ISRCTN67500535 https://doi.org/10.1186/ISRCTN67500535

The effects of adaptive servo ventilation on survival and frequency of cardiovascular hospital admissions in patients with heart failure and sleep apnea

Submission date
29/04/2010

Recruitment status
No longer recruiting

Registration date
30/04/2010

Overall study status
Completed

Last Edited
27/12/2023

Condition category
Circulatory System

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Heart failure is caused by the heart not pumping enough blood around the body at the right pressure. People with heart failure often have breathing problems while they sleep (sleep apnea), such as obstructive sleep apnoea, where the walls of the throat narrow and interrupt breathing, and central sleep apnoea, where the brain fails to send signals to the breathing muscles. Adaptive Servo Ventilation (ASV) machines can be used to treat sleep apnoea by providing support to regular breathing during sleep. This study will test whether ASV treatment improves outcomes for heart failure patients with obstructive sleep apnea and/or central sleep apnea.

Who can participate?
Heart failure patients aged 18 or over with obstructive sleep apnea and/or central sleep apnea.

What does the study involve?
Participants are randomly allocated to receive either standard treatment for heart failure or both standard treatment and an ASV machine to use during sleep.

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
Toronto Rehabilitation Institute (Canada)

When is the study starting and how long is it expected to run for?
May 2010 to September 2017

Who is funding the study?
1. Canadian Institutes of Health Research (CIHR) (Canada)
2. Philips Respironics Inc.

Who is the main contact?
Dr Douglas Bradley

Contact information

Type(s)
Scientific

Contact name
Dr Douglas Bradley

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT01128816

Secondary identifying numbers
IS2-95225

Study information

Scientific Title
Multi-centre, randomized study to assess the effects of adaptive servo ventilation on survival and frequency of cardiovascular hospital admissions in patients with heart failure and sleep apnea: the ADVENT-HF trial

Acronym
ADVENT-HF

Study objectives
This study will test the hypothesis that in a long-term multi-centre randomized clinical trial (RCT), treatment of Obstructive Sleep Apnea and/or Central Sleep Apnea with Adaptive Servo Ventilation in subjects with Heart Failure will:
1. Reduce the composite primary endpoint of death from all causes, cardiovascular

hospitalizations, new onset atrial fibrillation/flutter requiring anticoagulation but not hospitalization, or delivery of an appropriate shock from an ICD, not resulting in hospitalization
2. Cause regression of left ventricular remodelling
3. Reduce plasma levels of N-terminal pro-hormone of brain natriuretic peptide (NT-proBNP)
4. Improve submaximal exercise capacity
5. Improve quality of life

Ethics approval required
Old ethics approval format

Ethics approval(s)
University Health Network Research Ethics Board, University of Toronto, 11/03/2010, ref: REB # 09-0834-B

Study design
Multicentre randomized parallel-group open label 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 contact Dr. Douglas Bradley [douglas.bradley@utoronto.ca] for more information

Health condition(s) or problem(s) studied
Treatment of sleep apnea to improve outcomes in patients with heart failure

Interventions
Eligible participants will be randomized to receive either standard optimized treatment for Heart Failure conforming to national guidelines plus Adaptive Servo Ventilation to be worn during sleep or standard optimized treatment for Heart Failure conforming to national guidelines alone.

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Adaptive Servo Ventilation device

Primary outcome measure
Time from randomization to death from all causes or to the first hospitalization for a cardiovascular cause or new onset atrial fibrillation/flutter requiring anticoagulation but not hospitalization, or delivery of an appropriate shock from an ICD, not resulting in hospitalization. The trial will end when 540 primary outcomes have been adjudicated.

Secondary outcome measures
1. Time from randomization to death from any cause
2. Time from randomization to CV hospitalizations, new onset atrial fibrillation/flutter requiring anticoagulation but not hospitalization, or delivery of an appropriate shock from an ICD, not resulting in hospitalization
3. Number of days alive not hospitalised
4. Changes in left ventricular function at 6 months post randomization
5. Changes in plasma NT-proBNP levels at 6 months post randomization
6. Occurrence of CRT or AICD implantation
7. Change in 6-minute walk test distance at 6 months post randomization
8. Changes in American Heart Association/American College of Cardiology stages of HF and changes in New York Heart Association class measured at 1 month, 3 months, 6 months and every 6 months thereafter post randomization until study end
8. Changes in apnea-hypopnea index (AHI) measured at 1 month post randomization
9. Changes in quality of life assessed by the Minnesota Living With Heart Failure questionnaire and Epworth Sleepiness Scale measured at 1 month, 3 months, 6 months and every 6 months thereafter post randomization until study completion

Overall study start date
10/05/2010

Completion date
01/09/2017

Eligibility

Key inclusion criteria
1. Male or female 18 years or older
2. Documented American Heart Association Stages B, C and D HF due to ischemic, idiopathic or hypertensive causes for at least 3 months
3. Left ventricular ejection fraction (LVEF) ≤ 45%, as determined by echocardiography at screening
4. On optimal medical therapy conforming to contemporary national or American Heart Association guidelines, as determined by the patient's primary cardiologist
5. No changes in active cardiac medication during 2 weeks prior to randomization; if patient is on a beta-blocker, beta-blocker therapy must have been started at least 3 months prior to randomization
6. Sleep apnea with an Apnea/Hypopnea Index (AHI) ≥ 15, which will be divided into Obstructive Sleep Apnea (OSA) (greater than or equal to 50% events obstructive), or Central Sleep Apnea (CSA) (> 50% of events central in nature). For patients with OSA, an Epworth Sleepiness Scale (ESS) score of ≤ 10 and no or mild daytime sleepiness (by the International Classification of Sleep Disorders: occasionally falling asleep during passive situations, is considered mild and not pathological). For patients with CSA, no ESS or subjective sleepiness criteria will be used, since

there is very little evidence that CSA is associated with hypersomnolence, or that treating CSA reduces sleepiness.
7. Written informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
860 randomized participants

Total final enrolment
731

Key exclusion criteria
1. HF due to primary valvular heart disease
2. Presence of moderate to severe mitral insufficiency due to intrinsic mitral valve disease. If mitral insufficiency is secondary to the cardiomyopathic state, patients can be included
3. Hypertrophic obstructive or restrictive or post partum cardiomyopathy
4. Exercise capacity limited by class IV angina pectoris
5. Acute Myocardial Infarction (MI), cardiac surgery, Percutaneous Coronary Intervention (PCI), Automatic Implantable Cardioverter Defibrillator (AICD)-if implanted for pacing function or secondary prevention , or Cardiac Resynchronization Therapy (CRT) within 3 months of randomization; only a 2-week waiting period before randomization is required if the AICD is implanted for primary prevention
6. Active myocarditis
7. Planned AICD or CRT
8. Presence of a left-ventricular assist device (LVAD)
9. Transplanted heart or expected to receive a transplanted heart within the next 6 months
10. Pregnancy
11. Current use of ASV, BiPAP, CPAP or mandibular advancement device for treatment of sleep apnea or treatment with any investigational therapy during the last 4 weeks (including approved therapies being used in unapproved indications)
12. A clinical history that would interfere with the objectives of this study or that would in the investigator's opinion reduce 5 year life expectancy
13. Any other medical, social, or geographical factor, which would make it unlikely that the patient will comply with the study procedures (e.g. alcohol abuse, lack of permanent residence, severe depression, disorientation, distant location, or history of non-compliance)
14. Any contraindication to ASV therapy as detailed in the device provider manual

Date of first enrolment
10/05/2010

Date of final enrolment
30/04/2017

Locations

Countries of recruitment
Brazil

Canada

France

Germany

Japan

Spain

United Kingdom

United States of America

Study participating centre
University Health Network - Toronto Rehabilitation Institute
550 University Avenue
Toronto
Canada
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Sponsor information

Organisation
University Health Network/Toronto Rehabilitation Institute (Canada)

Sponsor details
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Sponsor type
Research organisation

ROR
https://ror.org/042xt5161

Funder(s)

Funder type
Research organisation

Funder Name
Canadian Institutes of Health Research (ref: IS2-95225)

Alternative Name(s)
Instituts de Recherche en Santé du Canada, Canadian Institutes of Health Research (CIHR), CIHR_IRSC, Canadian Institutes of Health Research | Ottawa ON, CIHR, IRSC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Canada

Funder Name
Unrestricted gift from Philips Respironics Inc.

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?
Other publications	Polysomnography results in participants with Cheyne-Stokes respiration with central sleep apnea (CSR-CSA)	15/11/2017	10/04/2019	Yes	No

Results article	21/12/2023	27/12/2023	Yes	No