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Marfan Syndrome and Quality of Life in the GenTAC Registry

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ABSTRACT

BACKGROUND Previous small studies suggested reduced quality of life (QOL) for people with Marfan syndrome (MFS) compared with those without MFS. The national registry of GenTAC (Genetically Triggered Thoracic Aortic Aneurysms and Cardiovascular Conditions) is a longitudinal observational cohort study of patients with conditions that predispose to thoracic aortic aneurysms and dissections, including MFS. At the time of registry enrollment, GenTAC study participants are asked to complete questionnaires about demographics, medical history, health habits, and QOL.

OBJECTIVES This study assessed QOL in GenTAC participants with MFS and identify associated factors using self-reported data.

METHODS QOL was assessed using the 4 subscales of the Physical Component Summary (PCS) of the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36): physical functioning; role limitations due to physical health; bodily pain; and general health. We studied the association of QOL with self-reported demographics, health behaviors, physical impairments, surgeries, comorbid medical conditions, medications, and MFS severity.

RESULTS In the GenTAC registry, 389 adults with MFS completed the SF-36. Mean age was 41 years, 51% were men, 92% were white, and 65% were college graduates. The mean PCS composite score was 42.3. In bivariate analysis, predictors of better QOL included college education, marital status, higher household income, private health insurance, full-time employment, moderate alcohol use, fewer prior surgeries, fewer comorbid conditions, absence of depression, and less severe MFS manifestations. In a multivariable analysis, insurance status and employment remained significant predictors of QOL.

CONCLUSIONS In a large cohort of patients with MFS in the GenTAC registry, health-related QOL was below the population norm. Better QOL was independently associated with socioeconomic factors, not factors related to general health or MFS severity. (J Am Coll Cardiol 2017;69:2821–30) © 2017 by the American College of Cardiology Foundation.

Marfan syndrome (MFS) is a hereditary, autosomal dominant disorder due to mutations in the fibrillin-1 gene, that affects connective tissue in multiple organs, most notably the eyes, skeleton, and aorta, with increased risk for thoracic aortic aneurysm and dissection. With advances in aortic surgery over the past 40 years, survival for people with MFS has increased from the third or fourth decade to the eighth (1). However, there continues to be substantial morbidity associated with MFS, including the sequelae of multiple surgeries and lifelong medical therapy (2–4). Not surprisingly, a growing body of literature suggests impaired quality of life (QOL) in patients with MFS

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ABBREVIATIONS AND ACRONYMS

BP = bodily pain subscale

GH = general health subscale

MFS = Marfan syndrome

PCS = Physical Component Summary

PF = physical functioning subscale

QOL = quality of life

RP = role limitations due to physical health subscale

SF-36 = Medical Outcomes Study 36-Item Short-Form Health Survey

(5-11), with most studies using the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) to assess QOL (5-13). Prior studies, however, were limited by small sample sizes and were therefore not able to identify independent factors associated with better or worse QOL.

The SF-36 is a widely used and extensively validated questionnaire that assesses health-related QOL. The questionnaire is subdivided into the Physical Component Score (PCS) and Mental Component Score. Because previous studies found that MFS predominantly affected the PCS (8,10,12,13), we used the PCS of the SF-36 to assess health-related QOL in patients with MFS, and we evaluated the association of QOL with self-reported demographic factors, health behaviors, physical impairments, clinical characteristics, and MFS severity.

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METHODS

The development and design of the GenTAC (Genetically Triggered Thoracic Aortic Aneurysms and Cardiovascular Conditions) registry have been previously described (14,15). Briefly, the GenTAC registry was created as a multicenter, longitudinal, observational cohort study of patients with aortic aneurysm and associated genetic conditions, including MFS. Patients were enrolled at 8 sites: Johns Hopkins University, Baylor College of Medicine, Oregon Health & Sciences University, University of Pennsylvania, University of Texas Health Science Center at Houston, Weill Cornell Medical College, National Institute of Aging-Harbor Hospital, and Queen's Medical Center. Each site obtained Institutional Review Board approval, and each participant patient provided informed consent. Standardized data collection included patient questionnaires, imaging studies, and information about prior surgical procedures. The Research Triangle Institute International in Rockville, Maryland, served as the data coordinating center and was responsible for data management and statistical design and analysis (14,15).

STUDY SUBJECTS. We included patients in the GenTAC database who had MFS diagnosed by Ghent or revised Ghent criteria and confirmed by a core phenotyping laboratory at Johns Hopkins University (16,17), were age 18 years or older, and had completed the SF-36. We excluded patients <18 years of age both to be consistent with the existing literature on QOL in MFS and because parents could complete questionnaires for pediatric patients in the GenTAC registry. This study used de-identified survey data from the GenTAC registry. Patients were enrolled in the GenTAC registry from 2006 through December 31, 2013. The most recent analyses of our data were performed in September 2016.

SF-36 SCALE SCORING. Our analyses focused on QOL, which was measured with the PCS of the SF-36 (18,19). The PCS comprises 4 subscales: physical functioning (PF); role limitations due to physical health (RP); bodily pain (BP); and general health (GH). Each score ranges from 0 to 100, and is standardized to the population norm of 50 with a SD of 10; higher scores indicate better QOL (18-20). Each of the 4 SF-36 subscales was standardized using a *z*-score transformation by subtracting the mean and SD from the 1998 general U.S. population. Composite PCS was computed using the score coefficients from the 1990 general U.S. population per the standard SF-36 scoring. The composite score is transformed to the norm-based scoring, where the norm is set as 50 with a SD of 10 (20).

VARIABLES. Self-reported variables were extracted from the Clinical Evaluation Form and the Enrollment Patient Questionnaire. The Clinical Evaluation Form includes questions about enrollment diagnosis, age at diagnosis, number of prior surgeries, number of medications, or use of specific medications. For the Enrollment Patient Questionnaire, patients provided their date of birth and answered multiple choice questions about sex, race/ethnicity (white, black or African American, Asian, American Indian, Native Hawaiian, or Pacific Islander), education, marital status, household income, health insurance status (employer private health insurance plan, Medicare, Medicaid, other), employment (full time, part time, unable to work, student, homemaker, unemployed, and retired); health behaviors, including use of cigarettes, alcohol, and illicit drugs; and vision or hearing impairment. This form asks about 47 medical conditions, including the genetic conditions associated with thoracic aortic aneurysms (numbers 1 through 7); cardiovascular history including murmur, palpitation, angina, heart attack, cardiomyopathy and others (numbers 8 through 16); hypertension; stroke; aneurysms; cancer; diabetes; bleeding or clotting disease; gastrointestinal disease; arthritis; autoimmune diseases; joint dislocations; cognitive issues; and depression.

To evaluate QOL data in the presence of phenotypic variability, we created a clinical severity scale to differentiate mild, typical, and severe disease. Two scores have been created previously, but neither has