Asian Sudden Cardiac Death in Heart Failure (ASIAN-HF) registry

NCT01633398

Synopsis

1. BACKGROUND

Heart failure (HF) is a major public health problem worldwide. The World Health Organization has projected that the largest increases in cardiovascular disease worldwide are occurring in Asia, due to rapidly increasing rates of smoking, obesity, dyslipidaemia, and diabetes among Asians. Thus the burden of HF is expected to reach epidemic proportions in Asia.

Yet in sharp contrast to the wealth of data regarding HF in Western nations, epidemiological data are scarce in Asian patients with HF. The limited available evidence suggests that there are important ethnic-related differences specific to this region, and a large treatment gap exists with regards to proven therapies that may contribute to the high mortality and morbidity rates of HF in Asia. The lack of data regarding the mortality burden of HF in Asians has contributed to underuse of potentially life-saving therapies. Sudden cardiac death (SCD) accounts for ~50% of deaths in HF according to Western statistics, with risk of death increasing particularly with LVEF<40%. The prophylactic implantation of a defibrillator in at-risk patients with reduced LVEF has been shown to reduce SCD and, therefore, has become standard practice in Western nations. However, in Asia there is resistance to adoption of similar preventive measures and continued controversy regarding the risk of SCD among Asians.

Given the public health importance of HF, the epidemic of cardiovascular disease in Asia, and the availability of potentially lifesaving drugs and devices, but ill-defined barriers to their application in Asians, there is an urgent need to fill the knowledge gaps regarding the mortality burden of HF, as well as to understand the barriers to preventive drug and device therapy, among Asian patients with HF. Such knowledge is critical to define the unmet clinical needs among Asian patients with HF, and to guide clinical decisions as well as healthcare resource planning to meet these needs. The Asian Sudden Cardiac Death in Heart Failure (ASIAN-HF) registry is being initiated to meet these manifest needs. This is a fundamental step towards the long-term goal of improving outcomes among the large and growing population of patients with HF in Asia.

2. AIMS AND OBJECTIVES OF THE ASIAN-HF STUDY

The Asian Sudden Cardiac Death in Heart Failure (ASIAN-HF) registry is the first prospective multinational Asian registry of patients with symptomatic HF (stage C) initiated towards determining the burden of morbidity and mortality in Asian patients. HF patients at least 18 years old were recruited from 46 medical centres across 11 Asian regions. Data on demographics, previous medical history, clinical symptoms, functional status, standard 12-lead electrocardiography and transthoracic echocardiography were collected.

In the HFrEF population, the *specific objectives* included:

I. The primary objective of this study is to determine the incidence of sudden cardiac death (SCD) in Asian patients diagnosed with HF and followed in representative Asian cardiovascular centres.
II. To determine the incidence of all-cause and cause-specific death and hospitalization among Asian patients with HF.
III. To determine the risk factors for SCD, all-cause death, other cause-specific death, and hospitalization among Asian patients with HF.

IV. To understand the socio-cultural barriers to device therapy among Asian patients.
V. To compare the genetic variants between the two phenotypes of reduced versus preserved ejection fraction (HFrEF versus HFpEF).

In 2013, a protocol amendment included patients with HFpEF (ejection fraction ≥50%).

3. STUDY DESIGN

This is a prospective, observational, multinational, multicentre Asian registry of patients with symptomatic HF (Stage C), including both HFrEF (ejection fraction <40%) and HFpEF (ejection fraction ≥50%). The study involved representative medical centres across Asia (China and Hong Kong, South Korea, Taiwan, Thailand, Indonesia, Philippines, India, Japan, Malaysia, and Singapore). Eligible sites were centres covering a broad spectrum of medical, cardiology, and HF specialty units that regularly admit patients with acute HF and follow patients with chronic HF in outpatient clinics. Site selection was based on size of the country, geographic location of the site within the country, patient population served, HF patient volume, and availability of expertise in echocardiography.

The study was conducted in compliance with the protocol, International Conference on Harmonization Good Clinical Practice, E6, and the applicable national regulations in each region as to assure that the rights, safety and well-being of the participating study patients are protected, in accordance with the ethical principles that have their origin in the Declaration of Helsinki (2008).

Publications from the ASIAN-HF registry are guided by a publication charter and overseen by a publications committee. Each outcome event and its cause were adjudicated by a central committee using pre-specified criteria.

4. ETHICS

Independent Ethics Committee (IEC) or Institutional Review Board (IRB)

At all regions and sites, IEC/IRB approvals were obtained for the study before any study activities commenced. All study amendments were submitted to IEC/IRB and approved prior to implementation of the amendment activities.

Ethical Conduct of the Study

The study was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki.

Patient Information and Consent

Patient informed consent was obtained prior to the commencement of any screening or study procedures. The investigator at each site provided full and adequate oral and written information about the nature, purpose and available details of possible risks and benefit of the study to each potential participant. Patients were also notified that they are free to discontinue from the study at any time.

5. STUDY INCLUSION AND EXCLUSION CRITERIA

Inclusion criteria

i. Adults (>18 years),

ii. Symptomatic HF (Stage C HF and any New York Heart Association [NYHA] class functional status). Patients should have a current diagnosis of symptomatic HF within 6 months of an episode of decompensated HF, which either:

a. resulted in a hospital admission (primary diagnosis) or

b. was treated in out-patient clinic,

iii. Left ventricular ejection fraction <40% (HFrEF) or left ventricular ejection fraction ≥50% (HFpEF) on baseline echocardiography,

iv. Available for follow-up over 3 years.

Exclusion criteria

i. Severe valve disease as the primary cause of HF,

ii. For the HFpEF population: a documented history of reduced ejection fraction (<50%) at any time prior to recruitment. In other words, patients with current HFpEF who previously had HFrEF will be excluded.

iii. Life threatening co-morbidity with life expectancy of <1 year,

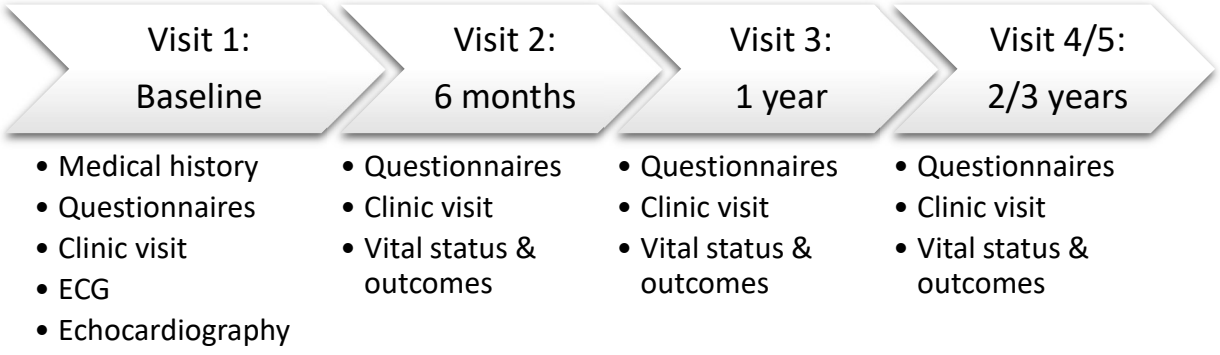
iv. Unable or unwilling to give consent,

v. Concurrent participation in a clinical therapeutic study which requires patient consent.

6. DATA COLLECTION

Study Schedule and Data Variables

Patients will be recruited over 2 years and followed up to 3 years, according to the schedule:



Demographic data and clinical data including previous medical, clinical signs/symptoms and functional status, and medication use will be collected. Standard 12-lead electrocardiography Standard resting 12-lead ECG will be performed at each centre and analysed for rate, rhythm, axes, intervals, conduction abnormalities and arrhythmias, and evidence of prior myocardial infarction or chamber enlargement. Standard transthoracic echocardiography will also be

performed at each centre according to internationally accepted guidelines and will include assessment of LVEF and dimensions, left atrial dimension, LV diastolic function, stroke volume, and cardiac output. Questionnaires administered during the study include the Patient Profile Questionnaire, Visual Analogue Scale (VAS) for Current Health Perception, Kansas City Cardiomyopathy Questionnaire (KCCQ) and the Device Therapy Perception Questionnaire.

Outcome determination and adjudication

The outcomes of interest are all-cause and cause-specific death and hospitalizations, diagnosed according to Framingham criteria for the clinical diagnosis of congestive HF. Each outcome event and its cause are adjudicated using pre-specified criteria by a central event adjudication committee comprising members of the Steering Committee. The data from the case report forms, death certificates, hospital discharge summaries will be reviewed independently by members of the event adjudication committee and adjudicated based on criteria outlined in the event adjudication committee charter. Briefly, all deaths and hospitalizations are classified as cardiac or noncardiac, with more specific categories assigned as permitted by the circumstances of the clinical event.

7. STUDY RECRUITMENT

Global Recruitment Summary

Total study recruitment – 6376 participants

Total HFrEF – 4779 participants

Total HFpEF – 1550 participants

EF criteria not met for HFrEF or HFpEF - 47 participants

Total genetic samples collected – 1034 samples

Recruitment by region

Region	Total Recruitment
China	488
Hong Kong	104
India	1920
Indonesia	295
Japan	678
Korea	382
Malaysia	638
Philippines	113
Singapore	700
Taiwan	845
Thailand	213
Total	**6376**