Heart Valve Prostheses in Pregnancy: Outcomes for Women and Their Infants

Claire M. Lawley, BSc(Med)Hons, MBBS(Hons); Charles S. Algert, BA, BSc, MPH; Jane B. Ford, BA(Hons), PhD; Tanya A. Nippita, BSc(Med), MBBS(Hons), FRANZCOG; Gemma A. Figtree, MBBS, DPhil (Oxon), FRACP; Christine L. Roberts, MBBS, DrPH, FAFPHM

Background—As the prognosis of women with prosthetic heart valves improves, and increasing number are contemplating and undertaking pregnancy. Accurate knowledge of perinatal outcomes is essential, assisting counseling and guiding care. The aims of this study were to assess outcomes in a contemporary population of women with heart valve prostheses undertaking pregnancy and to compare outcomes for women with mechanical and bioprosthetic prostheses.

Methods and Results—Longitudinally linked population health data sets containing birth and hospital admissions data were obtained for all women giving birth in New South Wales, Australia, 2000–2011. This included information identifying presence of maternal prosthetic heart valve. Cardiovascular and birth outcomes were evaluated. Among 1 144 156 pregnancies, 136 involved women with a heart valve prosthesis (1 per 10 000). No maternal mortality was seen among these women, although the relative risk for an adverse event was higher than the general population, including severe maternal morbidity (139 versus 14 per 1000 births, rate ratio [RR]=9.96, 95% CI 6.32 to 15.7), major maternal cardiovascular event (44 versus 1 per 1000, RR 34.6, 95% CI 14.6 to 81.6), preterm birth (183 versus 66 per 1000, RR=2.77, 95% CI 1.88 to 4.07), and small-for-gestational-age infants (193 versus 95 per 1000, RR=2.03, 95% CI 1.40 to 2.96). There was a trend toward increased maternal and perinatal morbidity in women with a mechanical valve compared with those with a bioprosthetic valve.

Conclusions—Pregnancies in women with a prosthetic heart valve demonstrate an increased risk of an adverse outcome, for both mothers and infants, compared with pregnancies in the absence of heart valve prostheses. In this contemporary population, the risk was lower than previously reported. (J Am Heart Assoc. 2014;3:e000953 doi: 10.1161/JAHA.114.000953)

Key Words: cardiovascular diseases • heart valve prosthesis • infant • perinatal mortality • pregnancy

With advances in surgical technique, prosthetic heart valve design, and anticoagulation, there has been an overall improvement in the prognosis and quality of life of young women with a prosthetic heart valve.1–4 There remains a paucity of data in regard to the maternal, fetal, and infant outcomes of the pregnancies of these women.

Normal pregnancy is a procoagulant state5,6 in which the body experiences an increased hemodynamic load.7–9 Tolerance of these changes by women with preexisting heart disease during pregnancy is known to vary.10 With gradual improvements in risk stratification and understanding of what conditions and cardiac parameters drive high risk during pregnancy, the number of these women counseled explicitly against pregnancy is decreasing.10,11 Current knowledge of pregnancy outcomes for women with a previous heart valve prosthesis implantation remains limited. Previous research on the outcomes of pregnancies in these women reflects a population of women with largely older, more thrombogenic mechanical valves and focuses on anticoagulation regimen.12–17 There is a need to examine pregnancy outcomes in a contemporary population, particularly given the increasing number of bioprosthetic valves implanted in women wishing to bear children, in accordance with international guidelines that advocate the consideration of this.11,16,19

Improvement in care for chronic and congenital cardiac disease, as well as the delayed age of childbearing, is expected to contribute to an increase in the number of
women with heart valve prostheses experiencing pregnancy. Routinely collected birth and hospital data represent an important resource for identifying women experiencing pregnancy with an existing heart valve prosthesis and provide data useful for exploring rare conditions, interventions, and subsequent health outcomes. Contemporary knowledge is vital in assisting prepregnancy counseling and guiding care for women with heart valve prostheses and their offspring during pregnancy and beyond. The aims of this study therefore were to assess the cardiovascular and birth outcomes of a contemporary population of women with a heart valve prosthesis undertaking pregnancy and to compare outcomes for women with mechanical and bioprosthetic valves.

Methods

The study population included all women giving birth in New South Wales (NSW), Australia, between 2000 and 2011. NSW is Australia’s most populous state, with >7 million residents (32% of the Australian population) and >95,000 births per annum.20

Data were obtained from 2 routinely collected population data sets: the NSW Perinatal Data Collection and NSW Admitted Patient Data Collection. The NSW Perinatal Data Collection, referred to as “birth records,” is a population-based surveillance system of all births (including all live births and stillbirths of ≥20 weeks gestation or 400 g in weight). The NSW Admitted Patient Data Collection, referred to as “hospital records,” is an administrative database of all public and private hospital admissions. It includes ≥20 diagnoses and procedures for each hospital admission, coded according to the International Classification of Diseases Version 10–Australian Modification (ICD10-AM) and the Australian Classification of Health Interventions. Record linkage of the NSW Perinatal Data Collection and NSW Admitted Patient Data Collection (including mothers’ and infants’ hospital admissions for the birth) and longitudinal linkage of hospitalizations up to 10 years before birth and 6 weeks postpartum) was undertaken by the NSW Centre for Health Record Linkage. Because Australia does not have a unique registration number for citizens, the separate data sets were linked using probabilistic linkage methods and a best-practice approach to preserving privacy.21-22 This involves a process of blocking and matching combinations of selected variables such as name, date of birth, address, and hospital and assigning a probability weight to the match. The validity of the probabilistic record linkage is extremely high.23 For this study, quality assurance assessments reported false-positive and -negative rates of 0.3% and <0.5%, respectively. More than 98% of birth records linked to a mother’s hospital record. The study was approved by the NSW Population and Health Services Research Ethics Committee (approval No. 2012/12/430).

Hospital records were used to identify women who had a heart valve prosthesis implanted before the time of giving birth. Separate procedure codes exist for heart valve prosthesis implantation surgery by valve location and type of prosthesis. Women who had a heart valve prosthesis implanted before 2000 could be identified only by a ICD10-AM diagnostic code indicating an extant prosthesis (Z95.2, Z95.3, T82.0) in the pregnancy/delivery hospital records, with no specification of valve type or location. After 2000, valve location and type of prosthesis were identifiable. Diagnoses of valvular disease and other maternal medical conditions, as well as cardiovascular outcomes, were also obtained from the hospital records; this information was not documented in the birth records. Valvular disease etiology was obtained taken from any admission record with the relevant code, before or after valve replacement, or during pregnancy.

Maternal cardiovascular outcomes evaluated included stroke, myocardial infarction, heart failure, a new arrhythmia, and endocarditis. Other vascular outcomes evaluated included new pulmonary embolism or other severe thromboembolic events. A composite outcome for any major cardiovascular event was used (stroke, myocardial infarction, heart failure, thromboembolic event, and endocarditis) during pregnancy or up to 42 days’ postpartum. Severe maternal morbidity during the birth admission was measured using a validated composite outcome indicator that was developed specifically for use in routinely collected population health data.24 Composite indicators overcome the problem of underascertainment of individual adverse events and reduce the need to rely on single ICD codes that have limited clinical detail, lack clear definitions, or are poorly validated.24

The hospital and birth records provided maternal characteristics (age, country of birth, medical conditions), while birth records provided pregnancy characteristics (parity, induction of labor, mode of delivery, place of birth) and birth outcomes (gestational age, birth weight, perinatal death) for women who had a birth ≥20 weeks’ gestation. The birth record was also a supplemental source to identify women who had chronic hypertension, pregnancy hypertension (including gestational hypertension, preeclampsia, and eclampsia), and diabetes (preexisting and gestational). Only miscarriages (spontaneous abortion before 20 weeks’ gestation) that resulted in admission to hospital were identifiable from hospital records. Stillbirth was defined as fetal death of ≥20 weeks’ gestation or 400 g birth weight. Neonatal death was defined as death of a live born infant during the first 28 days of life. Perinatal death included all stillbirths and neonatal deaths. Small-for-gestational-age (SGA), a proxy for intrauterine growth restriction, was defined as <10th birth weight percentile for gestational age and infant sex.25 Maternal length of stay and intensive care unit (ICU) admission data during the birth hospitalization (to discharge home) were obtained from the

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hospital data. Only pregnancy outcomes reliably reported in the population health data were included in the analyses. Information on medication use during pregnancy (ie, use of oral anticoagulant or heparin) was not available from either data set. No pregnancy or birth outcome information was missing for women with a heart valve prosthesis.

For the analysis of miscarriage and maternal characteristics, the study denominator was all pregnancies, including miscarriage. Because pregnancy losses before 20 weeks are not part of the population at risk for birth outcomes (such as SGA and perinatal death) and do not get a birth record, the analysis of delivery and birth outcomes was restricted to births ≥20 weeks’ gestation. Admission summaries for women experiencing a miscarriage were also searched for diagnoses of major cardiovascular events, but none of the miscarriages in the study population were associated with such an event. The rates of pregnancy and birth outcomes (per 1000) for women with and without a prosthetic heart valve prosthesis (and mechanical versus bioprosthetic valve type) were compared using contingency table analysis and by calculating rate ratios (RR) with 95% CIs. The comparisons of outcomes for women with mechanical prostheses versus bioprosthetic valves were similarly performed using contingency table analyses, because for almost all outcomes there were too few events to support a multivariable adjusted analysis.

**Results**

From 2000 to 2011, 87 women with heart valve prostheses experienced a total of 136 pregnancies. The prevalence of heart valve prostheses was approximately 1 per 10 000 pregnancies (136 per 1 144 156). Baseline characteristics of the pregnancies with and without heart valve prostheses are shown in Table 1.

Thirty-five women had an admission record for their valve implantation procedure; this group experienced 58 pregnancies subsequent to this surgery. The average age at time of surgery for these women was 26.0 years (SD ±6.2 years), and the mean interval between surgery and subsequent birth was 2.3 years (range 0.7 to 8.8 years). The remaining 52 women with a code identifying the presence of a heart valve prosthesis did not have an admission record for the valve insertion procedure, performed before 2000. The age of these 52 women as of 2000 ranged from 11 to 36 years, with a median age of 25 years. This group experienced 78 pregnancies during the study period. With the exception of 4 women (with 6 pregnancies) who had a diagnostic code indicating a xenograft valve, the valve prosthesis type and age at insertion in these women with pre-2000 valve prosthesis insertion were unknown. Combined with the 4 women identified as having a pre-2000 xenograft, the valve type (mechanical or bioprosthetic) was known for a total of 39 women experiencing 64 pregnancies. Valvular disease etiology could be ascertained.

**Table 1. Maternal Characteristics by Maternal Prosthetic Heart Valve Status for All Pregnancies**

<table>
<thead>
<tr>
<th>Maternal Characteristics</th>
<th>Any Prosthetic Valve, n=136 (87 Women)</th>
<th>Mechanical Valve, n=20 (14 Women)</th>
<th>Bioprosthetic Valve, n=44 (25 Women)</th>
<th>Valve Prosthesis Type Unknown, n=72 (48 Women)</th>
<th>No Valve Prosthesis, n=1 144 020 (651 072 Women)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age (mean±SD)</td>
<td>30.2 (5.6)</td>
<td>29.5 (7.4)</td>
<td>29.8 (4.5)</td>
<td>30.7 (5.7)</td>
<td>30.5 (5.7)</td>
</tr>
<tr>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>%</td>
</tr>
<tr>
<td>Nulliparous</td>
<td>48 (35)</td>
<td>9 (45)</td>
<td>12 (27)</td>
<td>27 (38)</td>
<td>42.1</td>
</tr>
<tr>
<td>Maternal birth in Australia/New Zealand</td>
<td>101 (74)</td>
<td>13 (65)</td>
<td>35 (80)</td>
<td>53 (74)</td>
<td>68.4</td>
</tr>
<tr>
<td>Valve disease etiology</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rheumatic heart disease</td>
<td>26 (19)</td>
<td>6 (30)</td>
<td>8 (18)</td>
<td>12 (17)</td>
<td>0.06</td>
</tr>
<tr>
<td>Nonrheumatic</td>
<td>49 (36)</td>
<td>12 (60)</td>
<td>25 (57)</td>
<td>12 (17)</td>
<td>0.21</td>
</tr>
<tr>
<td>Not recorded</td>
<td>61 (45)</td>
<td>2 (10)</td>
<td>11 (25)</td>
<td>48 (67)</td>
<td>—</td>
</tr>
<tr>
<td>Valve prosthesis location</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mitral</td>
<td>21† (15)</td>
<td>10 (50)</td>
<td>11† (25)</td>
<td>NA</td>
<td>—</td>
</tr>
<tr>
<td>Aortic</td>
<td>15† (11)</td>
<td>6 (30)</td>
<td>9† (20)</td>
<td>NA</td>
<td>—</td>
</tr>
<tr>
<td>Tricuspid or pulmonary</td>
<td>23 (17)</td>
<td>4 (20)</td>
<td>19 (42)</td>
<td>NA</td>
<td>—</td>
</tr>
<tr>
<td>Not recorded</td>
<td>78 (57)</td>
<td>0 (0)</td>
<td>6 (14)</td>
<td>72 (100)</td>
<td>—</td>
</tr>
<tr>
<td>Miscarriage admission</td>
<td>21 (15)</td>
<td>6 (30)</td>
<td>6 (14)</td>
<td>9 (13)</td>
<td>9.3</td>
</tr>
</tbody>
</table>

NA indicates not available; SD, standard deviation.

*Includes pregnancies ending in live birth, stillbirth, or hospital admission for miscarriage.

†One woman had both a mitral and an aortic bioprosthesis at the time of pregnancy.
for 75 (55%) pregnancies, and of these, 26 (19%) were attributed to rheumatic heart disease.

Of women with a known bioprosthetic valve, 46% experienced >1 pregnancy, as opposed to only 29% of those with a mechanical prosthesis. No pregnancies with prosthetic valves were complicated by preexisting diabetes, but 13 were complicated by chronic hypertension.

Twenty-one pregnancies among women with a heart valve prosthesis ended in a miscarriage, 19 before 14 weeks' gestation and 2 in the 14–19-gestational week category. A hospital admission with miscarriage was more frequent among women with valve prostheses than among those without (154 versus 93 per 1000 pregnancies, RR=1.65, 95% CI 1.12 to 2.45), and among those with mechanical valves compared with those with bioprosthetic valves, although this latter difference did not reach statistical significance (300 versus 140 per 1000, RR=2.20, 95% CI 0.81 to 5.98). For the 21 pregnancies ending in miscarriage with an associated hospital admission, no major cardiovascular events were identified, although 1 woman was diagnosed with a supraventricular tachycardia. Miscarriages not associated with a hospital admission were unable to be identified in women with or without prostheses.

Excluding miscarriages from further analysis, birth outcomes for births ≥20 weeks' gestation, with and without a prosthetic valve, are reported in Table 2. Compared with births where the mother did not have a prosthetic heart valve (n=1 037 159), those with valve prostheses (n=115) were more likely to have a hospital admission for arrhythmia (52 versus 3.3 per 1000 births, RR=16.0, 95% CI 7.35 to 35.0), have their pregnancy care in a tertiary center (713 versus 447 per 1000, RR=1.60, 95% CI 1.42 to 1.79), and be admitted to ICU during the birth admission (61 versus 8.3 per 1000, RR=7.34, 95% CI 3.58 to 15.1). One of the admissions for arrhythmia was an antenatal admission; the other 5 were during the birth admission; either just prior to giving birth or postpartum. Of the arrhythmias documented, 5 were atrial fibrillation; 1 was nonspecifically labeled as "tachycardia."

Severe maternal morbidity was experienced during 16 delivery admissions among women with heart valve prostheses. The events contributing to this were cardiovascular events, blood transfusions, and mechanical ventilation. Five births among women with prosthetic valves were complicated by a major cardiovascular event, including 4 with heart failure (3 among those with a bioprosthetic heart valves prosthesis and 1 among a woman with a mechanical heart valve prosthesis), and 1 stroke and heart failure occurred in the setting of a mechanical heart valve prosthesis. All major cardiovascular events occurred in the hospital admission at which delivery occurred. No diagnoses of endocarditis during pregnancy or the postpartum period were recorded among births to women with a prosthetic heart valve.

Births among women with valve prostheses were significantly more likely to be preterm (183 versus 66 per 1000 births, RR=2.77, 95% CI 1.88 to 4.07). These preterm deliveries were most commonly iatrogenic: by planned prelabor cesarean section or induction of labor (122 versus 28 per 1000, RR=4.37, 95% CI 2.68 to 7.14). Overall, infants of mothers with a heart valve prosthesis had an increased rate of SGA (193 versus 95 per 1000, RR=2.03, 95% CI 1.40 to 2.96).

Birth outcomes by mechanical versus bioprosthetic valve type, for the 52 births where valve type was known, are shown in Table 3. Numbers were small, with only incidence of cesarean section delivery and planned births (by labor induction or prelabor cesarean) reaching statistical significance, which was higher in the group with a mechanical prosthesis. The point estimates of risk for preterm birth—postpartum hemorrhage, ICU admission, and severe maternal morbidity—were all higher for mechanical valve births. The rate of major cardiovascular events was roughly comparable between births among women with mechanical versus those with bioprosthetic valve, although a major cerebrovascular accident attribute to thrombosis was seen in 1 woman with a mechanical valve. The 3 events among the births to women with bioprosthetic valves were all admissions due to congestive heart failure.

Discussion

From this large, contemporary, population-based study, the presence of a prosthetic heart valve increased the incidence of adverse pregnancy and birth outcomes compared with pregnancies in women without a prosthetic heart valve. Presence of a prosthetic heart valve at the time of childbirth increased risk of ICU admission, severe maternal morbidity, or a major maternal cardiovascular event. The infants were at increased risk of preterm birth and SGA. However, the frequency and RRs for these adverse outcomes were lower than previously reported in population studies\textsuperscript{29,30} and in a systematic review of women with mechanical heart valve prostheses only.\textsuperscript{17}

A previous systematic review of outcomes of women with heart valve prostheses undertaking pregnancy, focusing on the impact of anticoagulation regimen, found maternal mortality complicated 2.9% (95% CI 1.9 to 4.2) of pregnancies in women with a mechanical heart valve prosthesis. A higher prevalence of other adverse events in these pregnancies was also reported, including major bleeding (2.5%, 95% CI 1.7 to 3.5) and thromboembolic events (3.9% to 33.3%, dependent on anticoagulant regimen).\textsuperscript{17} While in this NSW study the incidence of perinatal mortality among births to women with a heart valve prosthesis was still higher than that among births

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to women without a maternal heart valve prosthesis, complications were much fewer, with no maternal mortality seen. This likely reflects the contemporary population of valve recipients, with fewer of the more thrombogenic cage-and-ball style valves, accounting for 49.7% of the valves in women in the previous systematic review, as well as the presence of bioprosthetic valve recipients. In addition to the higher rate of thromboembolic events, the higher level of anticoagulation required for cage-and-ball valves is associated with an increased incidence of hemorrhagic events and fetal death.17 Based on the use of cage-and-ball valves over time in Australia31,32 and the maternal age of the study population, we estimate that no more than 3 (2.2%) of the 136 pregnancies in this study are likely to have occurred in the context of these valves.

The choice of valve prosthesis type in women of reproductive age remains at the discretion of the physician and woman. International guidelines recommend that bioprosthetic valves be considered in women wishing to undertake pregnancy in the future to avoid the complications associated with anticoagulation required for mechanical valves.11,18,19 Current evidence suggests that there is no increase in the deterioration of bioprosthetic valves during pregnancy,33–35 although there is a noted propensity for earlier valvular dysfunction with bioprosthetic valves as opposed to mechanical valves, with implications for reoperation.36 From the population data evaluated in this study there was a trend toward mechanical valve association with higher relative risk of ICU admission, cardiac events, postpartum hemorrhage, and stillbirth, compared with bioprosthetic valves. Despite having 10 years of longitudinally linked birth data, a longer time-frame may be needed to have sufficient number of birth outcomes by valve type to draw conclusions about relative birth outcomes.

### Table 2. Birth Outcomes, by Prosthetic Heart Valve Status Among All Births ≥20 Weeks

<table>
<thead>
<tr>
<th>Birth Outcome</th>
<th>Valve Prosthesis (n=115), n (Rate per 1000)</th>
<th>No Valve Prosthesis (n=1 037 159), Rate per 1000</th>
<th>Rate Ratio* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy hypertension</td>
<td>17 (148)</td>
<td>95</td>
<td>1.56 (1.01 to 2.43)</td>
</tr>
<tr>
<td>Gestational diabetes</td>
<td>2 (17)</td>
<td>59</td>
<td>0.30 (0.08 to 1.17)</td>
</tr>
<tr>
<td>Induction of labor</td>
<td>32 (278)</td>
<td>252</td>
<td>1.10 (0.82 to 1.48)</td>
</tr>
<tr>
<td>Cesarean section</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prelabor</td>
<td>38 (330)</td>
<td>161</td>
<td>2.06 (1.59 to 2.67)</td>
</tr>
<tr>
<td>Intrapartum</td>
<td>14 (122)</td>
<td>119</td>
<td>1.02 (0.63 to 1.67)</td>
</tr>
<tr>
<td>Gestational age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20 to 27 weeks</td>
<td>3 (26)</td>
<td>6.6</td>
<td>3.94 (1.29 to 12.0)</td>
</tr>
<tr>
<td>28 to 33 weeks</td>
<td>6 (52)</td>
<td>14</td>
<td>3.72 (1.71 to 8.11)</td>
</tr>
<tr>
<td>34 to 36 weeks</td>
<td>12 (104)</td>
<td>45</td>
<td>2.31 (1.35 to 3.95)</td>
</tr>
<tr>
<td>37 to 38 weeks</td>
<td>41 (357)</td>
<td>221</td>
<td>1.61 (1.26 to 2.06)</td>
</tr>
<tr>
<td>≥39 weeks</td>
<td>53 (461)</td>
<td>713</td>
<td>0.65 (0.53 to 0.79)</td>
</tr>
<tr>
<td>Planned preterm birth†</td>
<td>14 (122)</td>
<td>28</td>
<td>4.37 (2.68 to 7.14)</td>
</tr>
<tr>
<td>Perinatal death</td>
<td>2 (17)</td>
<td>8.5</td>
<td>1.94 (0.49 to 7.67)</td>
</tr>
<tr>
<td>SGA infant‡</td>
<td>22 (193)</td>
<td>95</td>
<td>2.03 (1.40 to 2.96)</td>
</tr>
<tr>
<td>Birth admission</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe maternal morbidity</td>
<td>16 (139)</td>
<td>14</td>
<td>9.96 (6.32 to 15.7)</td>
</tr>
<tr>
<td>Length of admission (days: median, IQR)</td>
<td>4 (30 to 70)</td>
<td>4 (20 to 50)</td>
<td></td>
</tr>
<tr>
<td>ICU admission</td>
<td>7 (61)</td>
<td>8.3</td>
<td>7.34 (3.58)</td>
</tr>
<tr>
<td>Postpartum hemorrhage</td>
<td>17 (148)</td>
<td>71</td>
<td>2.09 (1.35)</td>
</tr>
<tr>
<td>Major maternal cardiovascular event to 42 days' postpartum</td>
<td>5 (43)</td>
<td>1.3</td>
<td>34.6 (14.6 to 81.6)</td>
</tr>
</tbody>
</table>

ICU indicates intensive care unit; IQR, interquartile range; SGA, small-for-gestational-age.

*Rate ratio of each outcome among births where the mother had a prosthetic heart valve compared with those who did not have a prosthetic valve.

†Induction of labor or prelabor cesarean section at <37 weeks.
‡Denominator for SGA infant is all births >24 weeks, n=114.
Recently published studies that examine contemporary pregnancies in the setting of maternal mechanical or bioprosthetic heart valves include only small numbers of women with bioprosthetic heart valves, precluding subgroup analysis.\textsuperscript{30,37,38} Larger studies focusing solely on pregnancies in those women with a bioprosthetic heart valve contain scant information on pregnancy and infant outcomes.\textsuperscript{33,34,39} The cohort presented in this study, containing 38 pregnancies in which the woman was known to have a bioprosthetic heart valve, represents the largest published series examining maternal, fetal, and infant outcomes in women with this type of prostheses with all pregnancies occurring in the contemporary setting (after 2000).

The propensity for development of congestive heart failure, seen in 79 per 1000 births among women with a bioprosthetic valve and in previous studies,\textsuperscript{40–42} supports the need for a structured regimen of cardiac surveillance during pregnancy. There has been limited work advocating the role of serial B-type natriuretic peptide (BNP) measurements in predicting cardiovascular adverse events in pregnancy,\textsuperscript{43} not yet explored in the prosthesis setting. B-type natriuretic peptide (BNP) has also been shown as a measure of valvular disease severity outside the pregnancy setting.\textsuperscript{44} Further work in this area may allow women to be better informed about the risks of undertaking pregnancy and guide both obstetricians and cardiologists.

Infants born to women with a heart valve prosthesis in this study had an increased incidence of preterm birth and SGA. Of the 21 preterm births, 14 were iatrogenic (122 versus 28 per 1000 births, RR 4.37, 95\% CI 2.68 to 7.14). In a large, population-based Danish study prematurity was also the predominant adverse neonatal event, affecting 49\% of live births. This was similarly iatrogenic, attributable to a high preterm cesarean section rate.\textsuperscript{30} This method of delivery allows control of the anticoagulation regimen and decreases the risk of intracerebral hemorrhage associated with vaginal delivery of an anticoagulated fetus. SGA infants may also have been delivered electively preterm due to concerns about intrauterine growth restriction or other fetal compromise, potentially contributing to the number of iatrogenic preterm births. The risk for extreme prematurity (gestational age 20 to 27 weeks), carrying the most significant morbidity, of infants born to mothers with a heart valve prosthesis in the NSW population was 26 per 1000 births, which is not insignificant.

The higher incidence of SGA infants seen has been noted in previous cohort studies examining populations of women with heart disease undertaking pregnancy\textsuperscript{10,45,46} and specifically in pregnancy in the setting of heart valve prostheses.\textsuperscript{40,42,47} A number of reasons have been proposed to account for this. First is the potential inability of women with a degree of cardiac insufficiency to increase requirements sufficient for normal fetal growth, as postulated in studies where having an SGA infant was used to predict later maternal cardiovascular mortality in healthy women.\textsuperscript{46} The second is a reflection of the poorer health status in general of women with chronic heart disease.\textsuperscript{46} There has been limited work examining the longitudinal outcomes of infants born to a woman with a heart valve prosthesis, a potentially important area of further research given the increase in number of women with any heart disease undertaking pregnancy.

The strengths of this study include the size of the population evaluated, representing one of the largest reported
series of pregnancies in contemporary heart valve recipients. This study also provides the most comprehensive consideration of cardiac and perinatal outcomes in pregnancies subsequent to 2000 where a maternal bioprosthetic heart valve is present. Another strength is the known reliability of the reporting of the perinatal factors in the NSW Perinatal Data Collection, used in this study. While the validity of the identification of valve prostheses in routinely collected data has not been evaluated, other cardiac procedures (e.g., angioplasty and coronary artery bypass graft surgery), the basis for billing, are reliably and accurately reported. The high quality of the record linkage for the study highlights the value of record linkage in exploring rare conditions, interventions, and subsequent health outcomes, with all women experiencing ongoing pregnancies in NSW and outcomes included.

While this study explores the pregnancy and birth outcomes for women with and without an existing prosthetic heart valve, it is unable to answer whether women with a prosthetic heart valve are less likely or unable to experience pregnancy. Other limitations include a lack of detailed clinical information; data on medication use or the temporality of events during an admission were unavailable. Information on specific heart valve type (mechanical or bioprosthetic) for some women undergoing valve prosthesis implantation before 2000 was also unavailable, contributing to an incomplete profile for these pregnancies. There is also underascertainment of miscarriages and terminations of pregnancy in both women with heart valve prostheses and the wider population, because this is only available if there is an associated hospital admission.

Conclusion

Pregnancies in women with a heart valve prosthesis, even in the contemporary setting, still demonstrate a higher incidence of adverse cardiovascular, pregnancy, and birth outcomes. The risk of these is relatively low and no maternal mortality was seen in this population. While these contemporary data support that bioprosthetic valves are safer during pregnancy, larger numbers of women are needed to confirm this, as well as longer follow-up of valve-related complications and childhood outcomes. Ongoing attention in this area is needed for the development of a structured, multidisciplinary regimen for obstetric and cardiac surveillance during pregnancy in women with a heart valve prosthesis.

Acknowledgments

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Disclosures

None.

References


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