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LGE and NT-proBNP Identify Low Risk of Death or Arrhythmic Events in Patients With Primary Prevention ICDs

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OBJECTIVES The aim of this study was to investigate whether late gadolinium enhancement (LGE) magnetic resonance imaging or N-terminal pro–B-type natriuretic peptide (NT-proBNP) could identify patients with a low risk of death or use of implantable cardioverter-defibrillator (ICD) in patients receiving a primary prevention ICD.

BACKGROUND ICDs reduce mortality in patients with heart failure (HF), although two-thirds may never use their device. Current risk stratification, based on New York Heart Association functional class and left ventricular ejection fraction, still leads to implantation of ICDs in patients who may never need their device.

METHODS We examined 157 patients with HF (61 with ischemic cardiomyopathy and 96 with dilated cardiomyopathy; mean age 50.5 years; 78% male) who underwent primary prevention defibrillator implantation. Presence and volume of LGE was measured before device implantation, and serum NT-proBNP level was measured before ICD implantation. The combined primary endpoint was cardiovascular death or appropriate ICD therapy (either appropriate shock or antitachycardia pacing).

RESULTS The primary outcome occurred in 32 patients (20.4%) over a median follow-up period of 915 days. Percentage of LGE (hazard ratio [HR]: per 1% increase: 1.06; 95% confidence interval [CI]: 1.04 to 1.09; $p < 0.001$) and (ln) NT-proBNP (HR: 1.44; 95% CI: 1.04 to 1.98; $p = 0.027$) were predictors of death or appropriate ICD activation and remained significant when entered into multivariable analysis. When the cohort was stratified into tertiles based on LGE percentage and NT-proBNP, we were able to identify a low-risk group (event rate 3% per year, compared with the intermediate- and high-risk groups [6% and 10% per year, respectively]).

CONCLUSIONS Both percentage of LGE and NT-proBNP were associated with higher risk of death or appropriate ICD activation. The use of these markers in combination may be useful in identifying individuals most likely to benefit from this costly intervention, and more specifically, in the identification of a group at lower risk in whom ICD implantation may be deferred. (J Am Coll Cardiol Img 2014;7:561–9)

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Implantable cardioverter-defibrillators (ICDs) and cardiac resynchronization therapy devices with a defibrillator function (CRT-Ds) have been shown to reduce mortality when implanted to prevent death in patients with heart failure (HF) who have not had a prior cardiac arrest (i.e., a primary prevention device) (1,2). The average annual rate of appropriate shocks in clinical trials is only 5.1%, and as many as two-thirds of patients may never use their ICD after implantation (2–4). Therefore, methods to improve the identification of individuals who may not be likely to benefit from ICD implantation meeting conventional criteria such as New York Heart Association (NYHA) functional class II to IV and reduced ejection fraction are needed.

Late gadolinium enhancement (LGE) by cardiac magnetic resonance (CMR) has been proposed as a potential marker of risk identifying individuals most likely to benefit from an ICD. The presence of LGE is associated with a higher risk of all-cause mortality, sudden cardiac death, appropriate ICD activation, and admissions for heart failure in patients with HF with both ischemic cardiomyopathy (ICM) and dilated cardiomyopathy (DCM) (5–11). However, LGE quantification has a number of limitations; furthermore, not all patients are able to undergo CMR due to relative or absolute contraindications or due to a contraindication to the administration of gadolinium.

ABBREVIATIONS AND ACRONYMS

CRT-D = cardiac resynchronization therapy (device with) defibrillator

DCM = dilated cardiomyopathy

HF = heart failure

ICD = implantable cardioverter-defibrillator

ICM = ischemic cardiomyopathy

LGE = late gadolinium enhancement

NT-proBNP = N-terminal pro–B-type natriuretic peptide

In contrast, B-type natriuretic peptide (BNP) and N-terminal pro-BNP (NT-proBNP) are easily measured and have been explored as a potential marker of risk in those receiving a primary prevention ICD and as predictors of sudden death in patients with HF (12–14). We assessed the association between LGE and NT-proBNP and death or appropriate ICD activation in individuals undergoing implantation of a primary prevention ICD, and specifically, hypothesized that the 2 markers may be combined to predict a group of patients who may be at low risk of ventricular arrhythmia and ICD activation.

METHODS

Patient selection. We prospectively evaluated 157 consecutive patients referred to our tertiary center for implantation of primary prevention ICD or CRT-D between January 2008 and December 2010. Patients with both ICM and nonischemic DCM were included. The diagnosis of ICM was made using either computed tomography (CT) coronary angiography or invasive coronary angiography in conjunction with CMR results. If patients were found to have a small area of LGE in an ischemic distribution that was thought not to be significant enough to cause the degree of left ventricular systolic impairment seen they were classified as DCM; conversely, in some patients, there was a definite regional wall motion abnormality in conjunction with a history of significant stenosis on invasive or CT coronary angiography (>70%), and we recorded these patients as having ICM. We excluded all patients referred for a secondary prevention ICD and those with renal impairment (estimated glomerular filtration rate <30 ml/min/1.73 m^2). The West of Scotland Research Ethics Committee approved the study.

CMR protocol. All patients underwent a clinically indicated CMR examination with a 1.5-T scanner (Avanto Siemens, Erlangen, Germany). The protocols, imaging sequences, and analysis have been previously described (15). Briefly, cine images were obtained using a steady-state free precession sequence in 3 long-axis planes (2-, 3-, and 4-chamber) and in short-axis slices through the left ventricle (echo time/repetition time/flip angle 1.4/3.5/50; spatial resolution 1.7 × 2 mm; slice thickness 8 mm). LGE imaging for myocardial infarction was acquired 10 min (after a total accumulative gadolinium–diethylene triamine pentaacetic acid of 0.15 mmol/kg) by an inversion recovery fast gradient echo sequence. Inversion time was adjusted to null normal myocardium—typically this was between 280 and 320 ms. CMR was carried out within a mean of 3 ± 1 days of defibrillator insertion.

All analyses were performed using commercially available proprietary software (Argus, Siemens). Left ventricular diameter, volumes, and function were derived from the short-axis slices using manual tracing of the endocardial contours, including papillary muscles as part of the ventricular volume. The presence of LGE was assessed by identification of areas of myocardium with a signal intensity of >5 SD above normal myocardium. Quantification of LGE was measured using manual planimetry in short axis and taking this area as a percentage of the total left ventricular area measured in short axis.

NT-proBNP sampling. Serum NT-proBNP was obtained within 2 ± 1 weeks of defibrillator implantation and analyzed in our local laboratory, the methods for which have been previously described (16). Blood samples were collected in ethylenediamine–tetraacetic acid–containing tubes before being centrifuged at 3,000 rpm for 10 min at