

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	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 30/04/2010	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 27/12/2023	Condition category Circulatory System	<input type="checkbox"/> 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

Contact details

Toronto Rehabilitation Institute
550 University Avenue
12 floor
Toronto
Canada
M5G 2A2

Additional identifiers

ClinicalTrials.gov (NCT)

NCT01128816

Protocol serial number

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

Study type(s)

Treatment

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(s)

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.

Key secondary outcome(s)

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

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) $\leq 45\%$, 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

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Sex

All

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

United Kingdom

Brazil

Canada

France

Germany

Japan

Spain

United States of America

Study participating centre

University Health Network - Toronto Rehabilitation Institute

550 University Avenue

Toronto

Canada

M5G 2A2

Sponsor information

Organisation

University Health Network/Toronto Rehabilitation Institute (Canada)

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, The Canadian Institutes of Health Research (CIHR), Canadian Institutes of Health Research (CIHR), Canadian Institutes of Health Research | Ottawa ON, CIHR - Welcome to the Canadian Institutes of Health Research, 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

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		21/12/2023	27/12/2023	Yes	No
Other publications	Polysomnography results in participants with Cheyne-Stokes respiration with central sleep apnea (CSR-CSA)	15/11/2017	10/04/2019	Yes	No