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# Biological versus mechanical heart valve prosthesis during pregnancy in women with congenital heart disease

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ABSTRACT

*Background:* We evaluate pregnancy outcome and anticoagulation regimes in women with mechanical and biological prosthetic heart valves (PHV) for congenital heart disease.
*Methods:* Retrospective multicenter cohort studying pregnancy outcomes in an existing cohort of patients with PHV.
*Results:* 52 women had 102 pregnancies of which 78 pregnancies (46 women) ≥20 weeks duration (59 biological, 19 mechanical PHV). Miscarriages ($n = 19$, ≤20 weeks) occurred more frequently in women using anticoagulation ($P < .05$). During 42% of pregnancies of women with mechanical PHV a combined low molecular weight heparin (LMWH) vitamin-K-antagonist anticoagulation regime was used ($n = 8$). Overall, cardiovascular, obstetric and fetal/neonatal complications occurred in 17% ($n = 13$), 68% ($n = 42$) and 42% ($n = 27$) of the pregnancies. Women with mechanical PHV had significantly higher cardiovascular (12% vs 32%, $P < .05$), obstetric (59% vs 85%, $P = .02$) and fetal/neonatal (34% vs 61%, $P < .05$) complication rates than women with biological PHV. This was related to PHV thrombosis ($n = 3$, $P < .02$), post-partum hemorrhage ($P < .02$), cesarean section ($P < .02$), low birth weight and small for gestational age (both $P < .05$). PHV thrombosis occurred in 3 pregnancies, including 2/5 pregnancies with pulmonary mechanical PHV. PHV thrombosis was related to necessary cessation of anticoagulation therapy or insufficient monitoring of LMWH. Other cardiovascular complications occurred equally frequent in both groups.
*Conclusion:* Complications occur more often in pregnancies of women with a mechanical PHV than in women with a biological PHV, mainly caused by PHV thrombosis and bleeding complications. Meticulous monitoring of anticoagulation in pregnant women is necessary. Women with a pulmonary mechanical PHV are at high risk of complications.



## 1. Introduction

A growing number of adult women with congenital heart disease (CHD) is treated with prosthetic heart valves (PHV). Still, the choice of type of valve prosthesis is difficult in young women with future desire to become pregnant.

While current European guidelines advise to consider implantation of a biological PHV in women with a pregnancy wish, the underlying evidence is limited [1]. The high deterioration rate of biological PHV at young age poses the woman at risk of going through pregnancy with a stenotic or regurgitant PHV [2]. Young women with a biological PHV inevitably face re-operation because of valve deterioration, with associated risks. Whether or not pregnancy itself accelerates the deterioration rate of PHVs is a debated controversy [2–5].

Mechanical PHV necessitate anticoagulation therapy, but there are no anticoagulation regimens that are sufficiently proven to be effective as well as safe for both mother and child [6–9]. Vitamin K antagonists

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(VKA) are associated with increased risk of pregnancy loss and with embryopathy, especially at higher dosages [10]. Anticoagulation with unfractionated or low-molecular weight heparin (UFH or LMWH) appears to be associated with increased risk of PHV thrombosis, even with monitoring of anticoagulation effect and dose adjusting. [9,11–13] Current anticoagulation advices are largely based on expert opinion since randomized studies are lacking and reported series are often small [6,14]. European and American guidelines advise the use of a combined regimen of VKA and LMWH in a substantial proportion of pregnancies, but there are relatively few data to support this advice [9,15]. Furthermore, data concerning outcome of pregnancies in women with right sided mechanical PHVs are scarce. [9,11,12,16] Even less is known about non-cardiac (obstetric and fetal/neonatal) complications and their relation with cardiac complications and PHV type in pregnant women with PHV. With insufficient evidence, an explicit preference for either biological or mechanical PHV in young women who wish to become pregnant is hard to substantiate. We therefore aim to perform a retrospective multicenter cohort study to evaluate and compare cardiovascular, obstetric and fetal/neonatal outcomes of pregnancy in women with mechanical and biological PHV for CHD and discuss anticoagulation regimen.

## 2. Methods

### 2.1. Patient inclusion

We recruited women with pregnancy after PHV implantation from the Dutch PROSTAVA (PROSTheses in Adult congenital heart VAlve disease) study. This study primarily aims to investigate functional outcome related to PHV characteristics in patients with CHD [17]. The secondary aim is to retrospectively evaluate PHV complications, including pregnancy-related complications, which was the primary goal of our sub study [18–20]. The study has been approved by the institutional review board of all participating centers. For the PROSTAVA study, patients with CHD and a PHV were identified through the Dutch national CONCOR database, founded in 2001 [21]. CONCOR registers all adults with CHD in the Netherlands with their informed consent [21]. All women enlisted in the PROSTAVA database who had been pregnant after PHV implantation were included in the current analysis. Data were collected from their medical files. A detailed and structured questionnaire was obtained from women who had given their consent to be contacted by PROSTAVA investigators, in order to clarify and supplement data from the medical files. Complications identified through the questionnaire were only registered when confirmed by medical files.

### 2.2. End points

Our primary endpoint consisted of cardiovascular complications during pregnancy and up to 6 months after pregnancy. Secondary endpoints were obstetric, fetal/neonatal and general pregnancy outcomes. Furthermore, we evaluated anticoagulation regimes in women with a mechanical PHV and the possible relation with complications.

### 2.3. Collected data

Only pregnancies after implantation of PHV were taken into account. Baseline characteristics included age, underlying heart disease, PHV characteristics (type, size, location, date of implantation and times of re-surgery), history of prosthesis-related complications as defined by previously published guidelines (including valve deterioration, valve thrombosis, embolism, hemorrhage and endocarditis), history of other cardiovascular complications (including documented and treated heart failure and any documented pre-pregnancy arrhythmias needing treatment) and general medical history [22]. Pregnancies were defined as completed (>20 weeks and not abortus provocatus) or incompleted (≤20 weeks or abortus provocatus).

Pregnancy related complications were collected for all pregnancies and analyzed for completed pregnancies and defined as occurring during pregnancy and up to 6 months postpartum. Pregnancy related complications were defined in accordance with our previous studies and according to guidelines [20,22,23]. We collected prosthesis related cardiovascular complications (including valve deterioration, valve thrombosis, embolism, hemorrhage, endocarditis and hemolytic anemia), other cardiovascular complications (including need for urgent invasive non-prosthesis related cardiovascular procedures, heart failure or arrhythmias requiring (change of) treatment, myocardial infarction, intensive care or coronary care unit (IC/CCU) admission). Furthermore we collected New York Heart Association (NYHA) class deterioration ≥2 points as a secondary cardiovascular outcome measure [22].

For evaluation of anticoagulation regimes data concerning anticoagulation medication and monitoring before and during pregnancy were retrieved from medical files. Obstetric complications were defined in line with previous papers of our group as primary obstetric events (including assisted delivery (forceps/vacuum extraction, elective or emergency Cesarean Section), pregnancy induced hypertension, (pre)eclampsia, HELLP syndrome, non-cardiac death, postpartum hemorrhage (blood loss >500 mL (vaginal delivery) or >1000 mL (cesarean section), >1 mmol/L drop in hemoglobin levels or need for transfusion therapy), hemorrhage from the placenta, premature labor, preterm prelabor rupture of membranes) and induction of labor as a secondary obstetric event. General maternal complications included hemorrhage (not postpartum, defined as an estimated loss of >0.5 L of blood, >1 mmol/L drop in hemoglobin levels or need for transfusion therapy or documented intracerebral bleeding), hospitalization >1 night, anemia, maternal infection and fever [23].

Fetal/neonatal complications were defined as previously described and included fetal/neonatal death (death after ≥20 wks. of gestation up to 28 days postpartum), neonatal respiratory distress syndrome, infection leading to hospital admission, neonatal intensive care unit (NICU) admission, premature birth (birth <37 wks. gestation, spontaneous or iatrogenic), low birth weight (birth weight < 2500 g), small for gestational age (birth weight < 10th percentile, adjusted for gestational age, based on population values), occurrence of CHD or other congenital disease in the offspring and Apgar-score < 7 (at one and five minutes after birth). [23]

### 2.4. Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics Premium' V 22 for Windows (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, version 22.0. Armonk, NY: IBM Corp.) Missing data were excluded for analysis. Continuous data are presented as mean with standard deviation (SD) or median with interquartile range (IQR) or range, depending on their distribution. Normality was tested with the Kolmogorov-Smirnov test with Lilliefors' correction. Absolute numbers and percentages

**Table 1**
Baseline characteristics for pregnancies in women with PHV for CHD.

| | Valve type | | |
|---|---|---|---|
| | All | Biological PHV only | Mechanical PHV/combined |
| Women, all (N) | 52 | 40 | 12 |
| Pregnancies, all (N) | 102 | 74 | 28 |
| Abortus provocatus (N) | 5 | 4 | 1 |
| Miscarriages (N, %) | 19 (19%) | 11 (16%) | 8 (30%) $P = .12$ |
| Women with completed pregnancies (N) | 46 | 36 | 10 |
| Completed pregnancies (N) | 78 | 59 | 19 |
| Underlying heart disease* (N women) | Congenital AOV | 20 | 8 |
| | ToF | 6 | 1 |
| | PS | 8 | 0 |
| | Marfan | 0 | 1 |
| | Other | 2 | 0 |
| Location of PHV* (N pregnancies) | AVR | 19 | 9 |
| | PVR | 26 | 2 |
| | MVR | 2 | 0 |
| | PVR + AVR | 12 | 3 |
| | MVR + AVR | 0 | 3 |
| | PVR + AVR + MVR | 0 | 2 |
| Pre-pregnancy re-surgery for PHV* (N pregnancies)(%) | 16 (21%) | 8 (14%) | 8 (42%)‡ $P < .02$ |
| Pre-pregnancy cardiovascular and prosthesis related history* (N pregnancies) | Rhythm disorder | 8 | 5 |
| | Heart failure | 3 | 4 |
| | Arterial thrombosis | 1 | 0 |
| | PVLeakage | 0 | 3 |
| | Infection | 0 | 3 |
| | Trombo-embolism | 0 | 1 |
| Gravida* | 1 (1–8) | 1 (1–6) | 2 (1–8) |
| Parity* | 0 (0–4) | 0 (0–4) | 1 (0–3) |
| Nulliparous* (%) | (39) 55% | 30 (58%) | 9 (47%) |
| Age at pregnancy* (years, range) | 29 (20–41) | 29 (20–41) | 30 (23–40) |
| Time between last PHV surgery and pregnancy* (years, range) | 6 (0−22) | 6 (0−21) | 6 (2−22) |

Completed pregnancies: >20 weeks and not abortus provocatus. Incompleted pregnancies: ≤20 weeks or abortus provocatus. Missing data were excluded for analysis. *Analysis performed in completed pregnancies, AVR = aortic valve replacement, CHD = congenital heart disease, Congenital AOV = congenital aortic valve disease including aortic stenosis, aortic regurgitation and bicuspid aortic valves, Cong PS = congenital pulmonic valve stenosis, MVR = mitral valve replacement, PHV = prosthetic heart valve(s), PVLeakage = paravalvular leakage, PVR = pulmonary valve replacement, ToF = Fallots tetralogy. ‡*Re*-surgery was related to deterioration of a biological PHV even before pregnancy could occur in 2 women.

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