Monitoring of hemodynamics in heart failure patients by intracardiac impedance measurement

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Primary objective:The primary objective is aimed at determining the comparability of intracardiac impedance (ICI) measurements to echocardiographic reference parameters in assessment of changes in stroke volume (SV) in an acute setting. It is...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON39966

Source
ToetsingOnline

Brief title
Bio.Detect HFII

Condition

- Heart failures

Synonym
Heart hailure; Decreased pump function of the heart

Research involving
Human

Sponsors and support

Primary sponsor: Biotronik
Source(s) of monetary or material Support: Biotronik SE & Co. KG

Intervention

Keyword: Heart failure, Hemodynamics, Intracardiac impedance measurement, Lumax 740 ICD

Outcome measures

Primary outcome

Intra-individual correlation coefficient r between stroke volume assessed by

echo Doppler aortic velocity- time-integral and stroke impedance assessed by

intracardiac impedance measurement in an acute setting.

Secondary outcome

1.Intra-individual correlation coefficient r between LVESV assessed by echo

2D-Biplane Simpson*s method and end-systolic impedance assessed by intracardiac

impedance measurement in an acute setting.

2. Intra-individual correlation coefficient r between SV assessed by the

Finapres®-method and stroke impedance assessed by intracardiac impedance

measurement in an acute setting.

Study description

Background summary

Heart failure (HF) is a syndrome with a broad spectrum of heterogeneous symptoms and signs caused by a cardiac dysfunction and resulting in a wide range of clinical expression. The overall mortality for the population is 50% in the first 4 years. 40% of the patients with HF-related hospitalizations have to be readmitted to hospital or die within one year. Cardiac Resynchronization Therapy (CRT) is used in order to synchronize interventricular and intraventricular contraction pattern of the heart in patients with HF in whom there is evidence of electrical dyssynchrony (QRS width >120 ms). The clinical benefits of long-term CRT have been evaluated in a large number of randomized multi-center trials. The results showed a significant alleviation of symptoms and an increase in exercise capacity for patients with CRT as well as a lowered

risk for all-cause mortality and HF-related hospitalizations. A consistent finding from the randomized trials has been an up to 15% absolute reduction in LV end-diastolic diameter and an up to 6% absolute increase in LVEF following initiation of CRT. These observations provide consistent evidence of a significant, progressive, and sustained reverse remodeling effect conferred by CRT. The management of patients with Heart Failure represents a substantial economic burden, and cost for inpatient treatment of the patients is responsible for >50% of this expense. The need for inpatient treatment arises from acute deterioration of cardiac function, called decompensation. By diagnosing an imminent cardiac decompensation in due time, acute decompensation and hospitalization might be prevented by an early and adequate adaptation of medical therapy. Improved diagnostic methods for assessment of the clinical status of HF patients are therefore warranted.

New diagnostic tools and a wide range of sensor technology are nowadays available for patients being implanted with a pacemaker, ICD or CRT-D device for therapeutic reasons. As a commonly used approach, accumulation of thoracic fluid can be detected by implants using thoracic impedance (TI) measurement. Its efficacy to predict cardiac decompensation was not yet satisfactory due to an insufficient sensitivity and specificity profile in clinical trials.
Therefore, for detection of imminent cardiac decompensation a continuous monitoring of the hemodynamic status of the heart may be a more adequate approach. At present, the assessment of the pump function of the heart can only be realized using time-consuming and sophisticated methods like e.g. echocardiography (which is the current standard) or invasive methods like catheterization. It is hypothesized that intracardiac impedance measurement (ICI) by Biotronik implemented in a new generation of CRT-D devices can be used for providing information of the hemodynamic status of the heart. The underlying working principle of the ICI is based on the different electrical conductance of blood and the surrounding cardiac tissue. A current is injected via the RV-lead coil and tip which is conducted by the blood and myocardial tissue between and around the injecting electrodes. Voltage is sampled via tip and ring of the LV-lead which is positioned in an epicardial vein on the left ventricle of the patient. As the current passes through the left ventricle of the patient, the measured intracardiac impedance is affected by the blood filling state and the diameter of the ventricle, the latter determines the distance of the RV- and LV-lead. The larger the left ventricle, and the more filled with blood, the smaller is the intracardiac impedance value. Constant current injections are performed at intervals of 8 ms so that impedance data for the whole heart cycle may be collected. Intracardiac impedance measurements do not provide absolute, but relative measurands of hemodynamic parameters. Therefore, serial measures recorded over a period of time or data collected prior to and after a change of conditions (like e.g. overdrive-pacing at higher heart rate for provoking immediate hemodynamic changes) are required for meaningful comparisons.

In animal and acute human studies, the impedance measurement proved to provide

reliable data for detection of LV-volume changes (especially stroke volume changes) in acute settings. This study was designed to non-invasively investigate the relationship of hemodynamic measurands and intracardiac impedance data in a larger patient collective. Echocardiography is the common non-invasive clinical standard for diagnosis of HF and allows the determination of SV. It is widely available, non-invasive, and safe. Therefore, echocardiography as the current non-invasive gold standard was chosen as the primary reference method. Additionally, the Finapres-method will be used in a subset of patients. This method records blood-pressure tracings from a finger cuff and allows the determination of SV in a non-invasive manner. The Finapres-method allows the continuous beat-to-beat evaluation of SV and may be valuable to understand SV variability due to external influences.

Study objective

Primary objective:
The primary objective is aimed at determining the comparability of intracardiac impedance (ICI) measurements to echocardiographic reference parameters in assessment of changes in stroke volume (SV) in an acute setting. It is expected that the mean intra-individual correlation coefficient between SZ and SV exceeds 0.65 (r>0.65):

h1-hypothesis: r(SV,SZ) > 0,65
h0-hypothesis: r(SV,SZ) < 0.65

Secondary objectives:
1. Determination of comparability of intracardiac impedance measurements to echocardiographic reference parameters in assessment of changes in left-ventricular end-systolic volume (LVESV) in an acute setting.
2. Determination of comparability of intracardiac impedance measurements to the Finapres®- method in assessment of changes in stroke volume (SV) in an acute setting.
3. Assessment of the ability of the ICI to detect mid-term hemodynamic changes during cardiac reverse remodeling.
4. Collection of additional clinical data for analysis in the context of their meaning to the ICI-trend curve. Identification of additional suitable parameters for hemodynamic monitoring of the heart.
5. Safety assessments: Incidence and severity of Adverse Events, Incidence and severity of Adverse Device Effects.

Study design

Multi-center, international, non-randomized, noncontrolled, open-label, interventional study.

Intervention

The diagnostic ICI sensor will be activated in study context after CRD-D device implantation in all patients by special release code for measurment of chonic hemodynamic changes (the ICI data is sent daily to the Home Monitoring Serive Center via the Home Monitoring system). For provocation of acute hemodynamic changes of the heart an overdrive-pacing protocol using the implanted CRT-D system is performed. Patients enrolled to BIO.Detect HF II will be subjected to the protocol 2 months after CRT-D implantation. In total, measurement at five different heart rates will be performed: at intrinsic heart rate, intrinsic heart rate plus 30 bpm, intrinsic heart rate plus 10 bpm, intrinsic heart rate plus 20 bpm, and intrinsic heart rate plus 40 bpm. Between the different heart rates the patient will be given time to recover (~1 min) at intrinsic heart rates. For every scheduled pacing rate 6 Ao-VTI, CW Doppler / stroke impedance (SZ) pairs will be collected. Additional echocardiographic parameters will be assessed for every frequency after the SV-values have been collected: LVESV index, LVEDV index, LVEF, Biplane stroke volume (calculated), MR dP/dtmax, calculated MR volume, visual classification of mitral regurgitation (color Doppler) and PW SV (measured via PW-Doppler). The overdrive-pacing will be terminated as soon as measurements at five different pacing rates have been collected if not terminated before due to other reasons (patients clinical condition, negative threshold test).

Study burden and risks

The associated risk with an ICD implanation in study context are not study specific and not different from risks associated during routine CRT-D device implantation. The risks associated with over-drive pacing as described in protocol section 6.2 are minimized due to the fact that the physician will evaluate the clinical condition of each participation patient prior to the over-drive pacing. The patient will not undergo the over-drive pacing protocol if his/her condition does not allow for further testing. In addition the intracadiac impedance measurement is code-protected and can only be release in study context. Prior to over-drive pacing an automatic threshold test will be performed. If succesful the protocol will be released. If the study demonstrates that the new hemodynamic sensor (intracardia impedance measurment) works effectivly and safly, the feature will be released in routine clincal practice. The patients may benefit from it by better diagnostic methods towards better managment of their heart failure status.

Contacts

Public
Biotronik

Woermannkehre 1 1

Berlijn D-12539
DE
Scientific
Biotronik

Woermannkehre 1 1
Berlijn D-12539
DE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* Patients with an indication for CRT-D device implantation according to the opinion of the treating physician who were not implanted with a CRT-device before (de novo CRT-patients only).
* Patients being implanted with single and dual chamber ICDs before may be included in the study.
* Patients who are planned to be implanted with a BIOTRONIK Lumax740 HF-T device (or successor).
* Patients planned to be implanted with a bipolar LV-lead with a minimum distance of 15 mm between tip and ring.
* Patients implanted (or planned to be implanted) with a true bipolar RV-lead.
* Patients with NYHA class II and III (with both ischemic or non-ischemic etiology or dilative cardiomyopathy as underlying disease)
* Patient is willing and able to comply with the CIP and has provided written informed consent.
* Patient accepts Home Monitoring concept and has sufficient GSM/GPRS net coverage.
* Evaluable echocardiographic measurements.
* Patients with LVEF >= 15% and <= 35%
* LVEDD >= 55mm

* QRS >= 150ms

Exclusion criteria

* Patients with diagnosed persistent or permanent atrial fibrillation.
* Patients suffering from aortic valve stenosis or from more than a trace of aortic valve insufficiency patients with aortic valve prosthesis.
* Heart surgery performed in the 3 months prior to enrollment or planned for the time of study participation.
* PTCA expected within the first 3 months of study participation.
* Post-HTX or listed for HTX.
* Non-ambulatory patients.
* Patients requiring chronic renal dialysis.
* Life expectancy < 1 year due to a noncardiac disease.
* Patient age < 18 years.
* Patient is addicted to alcohol, medical drugs or illegal drugs.
* Limited contractual capability.
* Pregnant or breast-feeding women.
* Participation in another clinical trial.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	28-11-2012
Enrollment:	20
Type:	Actual

Medical products/devices used

Generic name:	Intracardiac Impedance Measurement feature in ICD: Lumax

	740 HF-T
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	20-09-2012
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	07-10-2013
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	24-02-2014
Application type:	Amendment
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
Other	Indiening bij clinicaltrial.gov is gepland.
CCMO	NL40608.075.12