SPECTRUM OF HEART MALFORMATIONS IN PATIENTS WITH SITUS INVERSUS TOTALIS: LONG-TERM OUTCOME IN A TERTIARY CENTRE

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SITUS SOLITUS

SITUS INVERSUS

Prevalence ~ 1/8500
Background

- Despite being rare, the estimated incidence of Congenital Heart Defects (CHDs) in Situs Inversus is significantly higher than in patients with Situs Solitus (i.e., ~3% vs. ~0.08%) *

- The risk of developing laterality disorders and hence complex CHDs is greatly increased in families of individuals with Situs Inversus**

*Ferencz et al. BWIS 1985
**Gebbia Nat Gen 1997
Background

Left-Right Asymmetry and Cardiac Looping: Implications for Cardiac Development and Congenital Heart Disease

IRFAN S. KATHIRIYA AND DEEPAK SRIVASTAVA

Genetics of Human Situs Abnormalities

Brett Casey

Disorders of Left-Right Asymmetry: Heterotaxy and Situs Inversus

MARDI J. SUTHERLAND AND STEPHANIE M. WARE

- ZIC3
- ACVR2B
- LEFTYA
- CFC1 (Cryptic)
- NODAL
- FOXH1
- GDF1
- CRELD1
- GATA4
- NKX2.5
Background

The anatomic spectrum of organ laterality
Aim of the Study

- We sought to evaluate the spectrum of heart malformations and consequent outcome in patients with combined Situs Inversus and CHDs that underwent cardiac surgery at our institution.
Materials and Methods

- Familiar history of CHDs
- Karyotype
- Mutation analysis for ZIC3, CFC1 and NODAL genes
Results: Cardiac Phenotypes

39 PTS

17 \{ I,D,D \}  
\textit{ccTGA, UVH}

14 \{ I,L,L \}  
\textit{TGA, DORV, UVH}

8 \{ I,L,I \}  
\textit{TOF, DORV, AVC}
Results: Type of Surgery

39 PTS

- **GROUP I** (54%)
  - 21 pts with “single ventricle circulation” were staged toward
    - modified Fontan operation (19)
    - OHT (2)

- **GROUP II** (46%)
  - 18 pts
    - 15 biventricular repair
    - 3 one and a half ventricle repair
Results: Early Outcome

In-hospital Mortality 7.7%

- 3 deaths in Group I (2 at first stage palliation and 1 after Fontan operation)
- 0 deaths in Group II
Results: Follow-up

- 4 pts lost to FU after surgery
- Mean FU 10 yrs (range 1 - 381 months)
- Overall Kaplan-Meier event-free survival was 85.7%

(\textit{long-rank p value} = 0.011)
Results: Genetics

Genetic Analysis

- Available karyotype and screening for gene mutations in 43% of pts
- All probands negative for ZIC3, CFC1 NODAL mutations
- One pt affected by Kartagener’s Syndrome
- One pt affected by Oral-Facial-Digital Syndrome
- Two positive familiar history for complex CHDs and situs abnormalities
Conclusions

- Despite being rare, *Situs Inversus* is often associated with complex CHDs.
- Cardiac phenotype is heterogeneous, suggesting that mutations affecting L-R pathways may directly affect cardiogenesis through multiple mechanisms.
- In-hospital surgical mortality is not neglectable (7.7%) but limited to those with “single ventricle circulation.”
- Survival in both groups is excellent at long-term follow-up.
GRAZIE