

Optimisation and regulation of breathing in heart failure

Submission date 05/05/2010	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 06/05/2010	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 29/12/2020	Condition category Circulatory System	<input type="checkbox"/> Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
7352

Study information

Scientific Title

Optimisation and regulation of breathing in heart failure: a randomised interventional treatment trial

Acronym

DRN 370 (SRF Optimisation)

Study objectives

Evaluation of beat-by-beat continuous noninvasive blood pressure measurement by digital photoplethysmography to optimise haemodynamics in patients with an atrioventricular pacemaker for chronic heart failure:

1. Changes in atrioventricular and interventricular delays, within the range of settings typically used in clinical practice, will cause reproducible and significant changes in arterial pressure as measured by digital photoplethysmography (Finapres)
2. At higher heart rates, changes in atrioventricular and interventricular delay will have a more pronounced effect on arterial pressure than they do at lower heart rates
3. If echocardiographic measurement of stroke volume is able to identify an optimal setting for maximal stroke volume, that setting will correspond to a maximal or near-maximal systolic arterial pressure
4. Patients clinically considered non-responders will have a smaller increment in systolic arterial pressure than will the responders, when the device is switched from off to on
5. Dependency of haemodynamics on pacemaker settings will be similar, whether measured at rest or during exercise (low-level, steady state)

Immediate effects of higher-rate pacing or altered AV delay on periodic breathing:

6. Increasing heart rate through pacing significantly stabilises breathing pattern and reduces oxygen desaturation in awake patients with chronic heart failure and can also be used as a model of periodic breathing
7. The effect is prompt in effect, with a substantial stabilisation in the early few minutes after a change in heart rate
8. The effect is reversible, on a similarly rapid timescale, including with dynamic CO₂ administration
9. The stabilising effects are paralleled by a rise in cardiac output and fall in chemoreflex delay time, and the destabilising effects are paralleled by a fall in cardiac output and prolongation of chemoreflex delay time
10. Carefully-timed dynamic variation in rate or AV delay can achieve greater stability of breathing control than constant-rate pacing with the same mean rate

Dynamic therapy with inhaled carbon dioxide as a novel form of "pacing" to stabilise cardiorespiratory control in patients with chronic heart failure and periodic breathing:

11. In patients whose usual pattern of respiration is steady (i.e. non-periodic), alternating between CO₂ supplementation and normal inspired air for 30 second periods will generate a pattern resembling periodic breathing, which can be used as a model of periodic breathing
12. In patients with periodic breathing, dynamic intervention with alternation between CO₂ supplementation and normal air (with CO₂ given in the 30 seconds of the periodic breathing cycle with the lowest respiration) will worsen cardiorespiratory instability
13. In patients whose usual pattern of respiration is periodic, dynamic intervention with alternation between CO₂ supplementation and normal air (with CO₂ given in the 30 s with the highest respiration) will significantly stabilise cardiorespiratory control
14. Once the most effective timing strategy for dynamic therapy with CO₂ is determined by this study, application of this strategy achieves more stabilisation of cardiorespiratory control than is obtained by delivering the same average dose of CO₂ as a continuous stream

15. An automated algorithm, using respiratory excursion and/or end-tidal CO₂ data, can control the timing of delivery of CO₂ to improve cardiorespiratory control stability in a pacemaker model of periodic breathing

Ethics approval required

Old ethics approval format

Ethics approval(s)

Royal Brompton Hospital Research Ethics Committee approved (ref: 05/Q0404/018)

Study design

Single centre randomised interventional treatment trial

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied

Topic: Diabetes Research Network; Subtopic: Type 2; Disease: Cardiovascular disease

Interventions

All the sub-studies described below will be one-off visits for each patient with no long-term follow-up required.

Experimental design Study A (digital photoplethysmography to optimise haemodynamics in patients with atriobiventricular pacemaker):

Protocol for AV delay experiment: The experiment will be carried out at 4 heart rates: resting, 90, 110 and 130 bpm. At each rate, a series of AV delays will be trialled: 40 ms, 80 ms, 100 ms, 120 ms, 140 ms, 160 ms, 200 ms and 240 ms (if native AV conduction occurs at long AV delays, longer AV delay values will be omitted). A trial of an AV delay involves recording of a series of alternations of the pacemaker programming between that AV delay and a default values (120 ms). At each rate, a series of delays between ventricular activation (VV delays) will also be trialled (LV-RV delays of -40 ms, -20 ms, 4 ms [or nearest available value to 0], 20 ms, 40 ms) in a corresponding fashion. These will be performed with AV delay set to the value found to give the highest BP. The study will be repeated at 110 bpm (only).

Study B (Immediate effects of higher-rate pacing on periodic breathing in patients with chronic heart failure):

Protocol: With the patient positioned as indicated above, a pacemaker programmer telemetry

head will be secured over the pacemaker pulse. The programmed rate of the pacemaker in 16 periods of 10 minutes. This will comprise 4 cycles of 4 ten-minute periods, with each period consisting of resting rate, followed by 20 bpm above resting, followed by resting rate again, and then 40 bpm above resting. This protocol gives 80 minutes of resting rate, 40 minutes of 20 bpm above resting, and 40 minutes of 40 bpm above resting. It gives several onset and offset events, to allow time course of effect (if any) to be detected. It spreads out all like transitions over time, minimising the opportunity for secular changes in stability status to confound results. Dynamic CO₂ will then be applied to the induced oscillations.

Study C (Dynamic therapy with inhaled carbon dioxide as a novel form of "pacing"):

Protocol: Patients will be monitored as above. In addition, a loose-fitting, non-occlusive face-mask will be applied. A fine-bore catheter will be held in position by the mask, directing toward the left nostril a potential flow of humidified gas (3% CO₂, 21% O₂, balance nitrogen). The flow will be controlled by an electrical actuator and can change position in less than 0.5 s. Directed towards the right nostril will be an aspiration catheter allowing the metabolic cart to monitor gas concentration, and a thermistor. The analogue O₂ and CO₂ signals produced by the cart's gas sensors will be read via our custom real-time data-monitoring system, which also receives the signals from the respiratory strain gauge, earlobe oximeter and thermistor (and heart rate and blood pressure). A different module of the same software will control the electrical actuator that regulates delivery of CO₂. Delivery of CO₂ is programmable to be off, on at a constant level, alternating with a fixed period, or alternating in synchronisation to biosignal inputs. The regulatory algorithm can be programmed to utilise a combination of the inputs (including the system's knowledge of what therapy has been delivered) and to create independent cycling daemons that synchronise with and then track the rhythm of oscillation in the cardiorespiratory system, even when the externally-observable oscillations have been damped by therapy.

Intervention Type

Other

Phase

Not Applicable

Primary outcome measure

All parameters are measured continuously throughout the recordings:

Substudy 1: the effect on blood pressure of changes in AV and VV delay of a pacemaker

Substudy 2: the size of the change in end tidal carbon dioxide and ventilation achievable from a change in pacemaker setting and the application of dynamic CO₂

Substudy 3: the size of the change in ventilation achievable from administration of CO₂

Secondary outcome measures

No secondary outcome measures

Overall study start date

01/08/2005

Completion date

30/09/2010

Eligibility

Key inclusion criteria

1. Aged 18 - 80 years, either sex
2. Chronic systolic heart failure confirmed by transthoracic echo

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

Planned sample size: 140; UK sample size: 140

Key exclusion criteria

1. Severe lung disease
2. Any condition that would preclude participants from lying comfortably on a couch for the duration of the study

Date of first enrolment

01/08/2005

Date of final enrolment

30/09/2010

Locations**Countries of recruitment**

England

United Kingdom

Study participating centre

Imperial College London

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SW7 2AZ

Sponsor information**Organisation**

Imperial College London (UK)

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Sponsor type

University/education

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<http://www3.imperial.ac.uk/>

ROR

<https://ror.org/041kmwe10>

Funder(s)

Funder type

Charity

Funder Name

British Heart Foundation (BHF) (UK)

Alternative Name(s)

the_bhf, The British Heart Foundation, BHF

Funding Body Type

Private sector organisation

Funding Body Subtype

Trusts, charities, foundations (both public and private)

Location

United Kingdom

Results and Publications

Publication and dissemination plan

Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	dynamic CO2 therapy results	12/08/2014	29/12/2020	Yes	No