JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 72, NO. 14, 2018

The Mitral Annulus Disjunction Arrhythmic Syndrome

Lars A. Dejgaard, MD,[a,b,c] Eystein T. Skjølsvik, MD,[a,b,c] Øyvind H. Lie, MD,[a,b,c] Margareth Ribe, RN,[a,b] Mathis K. Stokke, MD, PhD,[a,b] Finn Hegbom, MD, PhD,[a,b] Esther S. Scheirlynck, MD,[a,b] Erik Gjertsen, MD,[d] Kristoffer Andresen, MD,[d] Thomas M. Helle-Valle, MD, PhD,[a,b] Einar Hopp, MD, PhD,[a,e] Thor Edvardsen, MD, PhD,[a,b,c,f] Kristina H. Haugaa, MD, PhD[a,b,c,f]

ABSTRACT

BACKGROUND Mitral annulus disjunction (MAD) is an abnormal atrial displacement of the mitral valve leaflet hinge point. MAD has been associated with mitral valve prolapse (MVP) and sudden cardiac death.

OBJECTIVES The purpose of this study was to describe the clinical presentation, MAD morphology, association with MVP, and ventricular arrhythmias in patients with MAD.

METHODS The authors clinically examined patients with MAD. By echocardiography, the authors assessed the presence of MVP and measured MAD distance in parasternal long axis. Using cardiac magnetic resonance (CMR), the authors assessed circumferential MAD in the annular plane, longitudinal MAD distance, and myocardial fibrosis. Aborted cardiac arrest and sustained ventricular tachycardia were defined as severe arrhythmic events.

RESULTS The authors included 116 patients with MAD (age 49 ± 15 years; 60% female). Palpitations were the most common symptom (71%). Severe arrhythmic events occurred in 14 (12%) patients. Longitudinal MAD distance measured by CMR was 3.0 mm (interquartile range [IQR]: 0 to 7.0 mm) and circumferential MAD was 150° (IQR: 90° to 210°). Patients with severe arrhythmic events were younger (age 37 ± 13 years vs. 51 ± 14 years; p = 0.001), had lower ejection fraction (51 ± 5% vs. 57 ± 7%; p = 0.002) and had more frequently papillary muscle fibrosis (4 [36%] vs. 6 [9%]; p = 0.03). MVP was evident in 90 (78%) patients and was not associated with ventricular arrhythmia.

CONCLUSIONS Ventricular arrhythmias were frequent in patients with MAD. A total of 26 (22%) patients with MAD did not have MVP, and MVP was not associated with arrhythmic events, indicating MAD itself as an arrhythmogenic entity. MAD was detected around a large part of the mitral annulus circumference and was interspersed with normal tissue. (J Am Coll Cardiol 2018;72:1600–9) © 2018 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Mitral valve prolapse (MVP) is relatively common, with a prevalence of about 2% and has a good overall prognosis (1–4). However, MVP has been associated with malignant ventricular arrhythmias and sudden cardiac death in a small subset of young and middle-aged patients (5–11). The mechanisms for arrhythmias in patients with MVP are unknown; however, bileaflet MVP, papillary muscle fibrosis, and mitral annulus disjunction (MAD) have been linked to increased arrhythmic risk (9–14).

MAD was first described more than 3 decades ago as an abnormal atrial displacement of the hinge point of the mitral valve away from the ventricular

Listen to this manuscript's audio summary by *JACC* Editor-in-Chief Dr. Valentin Fuster.

From the [a]Center for Cardiological Innovation, Oslo University Hospital, Rikshospitalet, Oslo, Norway; [b]Department of Cardiology, Oslo University Hospital, Rikshospitalet, Oslo, Norway; [c]Institute for Clinical Medicine, University of Oslo, Oslo, Norway; [d]Department of Medicine, Drammen Hospital, Vestre Viken Hospital Trust, Drammen, Norway; [e]Division of Radiology and Nuclear Medicine and The Intervention Centre, Oslo University Hospital, Rikshospitalet, Oslo, Norway; and the [f]Institute for Surgical Research, Oslo University Hospital, Rikshospitalet, Oslo, Norway. This work was supported by a public grant (203489/030) from the Norwegian Research Council, Norway. All authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received February 27, 2018; revised manuscript received June 13, 2018, accepted July 9, 2018.

ISSN 0735-1097 https://doi.org/10.1016/j.jacc.2018.07.070

myocardium (15), and has since been closely linked to MVP (11,12,16–19). Recent studies demonstrate an association among MAD, ventricular arrhythmia, and papillary muscle fibrosis, but only as a part of MVP disease and not in patients with MAD specifically (11,12,20). Some reports indicate that MAD also may appear without concomitant MVP, but the clinical relevance of this finding is unclear (19–22). Large clinical studies with MAD as the inclusion criterion are lacking, and standardized imaging protocols for detection and quantification of MAD are missing.

The aim of this study was to clinically characterize patients with MAD and to describe the MAD morphology by echocardiography and advanced cardiac magnetic resonance (CMR) imaging. We aimed to explore the relationship between MAD and MVP and to assess potential markers for ventricular arrhythmias.

SEE PAGE 1610

METHODS

STUDY POPULATION. In this cross-sectional multicenter study, we screened patients with possible MAD as previously defined (12) by echocardiography at 2 hospitals in Norway, Oslo University Hospital and Drammen Hospital, from August 2015 until June 2017. Sonographers and cardiologists at the 2 recruiting localizations were educated on how to identify MAD. If the echocardiographer suspected MAD, we invited the patient to a comprehensive study protocol evaluation including a new echocardiogram, CMR, 24-h electrocardiogram (ECG) recording, and clinical assessment at Oslo University Hospital. Patients were included if MAD was confirmed by either CMR or study echocardiogram (**Figure 1**).

The study complied with the Declaration of Helsinki and was approved by the Regional Committee for Medical Research Ethics (2015/596/REK nord). All study participants gave written informed consent.

ECHOCARDIOGRAPHY. Left ventricular and atrial volumes and ejection fraction were measured according to guidelines (Vivid E95 scanner, GE Healthcare, Horten, Norway) (23). Care was taken to identify the mitral annulus and include the basal sections of the left ventricle, but exclude prolapsed volume, in volumetric measurements. Data were analyzed offline (EchoPac version 201, GE Healthcare). MAD distance was measured from the left atrial wall-mitral valve leaflet junction to the top of the left ventricular wall during end-systole in the parasternal long-axis view (**Figure 2**) (12) and was defined as longitudinal MAD distance in the posterolateral wall. Presence of basolateral left ventricular wall curling motion (11,24) was identified by visual assessment (Online Videos 1A [echocardiogram, parasternal long-axis view], 1B [echocardiogram, apical long-axis view], 1C [echocardiogram, apical 4-chamber view], and 2 [CMR, 3-chamber view]). MVP was defined as superior displacement ≥2 mm of any part of the mitral leaflet beyond the mitral annulus according to the American Society of Echocardiography guideline (**Figure 3,** Online Figures 1 to 3) (25,26), and this MVP definition is used in the paper unless otherwise stated. We also classified patients according to the European Society of Cardiology guideline for comparison (27), which defines MVP as superiorly displaced mitral valve coaptation point relative to the mitral ring. We quantified mitral regurgitation according to guidelines (25,27). Echocardiographic analyses were performed by 2 independent echocardiography experts (L.A.D. and E.T.S.) blinded to all clinical data.

CMR IMAGING. The study protocol CMR was performed on a 3-T whole-body scanner (Ingenia, Phillips Healthcare, Best, the Netherlands) with a phased array body coil. To ensure the complete assessment of the mitral annulus circumference, we performed 6 left ventricle long-axis cine sequences with an interslice rotation of 30°. The first projection was aligned through the superior right ventricular free wall insertion into the septum, and was defined as 0° in the annular plane, followed by clockwise labeling of the long-axis slices. Longitudinal MAD distance was measured from the left atrial wall-mitral valve leaflet junction to the top of the left ventricular wall during at end-systole in all long-axis cine sequences and was defined as present if ≥1.0 mm. Longitudinal MAD distance in the posterolateral wall was measured at 120°. The circumferential extent of tissue disjunction along the mitral annulus was obtained from the combination of the 6 long-axis and was defined as circumferential MAD and expressed in degrees of the mitral annulus (Online Figure 4).

We recorded presence of late gadolinium enhancement in the left ventricular myocardium and the papillary muscles. Prior CMR examinations, if available, were analyzed for late gadolinium enhancement (n = 16) and for longitudinal MAD (n = 18) in patients who were not eligible for the study protocol CMR.

VENTRICULAR ARRHYTHMIAS. Patients with aborted cardiac arrest underwent thorough diagnostic workup, including genetic testing for channelopathies

ABBREVIATIONS AND ACRONYMS

CMR = cardiac magnetic resonance

ECG = electrocardiogram

IQR = interquartile range

MAD = mitral annulus disjunction

MVP = mitral valve prolapse