JACC: CARDIOVASCULAR IMAGING
VOL. 10, NO. 3, 2017

ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER
http://dx.doi.org/10.1016/j.jcmg.2016.11.015

ORIGINAL RESEARCH

Imaging-Guided Cardioprotective Treatment in a Community Elderly Population of Stage B Heart Failure

Hong Yang, BMED,[a] Kazuaki Negishi, MD, PHD,[a] Ying Wang, BMED, MS,[a] Mark Nolan, MBBS,[a] Thomas H. Marwick, MBBS, PHD, MPH[a,b]

ABSTRACT

OBJECTIVES The purpose of the study was to evaluate the benefit of care guided by the detection of stage B heart failure (SBHF) using advanced echocardiography for the reduction of new HF in the community.

BACKGROUND The detection of nonischemic SBHF has been facilitated by advanced echocardiographic imaging modalities. However, improved outcomes have not been proven as they are predicated on benefit of treatment.

METHODS Between September 13, 2013 and November 6, 2015, 618 asymptomatic community-based patients with HF risks (age 71 ± 5 years) were randomized to care guided by advanced echocardiography (myocardial deformation and detailed diastolic function) versus usual care. Evidence of SBHF led to advice to the patients and their primary physicians to initiate treatment with angiotensin-converting enzyme inhibition and beta-adrenoceptor blockade. The trial followed the PROBE (Prospective Randomized Open Blinded Endpoint) design. Participants were followed for 1 year for the primary composite endpoint of death from cardiovascular causes and new HF.

RESULTS Advanced echocardiography identified 219 as having SBHF and treatment was advised. Over a mean follow-up of 13 ± 6 months, 67 reached the primary endpoint. The incidence rate of HF was no different between the 2 arms ($p = 0.47$), likely because only 43% initiated therapy, and only 9% achieved target dose. Among subjects needing therapy on the basis of imaging and adherence to therapy, imaging-guided care showed a 77% lower hazard for the primary outcome ($p = 0.04$).

CONCLUSIONS The detection of SBHF from strain and diastolic function evaluation was associated with a higher incidence of incidence HF and death. The efficacy of pharmacological intervention with angiotensin-converting enzyme inhibition and beta-adrenoceptor blockade is limited by its uptake, and alternative strategies should be considered. (Tasmanian Study of Echocardiographic Detection of Left Ventricular Dysfunction [TAS-ELF]; ACTRN12614000080628) (J Am Coll Cardiol Img 2017;10:217–26) © 2017 by the American College of Cardiology Foundation.

Stage B heart failure (SBHF) has been defined in the American College of Cardiology/American Heart Association guidelines to include asymptomatic patients with abnormal left ventricular (LV) structure or function (1). Patients with SBHF are at higher risk for developing overt heart failure (HF) (2). In contrast to stage A HF ([SAHF], i.e., HF risk factors) (3), where therapy is directed toward the control

From the [a]Menzies Institute for Medical Research, Hobart, Tasmania, Australia; and the [b]Baker-IDI Heart and Diabetes Institute, Melbourne, Victoria, Australia. This study was partially supported by Tasmanian Community Fund, Hobart and Diabetes Australia, Melbourne and Siemens Healthcare Australia, Melbourne, Australia. None of the funding agencies had any role in design, analysis, or interpretation of this study. Dr. Yang is supported by a Health Professional Scholarship from the National Heart Foundation of Australia (100307). Dr. Negishi is supported by an award from the Select Foundation. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose. Pamela Douglas, MD, served as the Guest Editor for this article.

Manuscript received September 12, 2016; revised manuscript received November 1, 2016, accepted November 3, 2016.

ABBREVIATIONS AND ACRONYMS

A = peak late diastolic velocity

ACEi = angiotensin-converting enzyme inhibitor

AE = advanced echocardiography arm

AF = atrial fibrillation

ARB = angiotensin-receptor blocker

BB = beta-blocker

CV = cardiovascular

DD = diastolic dysfunction

E = mitral inflow peak early diastolic velocity

e' = peak early mitral annular tissue Doppler velocity

EF = ejection fraction

GLS = global longitudinal strain

HF = heart failure

HTN = hypertension

LV = left ventricular

SAHF = stage A heart failure

SBHF = stage B heart failure

UC = usual care arm

of cardiovascular (CV) risk factors, cardioprotective therapies are recommended in SBHF (1), on the basis of trials showing pharmacological interventions to delay and reduce the burden of HF in the SBHF population (4,5). The difference between SAHF and SBHF is a problem, because although highly prevalent, nonischemic SBHF requires an effective screening strategy for its recognition. Whereas modern imaging techniques may be able to provide this strategy, their incorporation into routine care needs evidence that management will be altered.

Accordingly, we developed a community-based screening program in elderly patients for detection of SBHF using echocardiography and subsequent cardioprotection. Our primary aims were to assess whether imaging-guided cardioprotective therapy, when added to usual care (UC), would reduce the rate of incident heart failure and to assess the feasibility of coupling an effective community screening program with interventional treatment in high-risk asymptomatic elderly individuals with SBHF.

METHODS

STUDY DESIGN. The TAS-ELF (Tasmanian Study of Echocardiographic Detection of Left Ventricular Dysfunction) is a community-based screening and interventional program. The study followed a PROBE (Prospective Randomized Open Blinded Endpoint) design (6). Individuals were randomized to either undergo an imaging-guided screening strategy for early detection and treatment of SBHF or to continue with usual care (7). The data were collected at various clinical sites within the State of Tasmania, Australia.

SEE PAGE 227

PATIENT SELECTION. Asymptomatic community-based patients (≥65 years of age) with HF risks volunteered for enrolment through local community presentations and media advertising. Patients were eligible for inclusion if they had SAHF risk factors (1), which include the following: hypertension ([HTN], based on blood pressure ≥140/90 mm Hg and self-report of HTN including antihypertensive medication); type 2 diabetes mellitus (based on self-report of diagnosis including medical management); obesity (body mass index ≥30 kg/m^2); previous chemotherapy; family history of HF; previous history of heart disease (but not existing HF). We excluded subjects with the following: symptoms or a known history of HF; known coronary artery disease; more than moderate valvular heart disease; reduced LV ejection fraction (EF) (<40%) on baseline echocardiography; already taking both trial medication, beta-blocker (BB) and angiotensin-converting enzyme inhibitor (ACEi)/angiotensin-receptor blocker (ARB), at baseline and contraindication of BB and/or ACEi and ARB. We also excluded those in whom we were unable to acquire interpretable images from baseline echocardiography (inclusion and exclusion in Online Table 1).

ENDPOINT. The primary composite endpoints were incident HF and death from CV causes. Potential HF symptoms were assessed through regular follow-up phone calls, followed by symptom surveillance questionnaires and clinical visits. New onset HF was adjudicated by a blinded endpoint committee using Framingham criteria at 1 year. Loss to follow-up was defined as not having replied for evaluation in ≥2 months.

SAMPLE SIZE. Sample size was calculated based on the following: 1) an expected prevalence of abnormal cardiac function in ~50% using advanced echocardiographic imaging; 2) an expected 7.5% annual rate of loss to follow-up; 3) a previously reported 12% annualized rate of incident HF among patients with evidence of SBHF who are receiving UC (8); 4) assumption of a 50% reduction of events with intervention compared with UC. A sample size of 400 in each randomized group would provide 80% power to document the benefit of therapy at a 2-sided $\alpha = 0.05$.

The trial was monitored by the Data and Safety Monitoring Board with termination guidelines for futility (if conditional probability of rejecting the null hypothesis was unlikely to achieve statistical significance) and feasibility (if recruitment or other aspects of its conduct were unable to fulfil requirements due to unforeseen circumstances).

RANDOMIZATION. Randomization was done using a central web-based program with adaptive allocation stratified by diabetes status. The eligible participants were randomized to advance echocardiographic (AE) imaging (involving measurement of global longitudinal strain [GLS] and diastolic function) versus UC (continuing with their UC treatment for primary risk factors such as HTN and diabetes). The randomization list and intervention list were prepared by assigned persons who were blinded to details of the investigations.

PATIENT REPORT OUTCOME MEASURES AND FUNCTIONAL CAPACITY. All participants enrolled in the study underwent a physical examination and