Sex Differences in the Cardiac Function of Ogden Syndrome

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Introduction

- Ogden Syndrome (OS) is an X-linked disease caused by variants in NAA10, the gene encoding the catalytic domain of the NatA N-α-terminal acetyltransferase[1]
- This disease is characterized by intellectual disability, developmental delay, hypotonia, dysphagia, ophthalmic manifestations[2]
- Case reports described cardiac manifestations such as cardiomyopathy and prolonged QT intervals[3,4].

Question

Is there a difference in OS cardiac pathology between males (M) and females (F)?

Methods

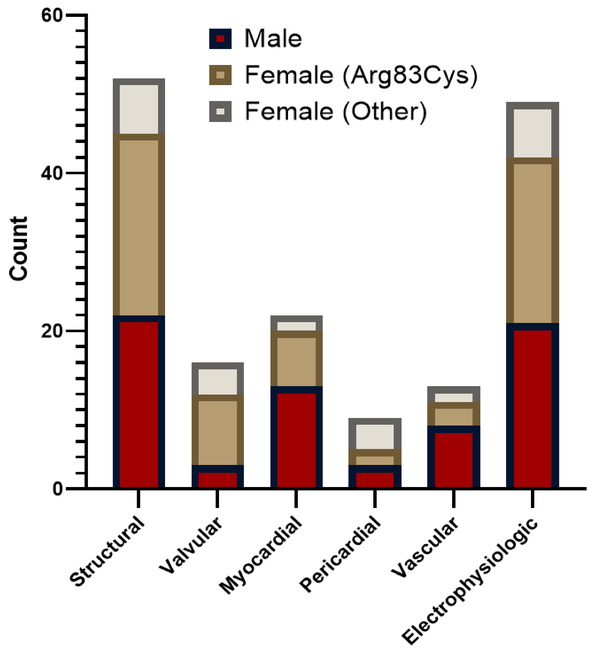
- Pathologies were grouped grossly into 6 categories: structural, valvular, myocardial, pericardial, vascular, and cardiac electrophysiologic.
- Two-sample unequal variance t-tests were calculated comparing the prevalence of each category pathology.
- All alpha values were set to .05

Results

Pathology Count	M (%)	F (%)
0	2 (10%)	28 (43.1%)
1	2 (10%)	12 (18.5%)
2	1 (5%)	11 (16.9%)
3	3 (15%)	6 (9.2%)
4	7 (35%)	4 (6.2%)
5	1 (5%)	2 (3.1%)
6	1 (5%)	1 (1.5%)
8	1 (5%)	0 (0%)
9	0 (0%)	1 (1.5%)
10	1 (5%)	0 (0%)
12	1 (5%)	0 (0%)
Total	20 (23.5%)	65 (76.5%)

Fig 1. Cardiac pathology Count by Sex

- 85 probands included in the study—65 females and 20 males
- The average number of pathologies present per proband was 2.1 (standard deviation (SD) = 2.4)
- Males on average had 4.1 (SD = 3.0) distinct cardiac abnormalities while females had 1.5 (SD = 1.8) **(p = .001)**
- Males had a greater number of myocardial abnormalities (n = .65; SD = .57) than females (n = .14; SD = .34; **p = .001**)
- Males also had more electrophysiological abnormalities (n = 1.1; SD = .97) than females (n = .43; SD = .66; **p = .02**).
- More males (n = .35; SD = .48) experienced cardiac arrest than females (n = .015; SD = .12; **p = .007)**.

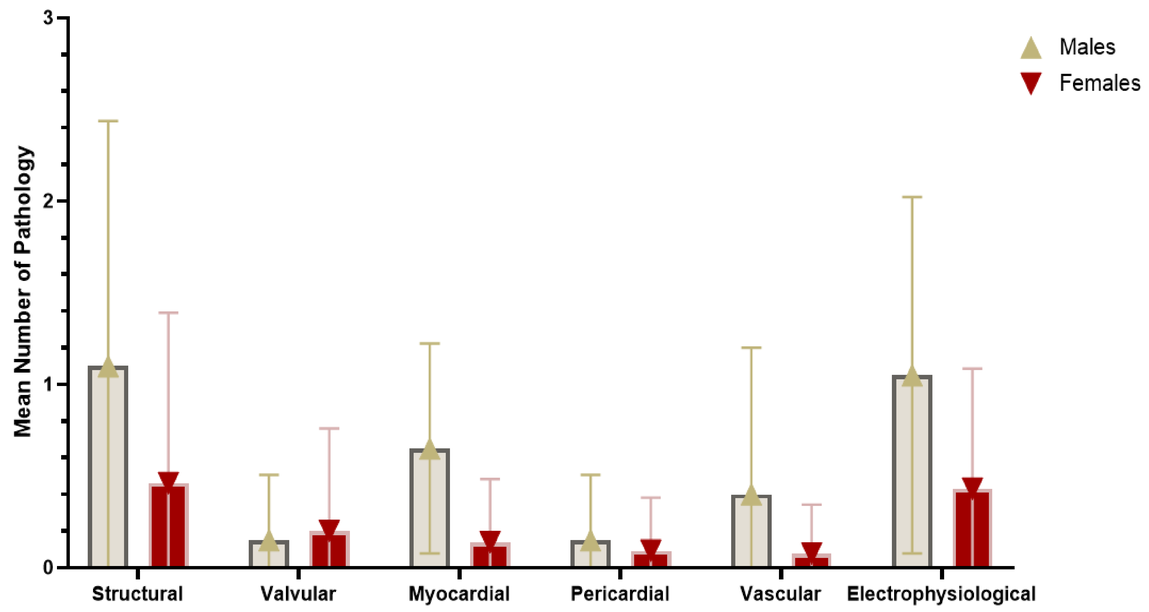


Sex	Structural	Valvular	Myocardial	Pericardial
Total	52	19	22	9
M	22	3	13	3
F	30	13	9	6

Sex	Vascular	Electrophysiologic	Total
Total	13	49	178
M	8	21	82
F	5	28	93

Fig 2. Total Cardiac Pathology Counts by Sex in Graphical and Tabular Format

Fig 3. Mean Cardiac Abnormalities Present in Individual Probands with OS by Sex



Mean (SD)	Structural	Valvular	Myocardial	Pericardial	Vascular	Electrophysiologic	Total
Total	0.61 (1.1)	0.22 (0.54)	0.26 (0.46)	0.11 (0.31)	0.15 (0.47)	0.58 (0.79)	2.1 (2.4)
Male	1.1 (1.3)	0.15 (0.36)	0.65 (0.57)	0.15 (0.36)	0.4 (0.8)	1.1 (0.97)	4.1 (3.0)
Female	0.46 (0.93)	0.20 (0.56)	0.14 (0.35)	0.09 (0.29)	0.08 (0.27)	0.43 (0.66)	1.5 (1.8)
p-values	0.03*	0.3	0.0006*	0.3	0.05	0.008*	0.0006*

Conclusion

- Males with OS had more severe mortality and morbidity than females, as evidenced by the greater average prevalence of myocardial, electrophysiologic, and total cardiac pathologies and greater number of cardiac arrests.
- This finding could be due to skewed X-inactivation in the females leading to more expression of functional NAA10[5]
- The worse cardiac presentation in the males contrasts with the neurodevelopmental and ophthalmic findings of the disease, where females tended to have more severe phenotypes[6,7].
- Physicians should give caregivers of children with OS anticipatory guidance surrounding myocardial and arrhythmogenic disease.

Citations

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