Fetal Counseling Provider Information
Last Updated: 10.08.21

Heterotaxy Syndrome

Definition/Anatomy

- Abnormal lateralization of the abdominal viscera, thoracic organs and cardiac atria
- Can be classified into two major subtypes
  - Right Atrial Isomerism (RAI)/Asplenia Syndrome
  - Left Atrial Isomerism (LAI)/Polysplenia Syndrome
- Associated with spectrum of congenital heart disease (see below for detailed list of associated cardiac findings)
  - Systemic venous abnormalities
  - Pulmonary venous abnormalities
  - Inlet abnormalities
  - Conotruncal defects

Incidence

- 1/10,000 live births [1-3]

Fetal Diagnosis

- 93% prenatal detection rate

Right atrial isomerism/Asplenia Syndrome

- Major cardiac defects in 98%
- Suspect if stomach and cardiac apex on opposite sides (viscerocardiac heterotaxy), single ventricle with AVSD or DORV/mitral atresia, if IVC and aorta are on the same side of spine.

Associated cardiac findings:

- Juxtaposition of aorta and IVC (82%) (major diagnostic feature)
- AVSD (73%)
- RV outflow tract obstruction (67%)
- TAPVR (42%), also small/absent pulmonary veins
- Conotruncal anomalies, especially DORV (40%)
- Absence of coronary sinus
- Interrupted IVC (4%), persistent LSVC (42%)
- Rhythm disturbances rare (1.3%), but can have bilateral sinus nodes or macroreentrant SVT

Associated noncardiac findings:

- Abnormal stomach (55%) and liver position (46%)
- Malrotation of gut (27%)
- Anal atresia
- Chromosomal abnormality (4%)
- Abnormal bronchial and lung lobation (bilateral right lungs)

Left atrial isomerism/Polysplenia Syndrome

- Major cardiac defects in 83%
- Suspect in viscerocardiac heterotaxy, interrupted IVC, Complete AV block (CAVB)

Associated cardiac findings:

- Interrupted IVC with azygos continuation (89%), persistent LSVC (29%)
- AVSD (59%)
- Arrhythmias 37%: most commonly CAVB (27%)
- RV outflow tract obstruction (36%)
- Conotruncal anomalies (especially DORV) (21%)
- Transposition or malrotation of the great arteries (11%)
- Anomalous pulmonary venous return (10%)
- LV outflow tract obstruction (8%)
- Coarctation of the aorta (5%)

Noncardiac associated findings:

- Abnormal stomach (59%) and liver position (33%)
- Polysplenia (57%) [4]
- Abnormal bronchial and lung lobation (bilateral left lungs)
- Malrotation of gut (14%) and GI obstruction (5%)
- Malformations of the biliary tract (8%) [5]
- Hydrops (12%), usually in those with CAVB
- Chromosomal anomalies (3%)

Prenatal Physiology

- Dependent on the cardiac anatomy

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Fetal Imaging Checklist [14]:

- Transverse view, Abdomen
  - Location of the abdominal organs (stomach and liver)
  - Situs determination
- Transverse view, 4-chamber + sweep to outflows
  - Cardiac position, segmental anatomy and connections A/AV/V(looping)/VA.
  - Pulmonary venous connection and drainage
  - Presence or absence of atrial septum (common atrium)
  - Ventricular size
  - Ventricular septal defect – size and location
  - AV valve connections and +/- valve regurgitation
  - Great artery position, relationship and relative size
  - Outflow tract obstruction
- 3 vessel view
  - Systemic venous connections – IVC vs Interrupted, RSVC and/or presence of LSVC
  - Great artery relationship and size
  - Main and branch pulmonary artery and size
  - Direction of flow across the ductus arteriosus (i.e., PA to Ao vs Ao to PA)
- Short axis
  - Ventricular size, position and function,
  - VSD shunting
  - Overriding/straddling of AV valve tissue.
- Others
  - Bicaval view
  - Aortic arch anatomy and size
  - Ductal arch - Direction of flow across the ductus arteriosus (i.e., PA to Ao vs Ao to PA)
  - Any abnormal venous structure highly suggestive of vertical vein from possible anomalous venous return
  - Rhythm assessment – presence of CAVB
  - Pleural/pericardial effusions, ascites, ductus venosus, umbilical artery/vein.

Postnatal Physiology/Management [14]

- Varies with underlying cardiac anatomy
  - RAI/Asplenia
    - If associated with single ventricle with pulmonary stenosis/atresia,
      - With obstructed TAPVC – severe cyanosis
        - PGE1 may not improve oxygenation
        - May need emergent surgical intervention
      - Normal pulmonary venous connection – mild cyanosis
        - PGE1 will provide hemodynamic stability
      - Single ventricle and ductal dependent will need surgical palliation after birth
      - If with PS/PA – may need modified Blalock-Taussig shunt
      - If without outflow tract obstruction – may need PA banding
      - Single ventricle with enough PS to protect vascular bed – initial surgical procedure not required.
      - HLHS variants will undergo 3-stage surgical palliation
  - LAI/Polysplenia
    - If associated with severe RVOTO or LVOTO
      - PGE1 after birth until surgical intervention
    - If associated with less severe CHD – may be asymptomatic
    - If associated with large VSD with no PS
      - Pulmonary overcirculation at 6-8 weeks
    - Single ventricle variants
      - PGE1 after birth until surgical palliation
      - Will undergo staged surgical palliation
  - For complex CHD with CAVB
    - Low cardiac output especially if HR < 55 bpm
    - May need inotropic support
    - May need pacing

- Other organ system abnormalities
  - Screening for functional asplenia
    - Antibiotic prophylaxis required and appropriate immunizations given
  - Screening for intestinal malrotation
    - Prophylactic Ladd procedure (controversial)
  - Screening for biliary atresia
    - Associated with polysplenia

Outcomes (*Results will vary at individual centers)

Metaanalysis of 647 Patients [4]

Perinatal Outcomes

	Right Atrial Isomerism	Left Atrial Isomerism
Termination of pregnancy	33%	25%
Fetal demise	4%	7%
Neonatal death	18%	11%
Late death	15%	6%

Surgical Outcomes

	Right Atrial Isomerism	Left Atrial Isomerism
Need for surgery	70%	73%
Biventricular repair	**7%**	**78%**
Univentricular repair	**93%**	**17%**
Death during or after surgery	28%	27%

*TAPVR is one of the major determinants of postnatal outcome in RAI, especially when obstructed.

Other literature:

Both LAI and RAI

- 5-year survival 53% for asplenia and 86% for polysplenia
- Single ventricle heterotaxy, 60% survival (median follow up 51mo), prenatal diagnosis did not improve survival[10].
- Risk factors for death: TAPVR, > mild AV valve regurgitation, common AVSD – 10-year survival of heterotaxy was 55% overall and 62% for those who underwent surgery [6].
- Bradyarrhythmia is associated with fetal death
- Of 22 pts with heterotaxy and bradycardia/AV block, 1-year survival rate for was 63%.

Right Atrial Isomerism

- 22% survival with a median follow-up of 13.8 years; 67% had some surgical intervention; TAPVR worsens outcomes [7].
- 69% mortality with a median 16 year follow-up [8].
- 68.7% 12-year survival; need for neonatal palliation was a risk factor and > moderate AV valve regurgitation for late [9].

Left Atrial Isomerism

- *Grim* prognosis if associated with CAVB (1/7 survived infancy in Pasquini series, none past 3 months of age in Cohen series and Arunamata) [10-12].
    - *Risk for pacemaker placement: 75% [*15]
- 68.7% 12 year survival overall; risk factors = >moderate AV valve regurgitation [7].
- *Median* follow up of 18 months, LAI overall survival 90%.
- Results of biventricular repair – 12/32 biventricular repair, of which 7/12 had complex intra-atrial baffles and 4/12 needed a pacemaker for CAVB. The remaining 20/32 needed single ventricle palliation [13].

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