JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
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PUBLISHED BY ELSEVIER

VOL. 68, NO. 16, 2016
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2016.07.750

Risk of Pregnancy in Moderate and Severe Aortic Stenosis

From the Multinational ROPAC Registry

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ABSTRACT

BACKGROUND Controversial results on maternal risk and fetal outcome have been reported in women with aortic stenosis (AS).

OBJECTIVES The authors sought to investigate maternal and fetal outcomes in patients with AS in a large cohort.

METHODS The Registry on Pregnancy and Cardiac Disease (ROPAC) is a global, prospective observational registry of women with structural heart disease, providing a uniquely large study population. Data of women with moderate (peak gradient 36 to 63 mm Hg) and severe AS (peak gradient ≥64 mm Hg) were analyzed.

RESULTS Of 2,966 pregnancies in ROPAC, the authors identified 96 women who had at least moderate AS (34 with severe AS). No deaths were observed during pregnancy and in the first week after delivery. However, 20.8% of women were hospitalized for cardiac reasons during pregnancy. This was significantly more common in severe AS compared with moderate AS (35.3% vs. 12.9%; $p = 0.02$), and reached the highest rate (42.1%) in severe, symptomatic AS. Pregnancy was complicated by heart failure in 6.7% of asymptomatic and 26.3% of symptomatic patients, but could be managed medically, except for 1 patient who was symptomatic before pregnancy and underwent balloon valvotomy. Children of patients with severe AS had a significantly higher percentage of low birth weight (35.0% vs. 6.0%; $p = 0.006$).

CONCLUSIONS Mortality in pregnant women with AS, including those with severe AS, appears to be close to zero in the current era. Symptomatic and severe AS does, however, carry a substantial risk of heart failure and is associated with high rates of hospitalization for cardiac reasons, although heart failure can nearly always be managed medically. The results highlight the importance of appropriate pre-conceptional patient evaluation and counseling.
(J Am Coll Cardiol 2016;68:1727–37) © 2016 by the American College of Cardiology Foundation.

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Manuscript received May 27, 2016; revised manuscript received July 7, 2016, accepted July 12, 2016.

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ABBREVIATIONS AND ACRONYMS

AS = aortic stenosis

AVR = aortic valve replacement

ESC = European Society of Cardiology

IQR = interquartile range

NYHA = New York Heart Association

OR = odds ratio

WHO = World Health Organization

Pregnancy carries a very low risk of death in developed countries, but overall, cardiac reasons remain the leading cause of maternal mortality (1). Consistent with this, women with pre-existing heart disease have 100 times greater mortality than normal (2). Pregnancy is associated with profound changes in hemodynamic parameters, perhaps explaining why pre-existing heart disease has such an adverse impact on morbidity and mortality in pregnant women (3). Although there is clear evidence that pregnancy is a high-risk endeavor in women with complex heart disease, and especially those with severe pulmonary hypertension (4,5), available data are limited in women with less complex heart disease. Obstructive heart lesions will be aggravated by the increase in stroke volume occurring with pregnancy, and are therefore of particular concern. Aortic stenosis (AS) is one of these lesions, but it is relatively uncommon in women of childbearing age. However, when present, it has been reported to be associated with an increased risk of maternal cardiovascular events, including death, obstetric morbidity (such as pre-term birth), and fetal complications, including growth restriction, miscarriage, and stillbirth (6). The evidence in this setting is nevertheless limited, and the results of published reports are conflicting. Unfortunately, prior studies either encompassed all forms of heart disease (7,8) or included mild AS (9). In addition, some series report on historic patient cohorts (6). As a consequence, the reported maternal mortality rate ranges between 2% and 17.4%, and the risk in contemporary cohorts of women presenting with severe AS remains unclear (6,9).

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The purpose of this study was therefore to investigate maternal and fetal adverse events in contemporary patients with moderate or severe AS on the basis of a prospective observational study of a large number of pregnancies in patients with AS included in ROPAC (Registry of Pregnancy and Cardiac Disease).

METHODS

ROPAC is a global, prospective, observational registry of women with heart disease. It was initiated by the European Society of Cardiology (ESC) working groups on congenital heart disease and valvular heart disease, and is part of the EURObservational Research Programme of the ESC. The registry allows for the inclusion of patients with structural or ischemic heart disease, aortic pathology, and pulmonary hypertension. The registry started in January 2008. Patients who were pregnant in 2007 could also be included retrospectively; from January 2008, patients were included prospectively. Patients were managed at the discretion of the attending physicians. The overall mortality during pregnancy and until 1 week after delivery in the registry has been reported at 1%. Further details on the registry and the institutional review board/ethical approval have previously been published (2,10). The current study is covered by approval under the umbrella of the general ROPAC project.

The present study retrospectively analyzed the outcome and complications in pregnant women with moderate or severe AS included in the registry up to April 2014. We focused exclusively on women with moderate or severe AS. Patients with additional congenital or acquired heart disease (with the exception of simple corrected pre-tricuspid shunts, aortic coarctation) were not included in the current study. The severity of AS was graded on the basis of available transthoracic echocardiographic data at baseline. Moderate AS was defined as a peak transaortic gradient ≥36 mm Hg (corresponding to a peak velocity ≥3 m/s), whereas severe AS was defined as a peak aortic gradient ≥64 mm Hg (corresponding to a peak velocity ≥4 m/s) using the simplified Bernoulli equation (11,12). This is in agreement with current guidelines and general recommendations for assessing the severity of AS in the presence of normal flow rate (13). Patients who had undergone aortic valve replacement before pregnancy were included if they fulfilled the hemodynamic criteria described in the preceding text. However, further analyses were also performed and presented separately because prosthetic valve-related risks require additional consideration. Repeated pregnancies were excluded from the analysis.

Baseline characteristics included maternal age, general cardiovascular risk factors, major noncardiac disease, cardiac diagnosis, prior interventions, cardiac symptoms, medication, and obstetric history. Heart failure before pregnancy was defined according to current guidelines clinically as a syndrome in which patients have typical symptoms (e.g., breathlessness, ankle swelling, and fatigue) and signs (e.g., elevated jugular venous pressure, pulmonary crackles, and displaced apex beat) (14). Maternal mortality was defined as death during pregnancy or up to 1 week after delivery. Miscarriage was defined as loss of pregnancy up to 24 weeks of gestation or a fetus weighting <500 g, whereas fetal mortality was defined as fetal loss beyond 24 weeks of pregnancy. Outcome measures included maternal mortality,