal amplitude-noise ratio and maximal variation of the T-wave during the recording. We will determine the

threshold of these quality indicators based on correlations between STV-QT and STV-ARIautomatic.

Furthermore we'll recording the following clinical characteristics:

- Age
- Sex;
- Left ventricular ejection fraction (LVEF) measured by MRI, nuclear imaging or echocardiography;
- NYHA class (II, III, ambulatory IV);
- Underlying cardiac disease (ischemic cardiomyopathy, dilated cardiomyopathy, other);
- Cardiovascular risk factors (smoking, hypertension, diabetes mellitus, peripheral artery disease)
- Relevant comorbidities (COPD, chronic kidney disease, malignancy)
- Medications (beta blockers, ACE-inhibitors/AT2-antagonists, aldosterone antagonists, diuretics, calcium blockers, digoxin, class I or III anti-arrhythmic drugs)
- ECG parameters (RR-interval, PQ-interval, QRS-duration, heart axis)

Study description

Background summary

Implantation of an Implantable Cardioverter-Defibrillator (ICD) is the mainstay of treatment in the prevention of Sudden Cardiac Death (SCD). While an ICD is highly effective in termination of sustained ventricular arrhythmias, it does not prevent arrhythmias from occurring. Prediction of imminent arrhythmias that

could trigger preventive treatment by the ICD would substantially increase its functionality. Short-term variability (STV) of repolarization has shown to be associated with a high risk of ventricular arrhythmias and SCD. Furthermore, it has been demonstrated that STV derived from the activation-recovery interval (ARI) of intracardiac electrograms (EGM) increases abruptly prior to the occurrence of arrhythmias in an arrhythmic animal model. Moreover, in this animal model it has been demonstrated that automatic STV-ARI measurements by an ICD can guide high-rate pacing to prevent imminent ventricular arrhythmias. To translate these findings to human application, we want to research if there is a correlation between the STV-ARIautomatic values and the STV values derived from our gold standard in humans, STV-QT. Furthermore, it is not known which intracardiac electrogram (unipolar/bipolar) should be used for STV analysis.

With this study (STV-ARI 2.0 study) we continue the STV-ARI clinical study, registered under number 17-732. The aim of the original STV-ARI study was similar to the aim of the STV-ARI 2.0 study, i.e. look into the possibility to automatically measure STV on human EGM signals by the ICD by demonstrating a correlation between STV-ARI,automatic and STV-QT. Unfortunately, due to significant injury current on the recordings obtained during de novo implantations, this goal was not achieved during the first STV-ARI study. STV analyses are not reliable on signals with such significant injury current. Based on the five recordings obtained during a replacement/upgrade procedure, we were however able to calculate a sample size estimation of how many study subjects we expect are needed to demonstrate a significant correlation coefficient.

The ultimate goal is to incorporate the STV-ARI,automatic technique in the ICD, in order for the ICD to start preventive therapy (temporary accelerated pacing) when the STV surpasses a certain arrhythmic threshold, in order to prevent imminent ventricular arrhythmias from occurring.

Study objective

Primary objective: to explore the application of automatic STV measurements by the ICD (STV-ARI,automatic), by correlating the STV-ARI,automatic values to the STV-values derived from our clinical gold standard, i.e. STV-QT (STV values derived from the ECG using the fiducial segment averaging technique) in sinus rhythm. Hence, our aim is to find out whether there is a statistically significant correlation between STV-ARI,automatic and STV-QT.

Secondary objectives:
- Explore the modulation of STV by pacing at different frequencies (80 beats per minute and [rate during sinus rhythm + 20 beats per minute]) and pacing modalities (AAI and DDD pacing), captured by both STV techniques (STV-ARIautomatic and STV-QT).
- Find the optimal ICD vector for each individual at each pacing modality,

based on quality indicators of the signal, i.e. minimal amplitude-noise ratio and maximal variation of the T-wave during the recording. We will determine the threshold of these quality indicators based on correlations between STV-QT and STV-ARIautomatic.

Study design

This study will be a cross-sectional, single center observational study with one time point of observation. The study will be performed in patients that are scheduled for true/integrated bipolar dual chamber ICD replacement/upgrade in the UMC Utrecht. During the replacement/upgrade procedure, additional measurements will be performed. No extra follow-up or test needs to be scheduled.

Study burden and risks

The study can only be done in these patients since they are the only patients with an RV lead in situ and a Right Atrium lead. The risks and burden for the patient will be minimal, since replacement procedure of the device will follow standard practice. The measurement of the intracardiac signals will increase the replacement procedure by approximately 30 minutes. No additional visits, blood samples, tests or administration of drugs are needed. The patients will not have a direct benefit from study participation. However, the results of the study might have benefit for future patients with an ICD, leading to prevention of ventricular arrhythmias.

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

- Carrying a dual chamber ICD with a true/integrated bipolar ICD lead scheduled for a generator replacement OR
- Carrying a single chamber ICD with a true/integrated bipolar lead, with an indication for a dual
chamber upgrade according to current guidelines
AND
- Sinus rhythm at upgrade/replacement with intrinsic AV conduction
- QRS <130 ms

Exclusion criteria

- Age <18 years old
- Permanent atrial fibrillation

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	28-06-2022
Enrollment:	15
Type:	Actual

Ethics review

Approved WMO Date:	14-04-2022
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	26-10-2022
Application type:	Amendment
Review commission:	METC NedMec

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	NL80446.041.22

Study results

Date completed:	19-04-2023
Actual enrolment:	7