Supplementary material

Milczanowski K, Tyczyński P, Kukuła K, et al. Pentalogy of Fallot. Pol Heart J. 2024

Table S1. Tetralogy of Fallot and associated anomalies (alphabetically). Brief review of the literature

Variant/anomaly	Prevalence, %	Author, year of publication
Absent PV	5	Nagao et al. 1967 [1]
	2	Piran et al. 2011 [2]
	1.3	Marino et al. 1996 [3]
ACA	36	Dabizzi et al. 1990 [4]
	6	Jost et al. 2010 [5]
	4.9	Sheikh et al. 2014 [6]
	4	Nagao et al. 1967 [1]
	4	Zakaria et al. 2011 [7]
	1.6	Erdogan et al. 2005 [8]
	0.7	Marino et al. 1996 [3]
Additional VSD	5.4	Sheikh et al. 2014 [6]
	0.4	Nollert et al. 1997 [9]
ALSA with RAA	5	Nagao et al. 1967 [1]
	4	Zakaria et al. 2011 [7]
	2.7	Prabhu et al. 2020 [10]
	1.1	Singh et al. 2019 [11]
ARSA	14	Piran et al. 2011 [2]
	13	Zakaria et al. 2011 [7]
	3.6	Singh et al. 2019 [11]
	1.3	Prabhu et al. 2020 [10]
	1	Nagao et al. 1967 [1]

ASD		23	Dabizzi et al. 1990 [4]
		16	Hashemzadeh. 2010 [12]
		14	Piran et al. 2011 [2]
		13	Zakaria et al. 2011 [7]
		11	Erdogan et al. 2005 [8]
		10	Nollert et al. 1997 [9]
		5	Nagao et al. 1967 [1]
		3.8	Singh et al. 2019 [11]
AVSD		6.7	Marino et al. 1996 [3]
AVSD	Complete	2.7	Marino et al. 1996 [3]
		1.5	Dabizzi et al. 1990 [4]
		1	Nagao et al. 1967 [1]
	Partial	0.8	Dabizzi et al. 1990 [4]
COCA		22	Zakaria et al. 2011 [7]
		3.8	Prabhu et al. 2020 [10]
DAA		1	Nagao et al. 1967 [1]
		0.5	Singh et al. 2019 [11]
		0.3	Prabhu et al. 2020 [10]
Dextrocardia		1	Hashemzadeh. 2010 [12]
		0.5	Singh et al. 2019 [11]
Levocardia with situs inversus		1	Nagao et al. 1967 [1]
MAPCAS		13	Sheikh et al. 2014 [6]
		8.7	Zakaria et al. 2011 [7]
PDA		48	Zakaria et al. 2011 [7]
		14	Nagao et al. 1967 [1]
		12	Hashemzadeh. 2010 [12]
		10	Dabizzi et al. 1990 [4]
		8.2	Singh et al. 2019 [11]
		5.4	Sheikh et al. 2014 [6]
		3	Erdogan et al. 2005 [8]
		2	Marino et al. 1996 [3]
PFO		36	Erdogan et al. 2005 [8]
		24	Nagao et al. 1967 [1]

	20	Nollert et al. 1997 [9]
	2.9	Hashemzadeh. 2010 [12]
	2.6	Dabizzi et al. 1990 [4]
	0.5	Singh et al. 2019 [11]
PLSVC	4.7	Erdogan et al. 2005 [8]
	3.1	Nollert et al. 1997 [9]
	9	Nagao et al. 1967 [1]
	1.9	Dabizzi et al. 1990 [4]
	1.9	Hashemzadeh. 2010 [12]
RAA	36	Piran et al. 2011 [2]
	33	Jost et al. 2010 [5]
	30	Zakaria et al. 2011 [7]
	25.7	Prabhu et al. 2020 [10]
	24	Singh et al. 2019 [11]
	21	Dabizzi et al. 1990 [4]
	14	Hashemzadeh. 2010 [12]
	13	Sheikh et al. 2014 [6]
	9.3	Marino et al. 1996 [3]
Situs inversus	0.8	Nollert et al. 1997 [9]

Abbreviations: ACA, anomaly of the coronary artery; ALSA, aberrant left subclavian artery; ARSA, aberrant right subclavian artery; ASD, atrial septal defect; AVSD, atrioventricular septal defect; COCA, common origin of carotid arteries; DAA, double aortic arch; MAPCAS, major aortopulmonary collateral arteries; PDA, patent ductus arteriosus; PFO, patent foramen ovale; PSLVC, persistent left superior vena cava; PV, pulmonary valve; RAA, right aortic arch; ToF, tetralogy of Fallot; VSD, ventricular septal defect

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Table S2. Congenital anomalies and anatomic variants (based on echocardiography, coronary computed tomography and cardiac magnetic resonance done in our center as well as historical imaging data from pediatric hospitalizations)

	Type of PoF				Overall *P*-value
	Total	ToF + ASD	ToF + PFO	PoF not specified	
	n = 53	n = 23	n = 20	n = 10	
Cardio-Vascular comorbidities, n (%)					
RAA	15 (28.3)	5 (21.7)	7 (35.0)	3 (30.0)	0.50
Pulmonary atresia	4 (7.5)	4 (17.4)	0 (0)	0 (0)	0.04[a]
PLSVC	4 (7.5)	4 (17.4)	0 (0)	0 (0)	0.04[a]
COCA	3 (5.7)	1 (4.3)	1 (5.0)	1 (10.0)	0.56
ACA	3 (5.7)	1 (4.3)	0 (0)	2 (20.0)	0.17
MAPCAS	3 (5.7)	2 (8.7)	0 (0)	1 (10.0)	0.84
ARSA	3 (5.7)	2 (8.7)	1 (5.0)	0 (0)	0.32
ALSA	1 (1.9)	1 (4.3)	0 (0)	0 (0)	0.31
ALVA	1 (1.9)	1 (4.3)	0 (0)	0 (0)	0.31
Other extra cardio-vascular comorbidities, n (%)					
Accessory spleens	2 (3.8)	0 (0)	2 (10)	0 (0)	0.64
Double RA	2 (3.8)	2 (8.7)	0 (0)	0 (0)	0.15
Duplex kidney	2 (3.8)	2 (8.7)	0 (0)	0 (0)	0.15
Hemiazygos lobe	2 (3.8)	0 (0)	2 (10)	0 (0)	0.64

[a]*P* = 0.03 for 1 group vs. 2 + 3 group

Abbreviations: ACA, anomaly of the coronary artery; ALSA, aberrant left subclavian artery; ALVA, aberrant left vertebral artery; ARSA, aberrant right subclavian artery; ASD, atrial septal defect; AVSD, atrioventricular septal defect; COCA, common origin of carotid arteries; MAPCAS, major aortopulmonary collateral arteries; PDA, patent ductus arteriosus; PFO, patent foramen ovale; PR, pulmonary regurgitation; PS, pulmonary stenosis; PSLVC, persistent left superior vena cava; RA, renal artery; RAA, right aortic arch; ToF, tetralogy of Fallot

Table S3. Interventions

		Type of PoF				Overall *P*-value
		Total	ToF + ASD	ToF + PFO	PoF not specified	
		n = 63	n = 25	n = 27	n = 11	
TSC						
Number of pts, n (%)		60 (95.2)	24 (96.0)	25 (92.6)	11 (100.0)	0.61
Age at TSC, years, median (range)		4 (0–28)	7 (0–28)	3 (1–16)	5 (0–25)	0.40
Ist correction						
Type of 1st correction, n (%)						
TSC		37 (58.7)	14 (56.0)	14 (54.8)	9 (81.8)	0.26
BT-shunt		22 (34.9)	10 (40.0)	10 (37.0)	2 (18.2)	
Another		3 (4.8)	0 (0)	3 (11.1)	0 (0)	
No intervention		1 (1.6)	1 (4.0)	0 (0)	0 (0)	0.47
Age at 1st intervention, years, median (IQR)		3 (1–7)	2.5 (1–7.5)	1 (1–4)	5 (3–9)	0.13
Re – interventions after TSC						
Number of pts, n (%)		31 (49.2)	18 (72.0)	9 (33.3)	4 (36.4)	0.014[a]
Age at 1st re-intervention, years, median (IQR)		21 (15–33)	20 (12–34)	21 (20–23)	32.5 (23.5–45)	0.29
Years from TSC to 1st re-intervention, median (IQR)		18.5 (12.5–26)	18 (11–26)	18 (30–20)	23 (19–32.5)	0.40
Type of correction, n (%)						
PR	Surgery only	12 (19.1)	5 (20.0)	3 (11.1)	4 (36.4)	0.20
	Surgery + percutaneous intervention	2 (3.2)	2 (8.0)	0 (0)	0 (0)	0.21
	Percutaneous intervention only	4 (6.3)	1 (4.0)	3 (11.1)	0 (0)	0.37
PS	Surgery only	3 (4.8)	1 (4.0)	2 (7.4)	0 (0)	0.61

	Surgery + percutaneous intervention	2 (3.2)	1 (4.0)	1 (3.7)	0 (0)	0.81
	Percutaneous intervention only	1 (1.6)	1 (4.0)	0 (0)	0 (0)	0.47
Complex PV disease	Surgery + percutaneous intervention	1 (1.6)	1 (4.0)	0 (0)	0 (0)	0.47
RVOT myectomy		9 (14.3)	5 (20.0)	3 (11.1)	1 (9.1)	0.57
Re-VSD closure		8 (12.70)	4 (16.0)	2 (7.4)	2 (18.2)	0.91
ASD closure		8 (12.70)	8 (32.0)	0 (0)	0 (0)	0.001[b]
TR surgery		2 (3.2)	1 (4.0)	0 (0)	1 (9.1)	0.34
Bentall procedure		1 (1.6)	1 (4.0)	0 (0)	0 (0)	0.47
PFO closure		1 (1.6)	0 (0)	1 (3.7)	0 (0)	0.51
ICD-implantation		4 (6.3)	3 (12.0)	0 (0)	1 (9.1)	0.20
PM-implantation		2 (3.2)	1 (4.0)	1 (3.7)	0 (0)	0.81

[a]*P* = 0.005 for ToF + PFO group vs. ToF + ASD group; [b]*P* = 0.001 for ToF + PFO group vs. ToF + ASD group

Abbreviations: ASD, atrial septal defect; BT, Blalock–Taussig; ICD, implantable cardioverter-defibrillator; IQR, interquartile range; PFO, patent foramen ovale; PM, pacemaker; PR, pulmonary regurgitation; PS, pulmonary stenosis; PV, pulmonary valve; RVOT, right ventricle outflow tract; ToF, tetralogy of Fallot; TR, tricuspid regurgitation; TSC, total surgical correction; VSD, ventricular septal defect

Table S4. Echocardiographic variables. Results of robust analysis of variance based on M estimation, adjusted for patient's age the at the echocardiographic assessment and time since the last intervention. Median predicted value with lower and upper quartiles. Time variables — median with lower and upper quartiles (Kruskall–Wallis and DSCF test)

	Type of PoF			Overall *P*-value
	ToF + ASD n = 25	ToF + PFO n = 27	PoF not specified n = 11	
Age, years[a]	35.0 (29.0–45.0)	26.0 (21.0–33.0)	39.0 (38.0–49.0)	0.001[b]

Time from the correction to the test performance, years	31.5 (24.0–39.0)	22.0 (19.0–30.0)	34.0 (33.0–39.0)	<0.001[c]
Time from the last intervention, years	12.0 (4.5–22.5)	19.0 (11.0–27.0)	30.0 (11.0–38.0)	0.167
LVEF, %	57.4 (56.8–58.6)	59.5 (59.2–60.4)	58.0 (56.4–58.4)	0.14
LVEDD, mm	48.9 (48.1–50.6)	46.1 (45.6–47.2)	44.7 (43.7–46.4)	0.18
LVESD, mm	32.5 (32.0–32.8)	30.2 (30.1–30.6)	31.3 (31.0–32.1)	0.63
RV diameter, mm	33.4 (31.7–38.2)	33.3 (31.6–35.2)	34.9 (33.4–35.8)	0.31
IVS, mm	10.5 (10.3–10.9)	10.0 (9.8–10.2)	10.5 (10.4–10.7)	0.87
LAAr, cm^2	20.4 (18.8–23.4)	17.9 (16.5–19.1)	20.4 (19.7–22.0)	0.66
RAAr, cm^2	22.3 (20.1–27.2)	18.4 (16.4–20.1)	25.1 (23.8–26.9)	0.71
AAo diameter, mm	36.5 (36.1–38.4)	33.7 (33.4–34.7)	36.6 (35.5–37.2)	0.14
Ao-arch diameter, mm	16.4 (13.0–19.8)	11.4 (7.9–14.9)	18.8 (13.1–24.6)	0.12
PT diameter, mm	26.4 (24.8–27.7)	24.0 (23.6–25.2)	30.2 (29.5–32.4)	0.10
TAPSE, mm	16.5 (15.8–17.8)	18.6 (17.6–19.4)	18.5 (16.6–19.7)	0.67
RVSP, mm Hg	45.7 (44.1–47.6)	35.4 (33.6–35.9)	39.6 (36.5–40.7)	0.001[d]
PG-peak, mm Hg	23.5 (22.6–25.4)	22.7 (22.2–24.0)	26.7 (24.5–27.5)	0.52
PG-mean, mm Hg	26.0 (22.7–27.2)	23.5 (21.4–24.8)	30.1 (24.8–31.1)	0.17

[a]At the time of the most recent transthoracic echocardiography; [b]P = 0.008 for ToF + PFO group vs. ToF + ASD group and ToF + PFO group vs. PoF not specified (Kruskall–Walis and DSCF test); [c]P = 0.01 for ToF + PFO group vs. ToF + ASD group and P = 0.03 for ToF + PFO group vs. PoF not specified (Kruskall–Walis and DSCF test); [d]P <0.001 for ToF + PFO group vs. ToF + ASD (Robust ANOVA)

Abbreviations: AAo, ascending aorta; Ao, aortic; ASD, atrial septal defect; IVS, interventricular septum; LAAr, left atrial area; LVEF, left ventricle ejection fraction; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; PFO, patent foramen ovale; PG, pulmonary gradient; PoF, pentalogy of Fallot; PT, pulmonary trunk; RAAr, right atrial area; RV, right ventricle; RVSP, right ventricular systolic pressure; TAPSE, tricuspid annular plane systolic excursion; ToF, tetralogy of Fallot; TR, tricuspid regurgitation; TTE, transthoracic echocardiography

Table S5. Pharmacological treatment (alphabetically)

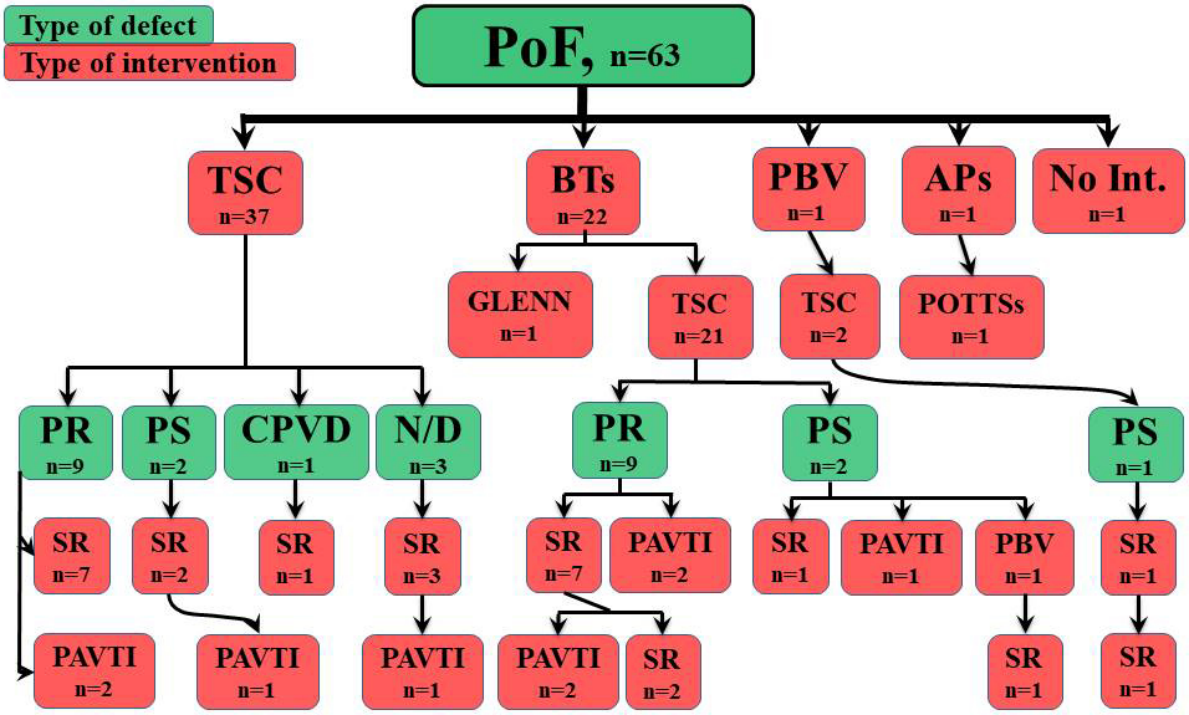
Drugs n (%)	ToF + ASD	PFO n = 27		Not specified n = 11	Overall *P*-value

	n = 25				
Acetylsalicylic acid	4 (16.0)	4 (14.8)		1 (9.1)	0.86
ACE-I or ARB	5 (20.0)	3 (11.1)		2 (18.2)	0.67
Aldosterone antagonist	7 (28.0)	2 (7.4)		3 (27.3)	0.13
Amiodarone	2 (8.0)	0 (0.0)		0 (0.0)	0.21
BB	15 (60.0)	7 (25.9)		5 (45.5)	0.048[a]
Clopidogrel	1 (4.0)	2 (7.4)		0 (0.0)	0.62
Digoxin	0 (0.0)	1 (3.7)		0 (0.0)	0.51
Loop diuretic	10 (40.0)	4 (14.8)		0 (0.0)	0.015[b, c]
OAC or NOAC	10 (40.0)	3 (11.1)		2 (18.2)	0.047[d]
Propafenone	0 (0.0)	0 (0.0)		1 (9.1)	0.09
Statin	3 (12.0)	3 (11.1)		1 (9.1)	0.97

Correction for multiple comparisons was waived due to small group sizes

[a]*P* = 0.01 for ToF + ASD group vs. PFO group; [b]*P* = 0.04 for ToF + ASD group vs. PFO group; [c]*P* = 0.02 for ToF + ASD group vs. PFO group; [d]*P* = 0.02 for ToF + ASD group vs. non-specified group

Abbreviations: ACE-I, angiotensin-converting-enzyme inhibitor; ARB, angiotensin receptor blocker; ASD, atrial septal defect; BB, beta-blokers; NOAC, non-vitamin K antagonist oral anticoagulant; OAC, oral anticoagulant; PFO, patent foramen ovale; ToF, tetralogy of Fallot



Abbreviations: APS- aorto-pulmonary shunt, BTs- Blalock-Tausig shunt, CPVD- complex pulmonary valve disease, GLENN- Glenn procedurę + VSD closure + RVOT myectomy, N/D- no data, No Int- no internetion, PAVTI- percutaneous pulmonary valve implantation, PBV- pulmonary baloon valvuloplasty, PoF- pentalogy of Fallot, POTTSs- Potts shunt, PR- pulomonary regurgitation, PS- pulomonary stenosis, SR- surgical repair, TSC- total surgical correction,

Figure S1. Diagram

Methods

Individual patient's discharge diagnoses collected in the electronic database from the National Institute of Cardiology in Warsaw, Poland were retrospectively screened for the presence of PoF in the consecutive patients, who were hospitalized from January 2008 to November 2020 for various reasons (mainly cardio-vascular). The key words: "pentalogy of Fallot" or "tetralogy of Fallot" and "atrial septal defect" or "tetralogy of Fallot" and "patent foramen ovale" (with their grammatical variations and abbreviations) were used to identify PoF.

Definitions

PoF was defined as either ToF with ASD (group 1) or ToF with PFO (group 2) or unspecified PoF (in the medical records), (group 3).

Patient charts and imaging data were reviewed in all identified cases. Demographics and clinical characteristics were collected. Every patient underwent at least one transthoracic echocardiography (TTE) at our center and the most recent TTE examination was evaluated.

The study was approved by the institutional Ethics Committee (IK.NPIA.0021.44.2033/23) and informed consent was waived because of the retrospective study design.

Statistics

Statistical software of SAS version 9.4 was used for data analysis. All the test performed were two-sided, where *P*-value of <0.05 was considered statistically significant. The following statistical methods were used: χ^2 test of independence, unless the number of events was less than 5, in which case Fisher's exact test; Cochran Mantel-Haneszel Modified Ridit Score for non-time to event categorical variables with >2 categories; Kruskall–Wallis tests and DSCF method for multiple comparison analysis, robust analysis of covariance based on M-estimation, logistic regression, log-rank test.

Continuous variables are expressed as median and 25^{th} and 75^{th} percentiles. Categorical data are reported as count and percentages. Quantitative echocardiographic variables were compared between groups using robust analysis of covariance based on M-estimation [1] (adjusting for age at the time of transthoracic echocardiography and time since the last intervention). The risk of developing valvular disease was compared between groups by estimating age- and time since the last intervention — adjusted odds ratios. The Kaplan–Meier plots (*Figures S2* and *S3*) were created to illustrate survival without intervention. The log-rank test (adjusted for multiple comparison was used to verify the homogeneity of the curves of time from the study groups).

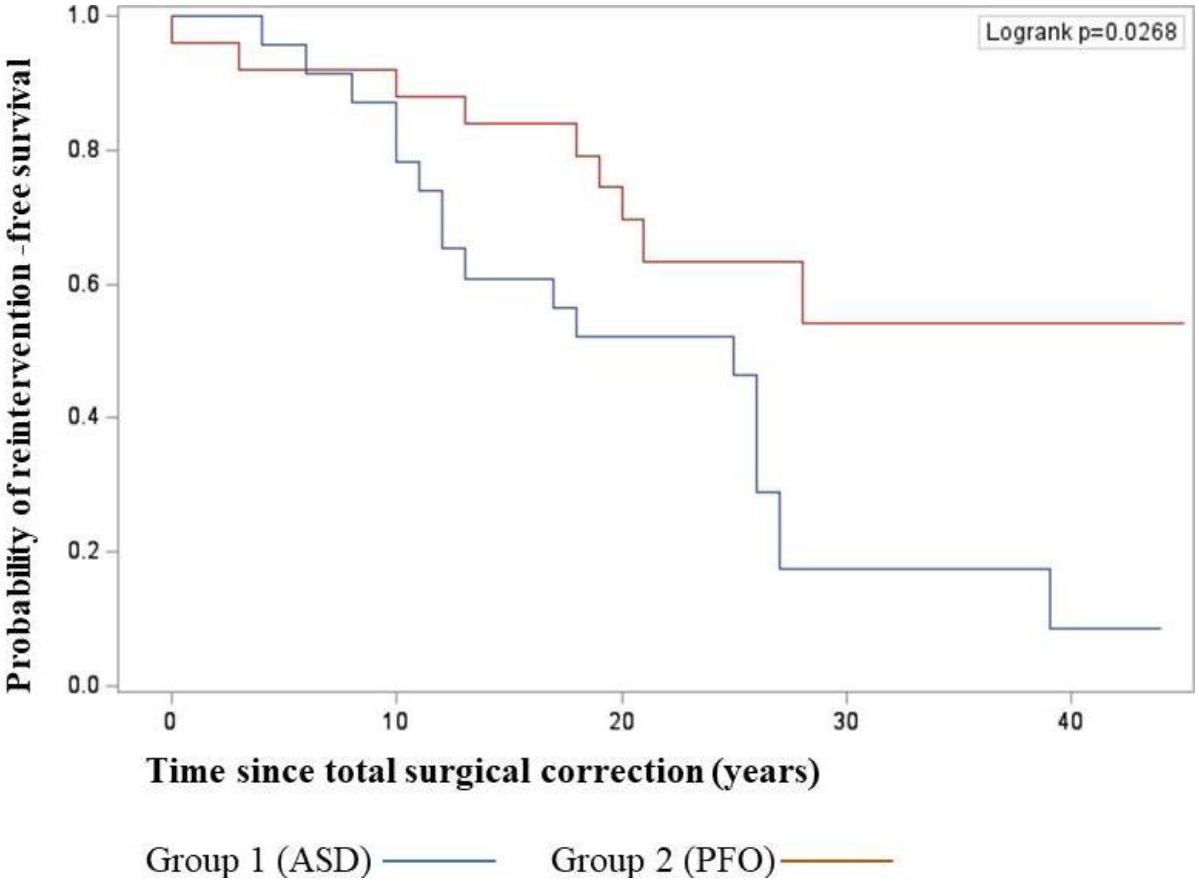

Logrank p=0.0268
Probability of reintervention -free survival
1.0
0.8
0.6
0.4
0.2
0.0
0
10
20
30
40
Time since total surgical correction (years)
Group 1 (ASD)
Group 2 (PFO)

Figure S2.

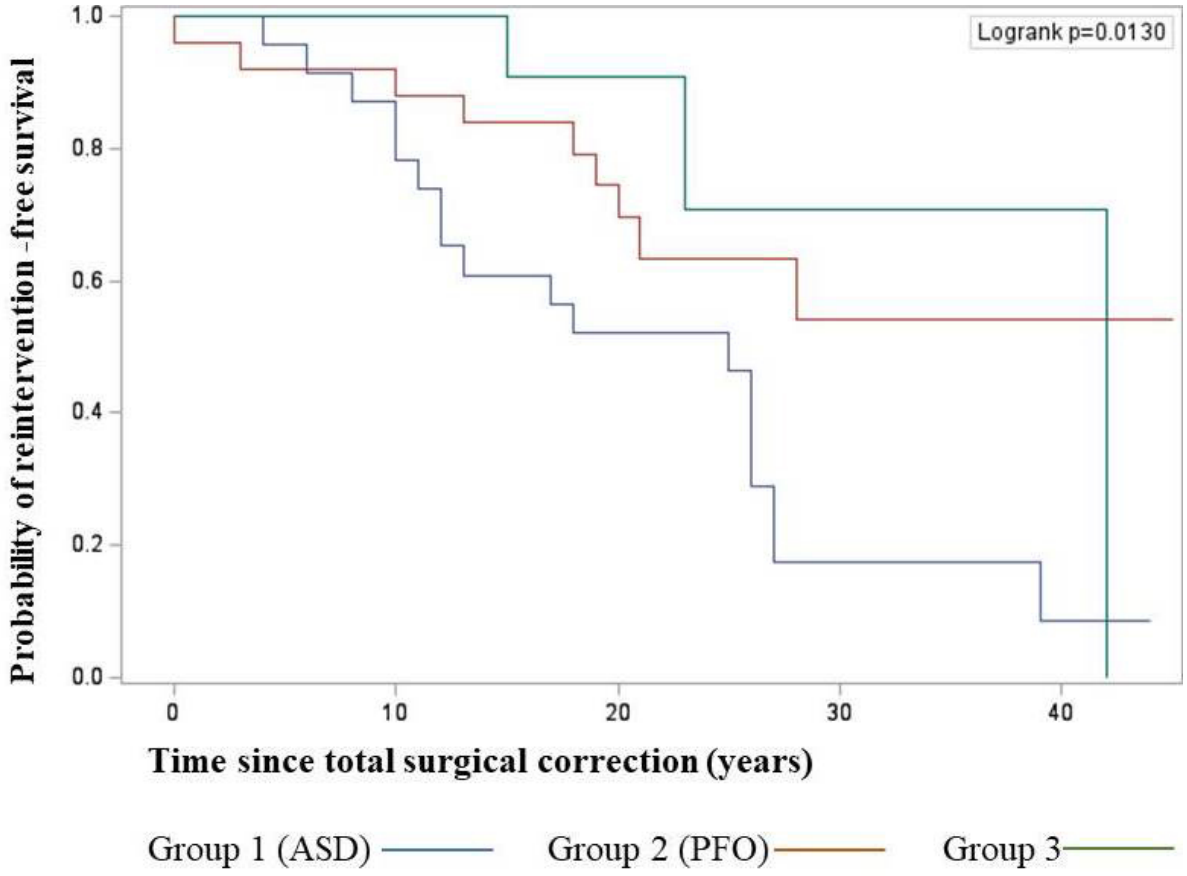


Figure S3.

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