Fetal Heart Society
IRB Working Draft (6-9-2015)

Short Title
Fetal Heart Society Collaborative Research Database Project

Full Study Title
Retrospective and prospective data collection of maternal, fetal, and neonatal variables from patients referred to Fetal Heart Society participant centers with a maternal or fetal abnormality affecting the cardiovascular system.

Summary/Abstract
The Fetal Heart Society facilitates collaborative research initiatives regarding abnormalities detected in prenatal life that affect the cardiovascular system. Such abnormalities are rare, and the FHS shares information regarding diagnosis, treatment, and outcomes of these diseases. This collaboration affords a better understanding of maternal and fetal disease, its effects on the cardiovascular system, and ultimately improves prenatal counseling and postnatal outcomes. To achieve this goal, the FHS maintains a secure, online data repository pertaining to these abnormalities.

Summary of the Research

Purpose

1) Retrospectively review patients referred to the Fetal Heart Society (FHS) participant sites for maternal and fetal abnormalities affecting the cardiovascular system and study their outcomes. The retrospective period is January 1, 1981 to the present. Clinical and demographic variables and diagnostic data will be reviewed.

2) Prospectively study pregnant women and their fetuses referred to FHS participant sites for maternal or fetal abnormalities affecting the cardiovascular system and to study their outcomes. The time frame is [the present date], through December 31, 2023.

Background and significance
The Fetal Heart Society was formed in 2015 by leaders in the field of fetal cardiology and maternal-fetal-medicine. The goal of the FHS is to foster collaborative multicenter investigations among fetal cardiovascular researchers from any relevant discipline, including pediatric and fetal cardiology, maternal fetal medicine, obstetrics and gynecology, neonatology, pediatrics, and neurology.

Fetal abnormalities affecting the cardiovascular system are rare. Collaborations such as the FHS allow a greater breadth of understanding of the spectrum of disease affecting the cardiovascular system. The goal of the FHS is to better understand maternal and fetal disease, its effects on the cardiovascular system, and to ultimately improve outcomes. The FHS facilitates collaborative research by maintaining a secure, centralized clinical data storage repository for the purposes of research.

In the past, many patients have been referred to Fetal Heart Society participant site for evaluation and treatment of maternal or fetal abnormalities. Until recently, most studies regarding maternal or fetal disease have been single-center studies. Many maternal and fetal

abnormalities are exceedingly rare. Due to the relative rarity of many forms of fetal congenital malformations, little collective short- and long-term data on outcomes exist. The Fetal Heart Society aims to collect data on a large cohort of patients and improve best clinical practice and improve outcomes for rare diseases.

Research design and methods
Information regarding maternal and pregnancy history, fetus, delivery, and neonatal course through hospital discharge will be studied.

Data will be analyzed and correlated to short- and/or long-term fetal/neonatal outcomes to provide further insight to diagnosis and treatment of fetal and neonatal disease. The retrospective and/or prospective data of approximately [#] patients from all Fetal Heart Society sites will be collected and analyzed.

Statistical Analysis:
Outcomes of interest are fetal survival, postnatal diagnosis, delivery course, surgical intervention, hospital length of stay, intensive care unit length of stay, and survival to hospital discharge.

Statistical Considerations:
Data will be analyzed and correlated with maternal, pregnancy, and neonatal outcomes.

Analyses will include:
1. Calculation of descriptive statistics such as mean, median, SD, range, tallies
2. Examination of graphs such as outcome vs time, as well as scatterplots of two variables
3. Estimation of differences between subject cohorts by t-test or Mann-Whitney test
4. Evaluated within-person changes using Wilcoxon rank sum
5. Multivariate and univariate data analyses

Inclusion criteria:
Inclusion criteria include the prenatal diagnoses of any maternal or fetal abnormality affecting the cardiovascular system. Patients will include fetuses of mothers usually aged 12 to 50 years old and newborns.

Exclusion criteria:
There are no exclusion criteria

Risk/Benefit Assessment
This study will be of less than minimal risk to the participants and will not affect the rights and welfare of the participants since the data will be protected by being de-identified and randomly assigned with a study number.

This study offers a benefit to the medical community in that it may allow for more informed counseling of pregnant women whose fetus is potentially affected by any abnormality affecting the cardiovascular system. Furthermore, it will allow practitioners to anticipate the severity of disease and accordingly tailor management strategies and initiate therapies in the delivery room, the perinatal period, and during the postnatal hospital course, thereby improving outcomes.

Subject Privacy & Data Confidentiality

Data which may be used to identify the patient will only be used at local FHS participant sites to obtain clinical data and to review medical records for details of history and clinical course. Once data has been obtained, all patient identifiers will be replaced by a randomly generated number which cannot be traced back to the individual patients. These de-identified data will then be uploaded to the FHS central database. No information which could be used to identify patients will be available once the data is uploaded. Patient identifiers on ultrasound studies will be automatically removed by commercially available software [name] capable of anonymizing such data.

No one outside the research staff at individual FHS participant sites will have access to PHI. PHI obtained for this research will be safeguarded from improper use because 1) only the researchers at local FHS sites will have access, 2) records containing PHI will be entered into local password protected computers only and not uploaded to the FHS database, and 3) there will be no hard copy documents that contain PHI.

HIPAA Waiver Request

We request a waiver of consent for the review of already obtained data given that it will be of less than minimal risk to the participants and will not affect the rights and welfare of the participants since the data will be protected by being de-identified and randomly assigned with a study number. In the case of prospective investigation, we request a waiver of consent, as all data obtained for this study would be obtained during the course of routine clinical care. Data will be protected in the same manner as for data previously obtained.

PHI including name, date of birth and medical record identifiers, is required to identify patients appropriate for the study. PHI will not be disclosed. After patients have been identified, they will be assigned a randomly generated number. This number will be used for each set of data. This randomly assigned number will not be recorded along with any information which could be used to identify the patient. No PHI will be available using the randomly assigned number. No data that could be used to identify the patient will be used in any phase of the study. No other individuals will have access to PHI.

No one outside FHS research staff participants at local FHS sites will have access to the PHI. PHI obtained for this research will be safeguarded from improper use because only the principal and co-investigators will be granted access, records containing PHI will be entered into local password protected computers only, and there will be no hard copy documents. Once submitted to the online database, no PHI will be associated with a given patient. PHI will not be reused or disclosed to third parties unless required by the law for authorized oversight of the research study.

This retrospective study cannot be carried out without the waiver since the families have already been discharged from the hospital and in some instances it will be difficult to locate and contact families for consent. PHI will be required to identify patients appropriate for this retrospective study.

Appendix: Data elements

Prenatal/maternal data:

1. Maternal age at diagnosis
2. Maternal gravida/para status
3. Maternal zip code data
4. Maternal predominant race
5. Maternal medications and doses
6. Maternal diagnosis
7. Maternal prior pregnancy history
8. Placental abnormalities
9. Uterine abnormalities
10. Family history of congenital heart disease
11. Gestational age at diagnosis
12. Genetic diagnosis
13. Extracardiac diagnosis
14. Delivery plan
15. Delivery location
16. Fetal mortality
17. Termination of pregnancy
18. Pregnancy complications
19. Postpartum complications

Fetal data:

1. Estimated date of delivery
2. Cardiac position
3. Cardiothoracic circumference ratio
4. Cardiothoracic area ratio
5. Mitral valve size
6. Mitral valve inflow pattern
7. Aortic valve size
8. Aortic valve flow pattern
9. Tricuspid valve size
10. Tricuspid valve flow pattern
11. Pulmonary valve size
12. Pulmonary valve flow pattern
13. Aorta size
14. Aorta flow pattern
15. Ductus arteriosus size
16. Ductus arteriosus flow pattern
17. Left ventricular long axis dimension diastole
18. Left ventricular short axis dimension diastole
19. Left ventricular long axis dimension systole
20. Left ventricular short axis dimension systole
21. Left ventricular end systolic volume
22. Left ventricular end diastolic volume
23. Right ventricular long axis dimension diastole
24. Right ventricular short axis dimension diastole
25. Right ventricular long axis dimension systole
26. Right ventricular short axis dimension systole
27. Ductus venosus flow pattern

28. Umbilical artery flow pattern
29. Umbilical vein flow pattern
30. Umbilical vein velocity
31. Middle cerebral flow pattern
32. Anterior cerebral flow pattern
33. Posterior cerebral flow pattern
34. Superior vena cava size
35. Superior vena cava vein flow pattern
36. Inferior vena cava size
37. Inferior vena cava vein flow pattern
38. Pulmonary vein flow pattern
39. Foramen ovale flow pattern
40. Femur length
41. Head circumference
42. Biparietal diameter
43. Abdominal circumference
44. Estimated fetal weight
45. Left ventricular function assessment
46. Right ventricular function assessment
47. Presence of extracardiac abnormalities
48. Evidence of hydrops
49. Placental characteristics
50. Umbilical cord insertion site
51. Lung-to-head ratio
52. Number of umbilical cord vessels
53. Presence of thoracic abnormalities
54. Presence of neurologic abnormalities
55. Presence of abdominal abnormalities

Delivery and Neonatal course data:

1. Gestational age at delivery
2. Live birth
3. Delivery room demise
4. Type of delivery
5. Reason for C-section
6. Gender
7. Birth weight
8. Birth length
9. Birth head circumference
10. 1 minute Apgar score
11. 5 minute Apgar score
12. Preductal saturations
13. Postductal saturations
14. Initial infant pH
15. Umbilical vein pH
16. Umbilical artery pH
17. Lowest systolic blood pressure
18. Lowest diastolic blood pressure
19. Need for supplemental oxygen
20. Need for CPAP
21. Need for intubation

22. Need for surfactant
23. Utilization of ECMO
24. Duration of ECMO
25. Diagnostic catheterization performed
26. Catheterization hemodynamic data
27. Interventional catheterization performed
28. Surgical intervention(s) performed
29. Major infections
30. Intensive care unit duration of stay
31. Hospital length of stay
32. Survival to hospital discharge
33. Oral feeding at discharge
34. G-tube feeding at discharge
35. Medications at discharge
36. In-hospital mortality
37. Autopsy performed
38. Autopsy results