ESTIM LVFP Synopsis

Observational Clinical Study for the Evaluation of Left Ventricular Filling Pressures Using the Apple Watch and 12-Lead ECG Enhanced by an Artificial Intelligence Algorithm

Version V3.1 — October 15, 2024
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Sponsor

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STUDY SUMMARY

Study Title

Observational Clinical Study for the Evaluation of Left Ventricular Filling Pressures Using the Apple Watch (ECG App Version 2.0) and 12-Lead ECG Enhanced by the Cardiologs Artificial Intelligence Algorithm.

Protocol Version and Date

Version 6.1 — October 15, 2024

Investigational Medical Device

Cardiologs Platform

Participating Center

Institut Cardiologique Paris Sud (Massy)

Clinical Investigation Objectives

Primary Objective

To evaluate the performance of detecting elevated left ventricular filling pressures from an Apple Watch ECG optimized by Cardiologs Artificial Intelligence (AI_AW), using conventional transthoracic echocardiography (TTE) as the reference standard.

Secondary Objectives

- Evaluation of elevated left ventricular filling pressure detection using an AI-enhanced 12-lead ECG (AI_12D) compared with conventional transthoracic echocardiography (TTE).
- Evaluation of elevated left ventricular filling pressure detection using AI-enhanced 12-lead ECG (AI_12D) in the cohort of patients classified as "indeterminate" by conventional TTE estimation methods.

Exploratory Analysis

- Evaluation of the accuracy of left ventricular ejection fraction (LVEF) detection from both 12-lead ECG and Apple Watch ECG optimized by AI (AI_12D and AI_AW), compared with standard transthoracic echocardiography (TTE), according to conventional heart failure classification thresholds:
    - LVEF > 50%
    - LVEF 40–50%
    - LVEF < 40%

Additional Objectives

- Evaluation of elevated left ventricular filling pressure detection using AI-enhanced 12-lead ECG and Apple Watch ECG (AI_12D and AI_AW) compared with standard TTE in a longitudinal cohort of patients admitted to a cardiac intensive care unit.

Methodology

This is an observational, non-interventional, prospective, open-label, single-center, non-randomized clinical investigation involving a CE-marked medical device used within its intended purpose.

Each patient referred for transthoracic echocardiography who consents to participate will undergo:

- simultaneous Apple Watch ECG recording,
- and 12-lead ECG recording,

performed before and/or after conventional transthoracic echocardiography (TTE).

Apple Watch ECG Recording

- Performed with the watch worn on the left wrist.
- Recording completed within a maximum of 3 minutes relative to the 12-lead ECG.

Echocardiography Timing

- TTE performed within approximately 6 hours of the ECG recordings.

All echocardiograms will include objective diastolic function quantification using conventional parameters for grading filling pressures.

Each echocardiogram will be blindly reviewed by an expert echocardiographer to determine left ventricular filling pressure status:

- elevated,
- normal,
- indeterminate.

Left ventricular ejection fraction will also be systematically assessed.

Endpoints

Primary Endpoint

- Detection of elevated filling pressures by AI_AW compared with conventional transthoracic echocardiography (TTE).

Secondary Endpoints

- Comparison of elevated filling pressure detection performance between AI_AW and AI_12D compared with conventional TTE.
- Classification of filling pressures (elevated, normal, indeterminate) by AI_AW and AI_12D compared with conventional TTE diagnosis.

Exploratory Endpoint

- Detection of left ventricular ejection fraction (LVEF) by AI_AW and AI_12D compared with transthoracic echocardiographic assessment according to conventional heart failure thresholds.

Statistical Analysis Methods

Data Description

Descriptive statistics will be provided for all collected data:

Quantitative Variables

- number of observations,
- mean,
- standard deviation,
- median,
- quartiles,
- minimum and maximum observed values,
- number of missing values.

Qualitative Variables

- number of observations,
- frequency and percentage by category,
- number of missing values.

Diagnostic Performance Evaluation

Classification according to the measurement method:

- AI_AW wrist,
- AW wrist,
- AI_12D,

compared with conventional echocardiography interpreted blindly by the expert echocardiographer for detecting elevated filling pressures.

Associated indicators will be calculated:

- sensitivity,
- specificity,
- Youden index,
- misclassification rate,
- positive predictive values,
- kappa coefficient.

Diagnostic performance for elevated filling pressure detection will be assessed using sensitivity and specificity values with associated 95% confidence intervals.

The frequency of uninterpretable Apple Watch ECGs will also be described.

Descriptions of adverse events and concomitant treatments occurring during the clinical investigation will also be provided.

Exploratory retrospective analyses may be conducted on 12-lead ECG and Apple Watch data for left ventricular ejection fraction detection performance.

Eligibility Criteria

Inclusion Criteria

1. Patient aged 18 years or older, capable of providing informed consent and willing to participate.
2. Outpatient referred for conventional cardiac echocardiography.
3. Hospitalized patient in medical or surgical units, including cardiac intensive care and postoperative cardiac surgery units, referred for conventional echocardiography.
4. Emergency department patient referred for conventional echocardiography.
5. Patient who has read the information notice and provided written informed consent before any study-related procedure.
6. Patient affiliated with a social security system.

Exclusion Criteria

1. Patient with complex congenital heart disease.

2. Heart transplant recipient.
3. History of mitral valve surgery (mechanical valve, bioprosthesis, annuloplasty).
4. Patient with pacemaker/implantable cardioverter-defibrillator.
5. Significant degenerative mitral annular calcification (MAC).
6. Subject related to the investigator or directly involved study personnel.
7. Patient unable to provide consent, minors, or legally protected adults.

Number of Patients

A 12-month inclusion period is planned to enroll a total of **200 patients**, including:

- outpatients,
- hospitalized patients,
- emergency department patients.

Duration of Clinical Investigation for Patients

Minimum Study Duration

- 1 day

Maximum Study Duration

- Main cohort: 1 day
- Longitudinal cohort: 2 or 3 one-day visits according to routine patient follow-up.

Patients referred for conventional echocardiography will undergo simultaneous 12-lead ECG and Apple Watch recordings before and/or after echocardiography.

No additional procedures will be performed after hospital discharge.

The clinical investigation begins when the first patient is enrolled and ends when the last patient completes the final recording.

Benefits / Risks / Constraints

Benefits

No immediate direct clinical benefit is expected for participants, as this is an observational study only.

Potential future benefits include the use of AI-enhanced smartwatch recordings as an autonomous monitoring device capable of detecting potentially reversible cardiac conditions in hospitalized or ambulatory cardiovascular patients.

Risks

No risks are expected for study participants.

No additional risk is anticipated from extra Apple Watch recordings or analyses.

The Cardiologs AI analysis will not be used to guide medical decisions. All medical decisions will rely solely on conventional echocardiographic interpretation by the treating cardiologist.

Data will be analyzed retrospectively for research purposes only.

Constraints

No medical constraints. All investigations will be performed according to routine clinical practice.

Clinical Investigation Timeline

- Total planned duration: 14 months
- Start of enrollment: July 1, 2024
- Enrollment duration: 12 months
- Planned end of enrollment: July 1, 2025
- Planned end of data collection: September 1, 2025

Clinical Investigation Flow Chart

Main Cohort — Visit 1 (Day 1)

- Patient informed consent
- Inclusion/exclusion criteria review
- Physical examination*

- Medical history*
- Concomitant treatments*
- 12-lead ECG*
- Apple Watch ECG
- TTE
- Adverse events recording

Longitudinal Cohort — Visits 2 and 3 (if applicable)

- Repeat ECG and echocardiographic evaluations according to routine follow-up.

* Procedures performed according to standard care.

Notes:

1. Inclusion/exclusion criteria must be verified before the first Apple Watch ECG.
2. Apple Watch ECG recorded simultaneously with 12-lead ECG.
3. One or more ECGs may be performed according to routine practice.
4. Adverse events are recorded from consent until the final ECG.
5. Visits V2 and V3 each correspond to one day according to routine patient follow-up.

List of Abbreviations

- AW: Apple Watch
- CE: European Conformity
- CPP: Ethics Committee
- eCRF: Electronic Case Report Form
- ECG 12D: 12-lead Electrocardiogram
- AE: Adverse Event
- SAE: Serious Adverse Event
- PVC: Premature Ventricular Contractions
- AF: Atrial Fibrillation

- AI: Artificial Intelligence
- RM: Reference Methodology
- VT: Ventricular Tachycardia
- TTE: Transthoracic Echocardiography