PRegnancy **O**utcomes in **F**ontans with **A**nticoagulation **T**herapy (**PROFAT)**. An **ISACHD** sponsored Multi-institutional Retrospective Study

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Background

- The success of the Fontan operation has resulted in an increasing number of patients reaching childbearing age
- There is limited information about the overall risks for Fontan patients who become pregnant.
- Fontan patients and pregnant patients are both at increased thrombosis risk, but overall risk and management of the combined state is poorly understood.
- ESC guidelines advise anticoagulation for all pregnant Fontan patients, but this is not evidence based

Thrombosis in Fontans

- Risk factors
  - Low cardiac output
  - Less pulsatile pulmonary blood flow
  - Chronic venous hypertension
  - Greater degree of inflammation
- Coagulation abnormalities
  - Decreased Protein C and Protein S
  - Increased circulating vWF and Factor VIII
  - Evidence of platelet activation

CPP congress Venice 2014

Subplacental bleeding in two pregnant women with a Fontan circulation

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Fontans in CHD/Pregnancy Literature:

- CARPREG (Siu 2001)
  - 5 Univentricular patients; 2 SVT episodes
- ZAHARA (Drenthen 2010)
  - 9 “Complex Cyanotic Heart Disease”, including Fontan palliation; complications included arrhythmia and heart failure
- Khairy
  - 4 Fontan patients; 1 arrhythmia reported
- Balci 2014
  - 3 Fontan patients; 1 primary CV event recorded

Fontan and Pregnancy in Literature

- Multiple case reports focusing on cardiac, obstetric, or anesthetic management
- Canobbio (1994): Questionnaire based study on pregnancy outcomes in Fontan patients
  - 21 women with 33 pregnancies
- Drenthen et al (2006): Series of 6 women with 10 pregnancies
- Gouton (2015): The largest study on this topic to date is a retrospective analysis of 37 patients with 59 pregnancies.
  - Thrombosis identified as an area of concern, but larger numbers are needed to further clarify risks and management strategies
- Most common maternal complications observed were arrhythmia and CHF.
- There is a high rate of offspring complications, including miscarriage, preterm delivery, and SGA

Data for Thrombosis and Bleeding

- In Gouton et al (2015):
  - 46% of pregnancies received prophylactic anticoagulation; 22% received therapeutic anticoagulation
  - 6 hemorrhagic events (2 with antiplatelet therapy, 1 with prophylactic anticoagulation, 3 with therapeutic anticoagulation)
  - 3 thrombotic events (1 with no anticoagulation, one with antiplatelet therapy, one with prophylactic anticoagulation
- Not enough data to draw conclusions to guide future therapy

Fontan and Pregnancy in Literature

- Cauldwell (2016):
  - Retrospective review focusing on prenatal counseling and pregnancy outcomes in Fontan patients
  - 8 women had 14 live births and 9 miscarriages
  - Pregnant patients maintained on prophylactic LMWH
  - One thrombotic event (PE), 50% of deliveries with PPH
  - This congress: presented data that Fontan circulation is a risk factor for increased peripartum bleeding
- Zentner (2016)
  - Questionnaire based study examining prepregnancy management and pregnancy outcomes in the Australia-New Zealand Fontan Registry
  - 11 women had 14 live births and 9 miscarriages
  - 3 pregnancies with no anticoagulation, 6 with antiplatelet therapy, 5 pregnancies with LMWH/Coumadin
  - Antepartum bleeding reported in 4 patients, postpartum bleeding in 6 patients

Study Aims

- Primary: To define outcomes and complications in pregnant women with a Fontan circulation relative to their associated use of antiplatelet and antithrombotic therapy. Complications related to both bleeding and thrombosis will be evaluated.
- Secondary:
  - To determine risk factors for adverse maternal and fetal outcomes in women managed on anticoagulation and/or antiplatelet therapies
  - To further define cardiovascular, obstetric and neonatal outcomes in this population

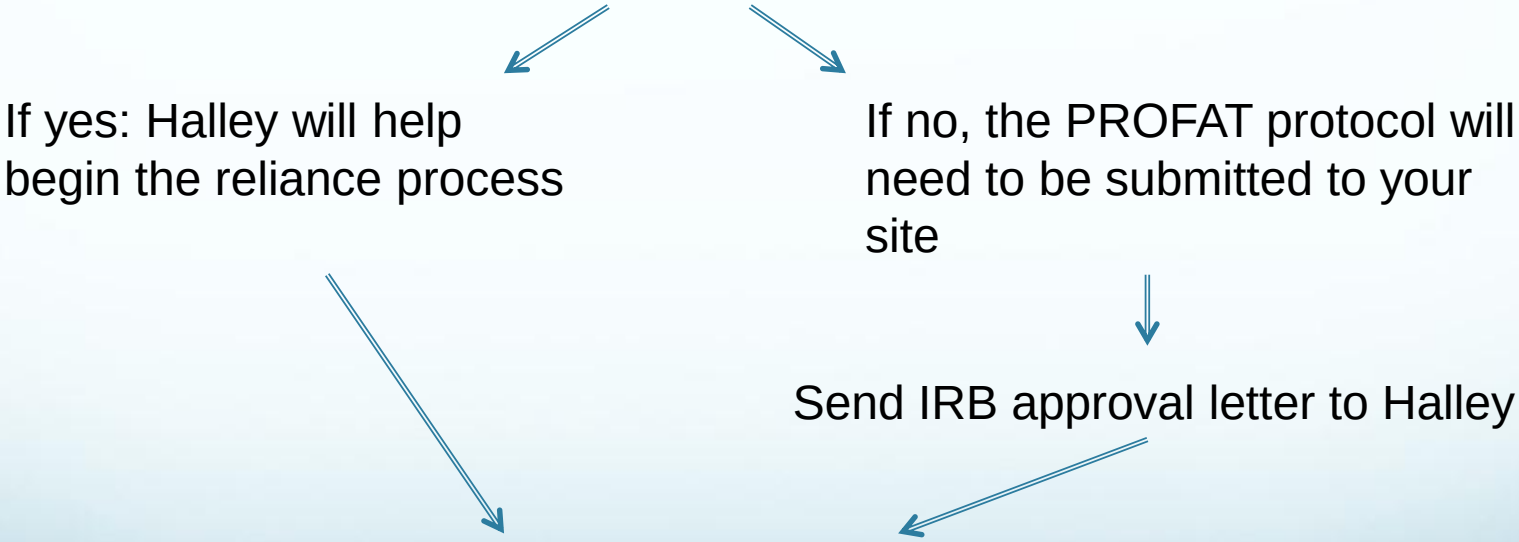
Data to be collected

- Deidentified data on patients with a Fontan who have undergone one or more pregnancies
  - Maternal baseline characteristics
  - Anticoagulation or antiplatelet regimen, if any
  - Bleeding and thrombosis complications (type, severity, and treatment)
  - Maternal cardiac complications
  - Maternal obstetric complications
  - Neonatal baseline data and complications
  - Pathological placental findings (if available)

- Eligible Data: 2005-2015

Process to Participate

1. Indicate agreement to participate in PROFAT by email to Halley.estridge@cchmc.org.
2. Determine you would like to rely on CCHMC's IRB



Logistical Information

- Currently IRB (Ethics Board) approved at Cincinnati Children's Medical Center
- Data will be collected via REDCap, a secure web based data collection application. Once the site's IRB and approval process is complete, we will contact each site about access to the database.

Currently Participating Centers

Items to Discuss

- Control Population
  - Current ideas: control group of age matched nonpregnant Fontan patients

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