How Pregnancy Impacts Adult Cyanotic Congenital Heart Disease

A Multicenter Observational Study

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Survival into adulthood of patients with unrepaired cyanotic congenital heart defects (CHDs) is possible when cyanotic CHDs are deemed unsuitable for radical surgical repair but are compatible with survival. These situations include, for example, complex pulmonary atresia with aortopulmonary collaterals and single-ventricle hearts (with and without earlier palliation). This is also the case when patients with cyanotic CHDs reach adulthood without serious symptoms requiring surgery, such as those with mild tetralogy of Fallot, Ebstein's anomaly, and some cases of corrected transposition of the great arteries with pulmonary stenosis and ventricular septal defect. Many women with these heart conditions wish to become pregnant, which creates a situation of high maternal and fetal risks of complications.[1] Management of these patients before, during, and after pregnancy has improved, with an earlier recognition of the underlying disease, improved understanding of cardiopulmonary physiopathology, better prenatal and peri-partum obstetric/anesthetic management, and the introduction of a multidisciplinary approach.[2]

We retrospectively reviewed the charts of all pregnant women with cyanotic CHDs (n=51) who were followed in 11 adult CHD referral centers from the M3C French network (Center de référence des Malformations Cardiaques Congénitales Complexes) between 1997 and 2015. We included patients with central cyanosis on effort or at rest, with appropriate cardiac anatomy underpinning this condition. We excluded for this study patients with pulmonary arterial hypertension, which concerned patients with either Eisenmenger syndrome (n=17) or segmental pulmonary hypertension confirmed invasively (group 5 according to the latest classification of pulmonary hypertension,[3] n=3). The ethical review board of each institution approved the study, and all patients provided written informed consent. The study population was divided into 4 groups according to the cyanosis mechanism as previously described by Presbitero et al (Table).[1] We collected data on the demographic, clinical, and biological characteristics. Cardiac complications (arrhythmia, heart failure requiring treatment, systemic thromboembolic complication, worsening of hypoxemia [decrease in saturation at rest >5% compared with basal saturation, leading to a hospitalization], and infective endocarditis) were documented. A mixed logistic regression, with number of pregnancies nested within each individual, was used to determine risk factors for maternal cardiovascular complications.

Our population consisted of 71 pregnancies in 31 patients (Table). Fifteen patients (48%) had undergone previous palliative shunts and remained cyanotic. Systemic ventricle function was normal in all but 2 patients with moderately to severely impaired systolic function before pregnancy. No patient died during pregnancy or the postpartum period. Cardiovascular complications occurred in 13 completed pregnancies (27%, 95% confidence interval, 14–46) in 10 patients (32%, 95% confidence interval, 17–51). Three patients developed heart failure and 2 experienced de novo supraventricular tachycardia. The more common complication was worsening of hypoxemia (n=7), requiring hospitalization in 3 cases. No maternal baseline char-

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Table 1. Baseline Maternal Characteristics and Maternal Outcomes

	Group 1 (n=7): ventricular R-L shunt and systemic LV	Group 2 (n=18): univentricular heart	Group 3 (n=4): ventricular R-L shunt and systemic RV	Group 4 (n=2): atrial R-L shunt	Global (n=31)
Principal cardiac lesions and baseline maternal characteristics					
Principal cardiac lesions	4 tetralogy of Fallot; 3 pulmonary atresia+VSD+MAPCA	18 congenital heart diseases with single-ventricle physiology	3 L-TGA+VSD+PS or pulmonary atresia; 1 D-TGA+VSD	2 Ebstein's anomaly+ASD	
Cardiac surgeries	1 BT; 2 RV-PA stenotic conduit	4TCPC; 2 Blalock-Taussig; 1 pulmonary banding; 2 Glenn; 1 SV-PA stenotic conduit	1 Mustard; 1 LV- PA stenotic conduit; 1 repair*	0	16 (52%)
History of cardiovascular event†	2	4	1	1	8 (26%)
Systemic ventricular function					
Normal	7	17	2	2	28 (90%)
Moderately impaired	0	1	1	0	
Severely impaired	0	0	1	0	
Maternal treatment					
None	6	7	1	2	16 (52%)
Diuretics	0	1	0	0	1 (3%)
Antiarrhythmics	0	5	2	0	7 (23%)
Receiving anticoagulants or antiplatelet drugs	1 ASA	8 ASA and 1 VKA	1 ASA	0	11 (35%)
Risk scores,[2] mean [max to min]					
CARPREG	1	1.25 [1 to 3]	1.2 [1 to 3]	1	1.11 [1 to 3]
ZAHARA	2.29 [1 to 3.25]	2.70 [1 to 4.75]	2.88 [1 to 4.75]	1.36 [1 to 1.75]	2.3 [1 to 4.75]
Age, y	28±8.0	26±5.5	27±11.4	22.8	27±6
Pregestational body mass index, kg/m^2	25.8±8.4	22.6±5.4	19.5±0.8	19.0	22.4±4.5
NYHA I/II/III/IV	1/6/0/0	4/13/1/0	1/2/1/0	0/2/0/0	6/22/3/0
Oxygen saturation at rest, %	88±7	88±4	91±1	92 and 95	89±2
Hemoglobin, g/dL	16.1±1.1	15.7±2.6	14.6±1.3	14.9 and 15.0	14.9±1.8
Maternal outcomes of completed pregnancies, n/n' completed pregnancies, %					
Maternal cardiac complications	4/13 (31%)	7/25 (28%)	2/8 (25%)	0/2	13/48 (27%)
Heart failure	1	2	1	0	
Arrhythmia	1	1	0	0	
Deep hypoxemia‡	2	3	1	0	
Infective endocarditis	0	1	0	0	
Anticoagulation therapy					
Prophylactic	1	9	1	0	11 (23%)
Curative	0	1	1	0	2 (4%)

(*Continued*)

Table 1. Continued

Antiplatelet drugs	1	3	1	0	5 (10%)
No anticoagulation or antiplatelet drug	11	12	5	2	30 (63%)
Cardiac treatment					
Diuretics	0	3	0	0	
Antiarrhythmics	1	2	1	0	
Maternal characteristics at last follow-up					
Cardiovascular event†	3	5	2	1	11/31 (35%)
Systemic ventricular systolic function					
Normal	5	16	2	2	25/31 (81%)
Moderately impaired	2	2	0	0	
Severely impaired	0	0	2	0	
NYHA I/II/III/IV	0/4/3/0	4/11/3/0	1/1/2/0	0/2/0/0	5/18/8/0
Oxygen saturation, %	88±6	90±2	92±1	93 and 95	89±5

ASA indicates acetylsalicylic acid; ASD, atrial septal defect; BT, Blalock-Taussig anastomosis; CARPREG, Cardiac Disease in Pregnancy; LV-PA, left ventricle-pulmonary artery; MAPCA, major aortopulmonary collateral artery; NYHA, New York Heart Association; PB, pulmonary banding; PS, pulmonary stenosis; R-L, right to left; RV, right ventricle; RV-PA, right ventricle-pulmonary artery; SV-PA, single ventricle-pulmonary artery; TCPC, total cavopulmonary connection; TGA, transposition of the great arteries; VKA, vitamin K antagonist; VSD, ventricular septal defect; and ZAHARA, Zwangerschap bij Aangeboren Hartafwijkingen. No significant difference was observed among the 4 groups. n indicates the number of completed pregnancies.

*Repair consisted of closure of VSD and a conduit placement between the left ventricle and the main pulmonary artery.

†Cardiovascular events included heart failure, arrhythmia, thromboembolism, and infective endocarditis.

‡Deep hypoxemia was defined by a decrease in saturation at rest >5% compared with basal saturation or leading to a hospitalization.

acteristics, listed in Table, were statistically predictive of cardiovascular complications. Anticoagulation treatment was given in 13 pregnancies and antiplatelet agents in 5. No thromboembolic complication was recorded during pregnancy or the postpartum period. *Streptococcus milleri* infective endocarditis occurred in the postpartum period in 1 patient who did not receive peripartum antibiotic prophylaxis. At last follow-up (median 3.8 years, 95% confidence interval, 0.9–14.8), no patients died, but 4 (13%) developed chronic heart failure, with deterioration in New York Heart Assocation functional class from II to III, associated with a decrease in systolic ventricular function on echocardiography, from normal before pregnancy to moderately impaired at last follow-up in 3 patients and from moderately impaired to severely impaired in 1. Furthermore, New York Heart Assocation functional class was impaired in 3 other patients without documented systolic ventricle dysfunction and without significant decrease in oxygen saturation. Moreover, atrial arrhythmia occurred in 8 patients, ventricular tachycardia in 1, and stroke in 5. Among the 10 patients who experienced cardiovascular complications during pregnancy, 3 had subsequent heart failure or arrhythmia.

These findings, with no maternal death, indicate that patients with cyanotic CHDs can carry a pregnancy and deliver with lower maternal risks than previously described.[1] This difference may be explained by recent improvement of the high-risk pregnancies prenatal and peripartum management with a multidisciplinary approach[2] and impact of preconception counseling. With only a quarter of our population receiving anticoagulation or antiplatelet therapy, it is difficult to associate this treatment with the absence of thromboembolic complications. Prophylactic anticoagulation may be more relevant during the postpartum period because postpartum maternal thromboembolic risk is increased at least 3-fold compared with the risk during pregnancy.[4]

Long-term outcome in this cohort is characterized by 13% risk of late chronic heart failure. Systemic ventricle function was semiquantitatively assessed with echocardiography. This method is limited in complex CHDs, and heart failure diagnosis could be underestimated. Larger prospective studies on pregnancy-related complications of patients with cyanotic CHDs are needed to develop more rigorous conclusions and elucidate the impact of pregnancy on this unique patient population with cyanotic CHDs.

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DISCLOSURES

None.

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FOOTNOTES

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