JACC: CARDIOVASCULAR IMAGING
VOL. 9, NO. 6, 2016

ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER
http://dx.doi.org/10.1016/j.jcmg.2015.10.027

LGE Provides Incremental Prognostic Information Over Serum Biomarkers in AL Cardiac Amyloidosis

Samuel J. Boynton, MD,[a] Jeffrey B. Geske, MD,[b] Angela Dispenzieri, MD,[c] Imran S. Syed, MD,[b] Theodore J. Hanson, MD,[a] Martha Grogan, MD,[b] Philip A. Araoz, MD[a]

ABSTRACT

OBJECTIVES This study sought to determine the prognostic value of cardiac magnetic resonance (CMR) late gadolinium enhancement (LGE) in amyloid light chain (AL) cardiac amyloidosis.

BACKGROUND Cardiac involvement is the major determinant of mortality in AL amyloidosis. CMR LGE is a marker of amyloid infiltration of the myocardium. The purpose of this study was to evaluate retrospectively the prognostic value of CMR LGE for determining all-cause mortality in AL amyloidosis and to compare the prognostic power with the biomarker stage.

METHODS Seventy-six patients with histologically proven AL amyloidosis underwent CMR LGE imaging. LGE was categorized as global, focal patchy, or none. Global LGE was considered present if it was visualized on LGE images or if the myocardium nulled before the blood pool on a cine multiple inversion time (TI) sequence. CMR morphologic and functional evaluation, echocardiographic diastolic evaluation, and cardiac biomarker staging were also performed. Subjects' charts were reviewed for all-cause mortality. Cox proportional hazards analysis was used to evaluate survival in univariate and multivariate analysis.

RESULTS There were 40 deaths, and the median study follow-up period was 34.4 months. Global LGE was associated with all-cause mortality in univariate analysis (hazard ratio = 2.93; $p < 0.001$). In multivariate modeling with biomarker stage, global LGE remained prognostic (hazard ratio = 2.43; $p = 0.01$).

CONCLUSIONS Diffuse LGE provides incremental prognosis over cardiac biomarker stage in patients with AL cardiac amyloidosis. (J Am Coll Cardiol Img 2016;9:680–6) © 2016 by the American College of Cardiology Foundation.

Amyloid light chain (AL)-type amyloidosis is a rare systemic disease with an incidence of approximately 1 per 100,000 person-years (1). It is characterized by tissue deposition of insoluble fibrils made up of plasma cell-derived immunoglobulin light chain precursor proteins (2). Cardiac involvement, found in up to 60% of patients with AL type amyloidosis, is a major determinant of morbidity and mortality (3).

Cardiac magnetic resonance (CMR) late gadolinium enhancement (LGE) has been shown to be associated with myocardial amyloid deposition (4), and it has been associated with all-cause mortality (5–8). However, with the advent of staging systems using serum biomarkers as their basis (9), it has become important that CMR findings be shown to be incrementally prognostic for serum biomarkers. Therefore, the purpose of this study was to evaluate retrospectively

From the [a]Department of Radiology, Mayo Clinic Rochester, Rochester, Minnesota; [b]Department of Medicine, Division of Cardiovascular Diseases, Mayo Clinic Rochester, Rochester, Minnesota; and the [c]Department of Medicine, Division of Hematology, Mayo Clinic Rochester, Rochester, Minnesota. This work was made possible by Clinical and Translational Science Awards (CTSA) Program grant UL1 TR000135 from the National Center for Advancing Translational Sciences (NCATS), a component of the National Institutes of Health (NIH). The contents of this paper are solely the responsibility of the authors and do not necessarily represent the official view of the NIH. All authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received February 23, 2015; revised manuscript received October 16, 2015, accepted October 21, 2015.

the prognostic value of CMR LGE for determining all-cause mortality in AL amyloidosis and to evaluate the prognostic value with serum biomarker stage.

METHODS

PATIENT SELECTION. Institutional Review Board approval was obtained. Written informed consent was not required for retrospective medical review. This study is a follow-up investigation of a cohort of patients with amyloidosis originally described by Syed et al. (4), who compared CMR LGE patterns with clinical and echocardiographic findings in cardiac amyloidosis.

SEE PAGE 687

Inclusion criteria for this study were as follows: 1) CMR ordered for evaluation of cardiac amyloidosis between January 1, 2006 and December 31, 2007; 2) age ≥18 years; 3) histologically proven AL-type amyloidosis; 4) the presence of a monoclonal protein in the urine or serum or a monoclonal population of plasma cells in the bone marrow, or both; and 5) CMR performed within 3 months of diagnosis.

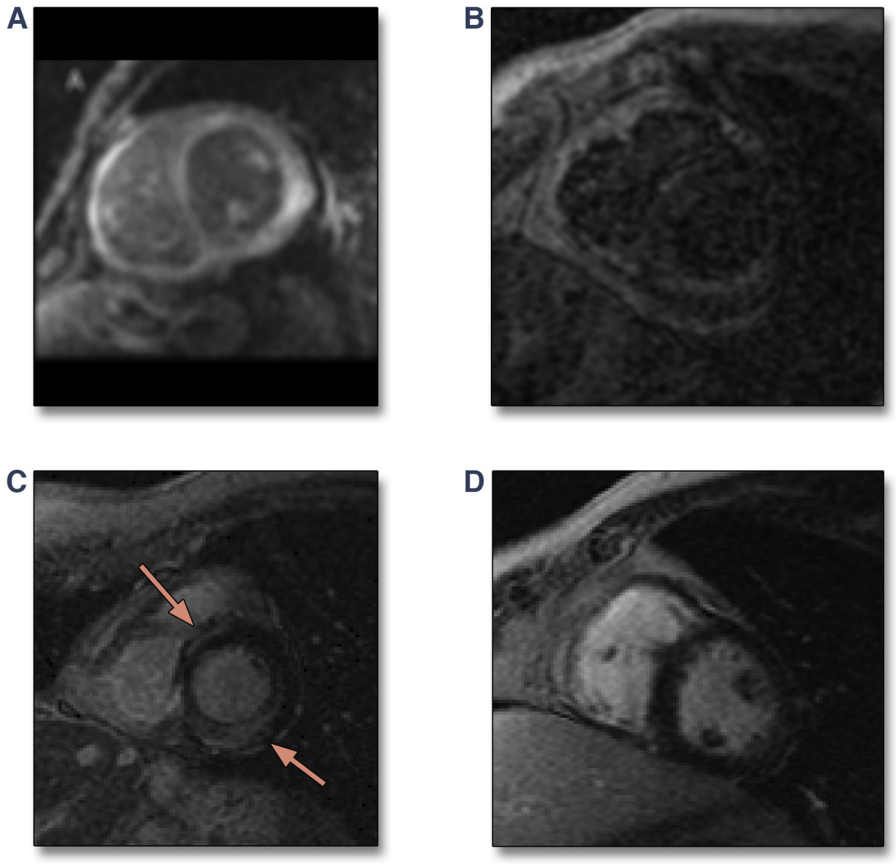
Exclusion criteria were as follows: 1) history of myocardial infarction or myocarditis; 2) previous peripheral blood stem cell transplant; or 3) history of previous heart transplant. Of 151 patients with documented amyloidosis who underwent CMR at our institution (Mayo Clinic Rochester, Rochester, Minnesota) during this time frame, 76 were included in this study.

ABBREVIATIONS AND ACRONYMS

AL = amyloid light chain
CMR = cardiac magnetic resonance
CTnT = cardiac troponin T
ECG = electrocardiogram
HR = hazard ratio
LGE = late gadolinium enhancement
LV = left ventricular
NT-proBNP = N-terminal probrain natriuretic peptide
TI = inversion time

CMR MYOCARDIAL LATE GADOLINIUM ENHANCEMENT PATTERNS. CMR image acquisition was performed as described by Syed et al. (4). Electrocardiogram

FIGURE 1 LGE Patterns



Late gadolinium enhancement (LGE) classification: "global" was defined as **(A)** diffuse enhancement or **(B)** inability to null the myocardium on multiple T1 sequences or if the myocardium nulled before the blood pool on a multiple TI cine fast gradient echo sequence (not shown). **(C)** "Focal patchy" was defined as nondiffuse, discrete areas of LGE **(arrows)**. **(D)** "None" was normal myocardial nulling without any delayed enhancement.