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Impact of Valvular Heart Disease (VHD)in Adult Congenital Heart Disease (ACHD)

Francesca Graziani, MD, PhD
Policlinico Universitario A. Gemelli IRCCS, Rome
Ambulatorio Cardiologico Difetti Congeniti e Malattie Rare

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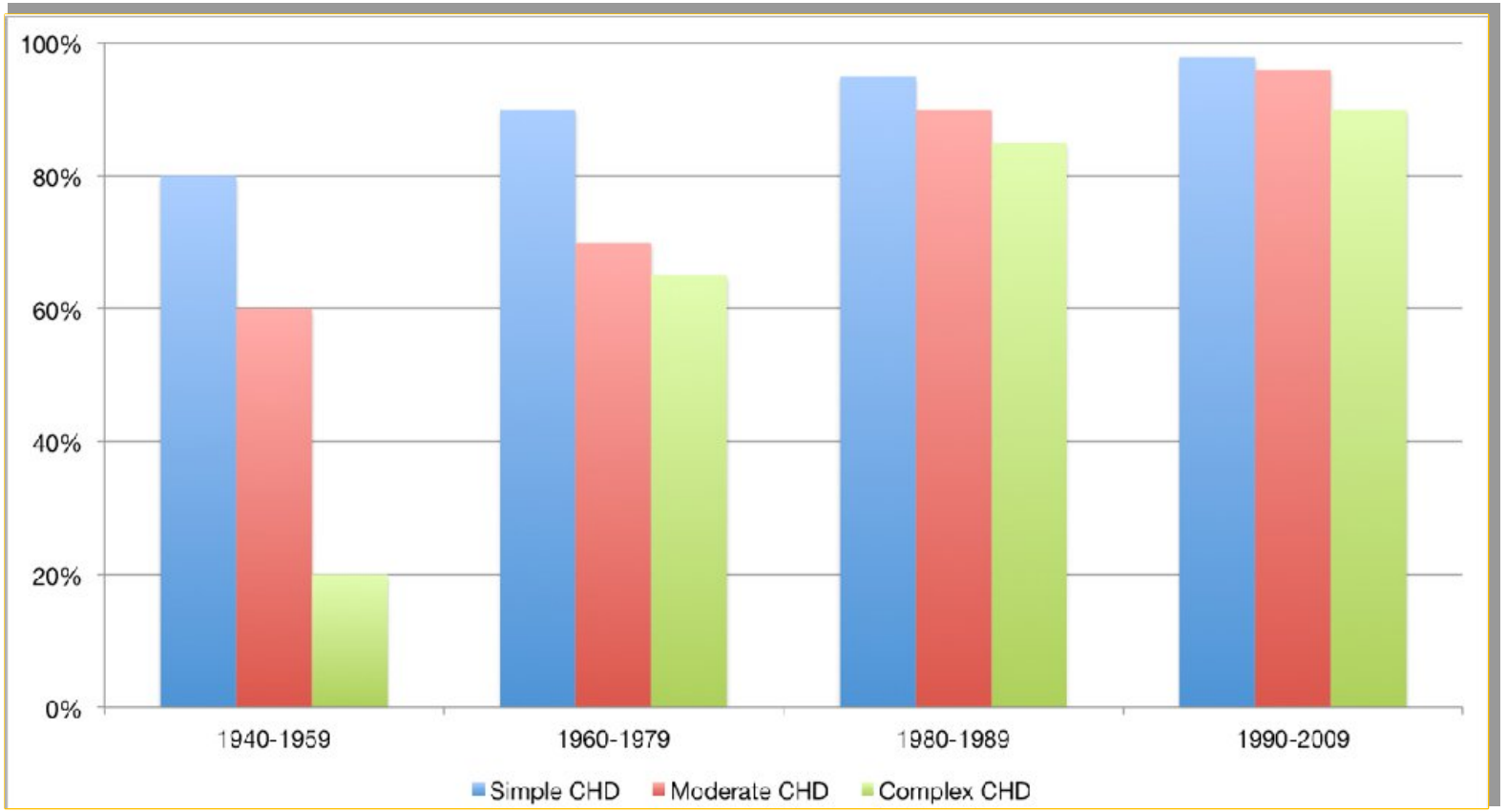
ACHD-The Burden



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ACHD-The Burden

- ✓ Increased knowledge ☾ prenatale dx= early treatment
- ✓ Improvement of neonatal/pediatric care, including percutaneous and surgical treatments
- ✓ Improvement of medical therapies for the management of short- and long-term complications
- ✓ Prevention of arrhythmias/sudden cardiac death
- ✓ Dedicated clinical pathways and cardiac and non-cardiac specialists

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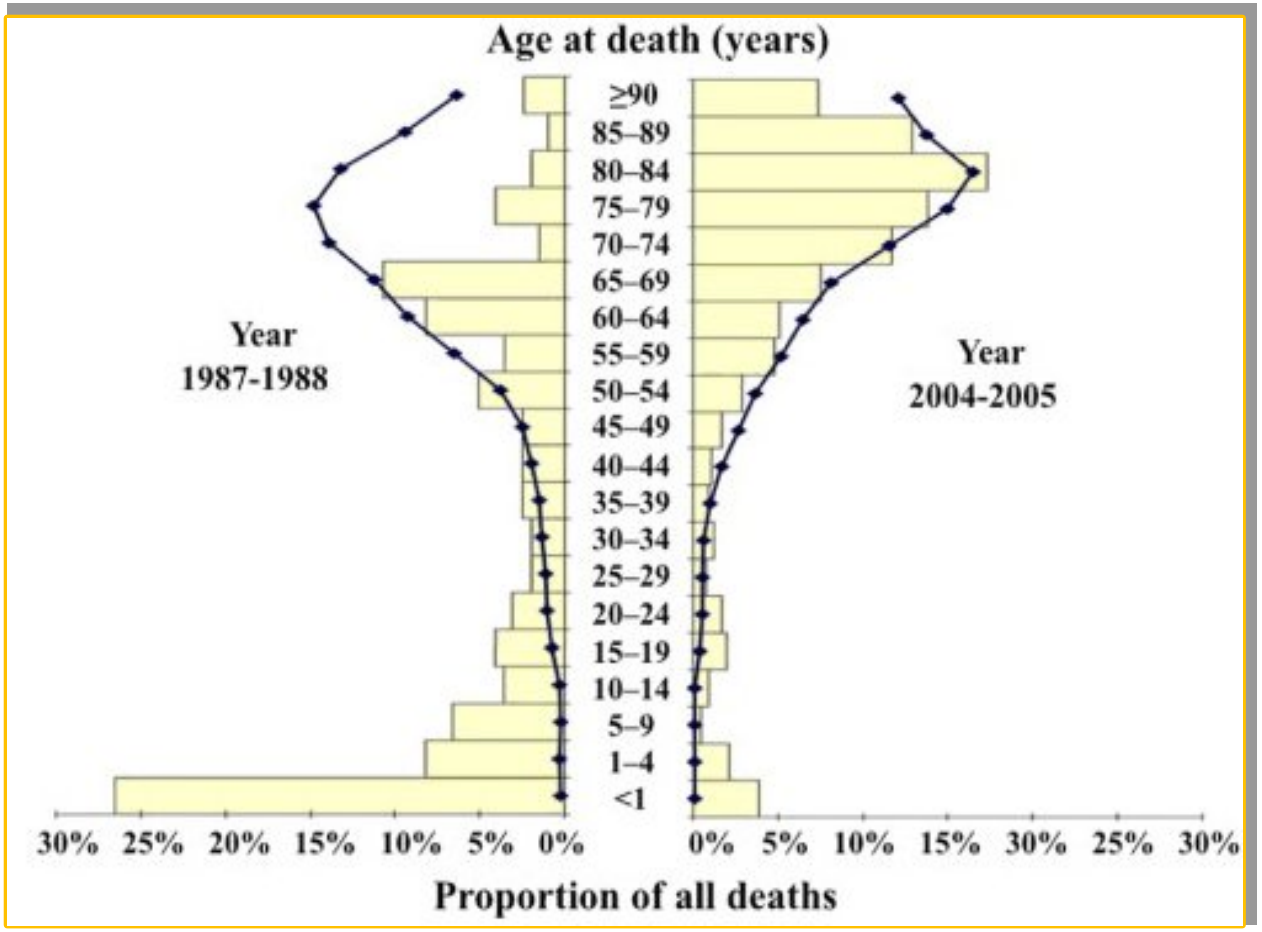
ACHD Life-expectancy



Khairy et al., J Am Coll Cardiol, 2010

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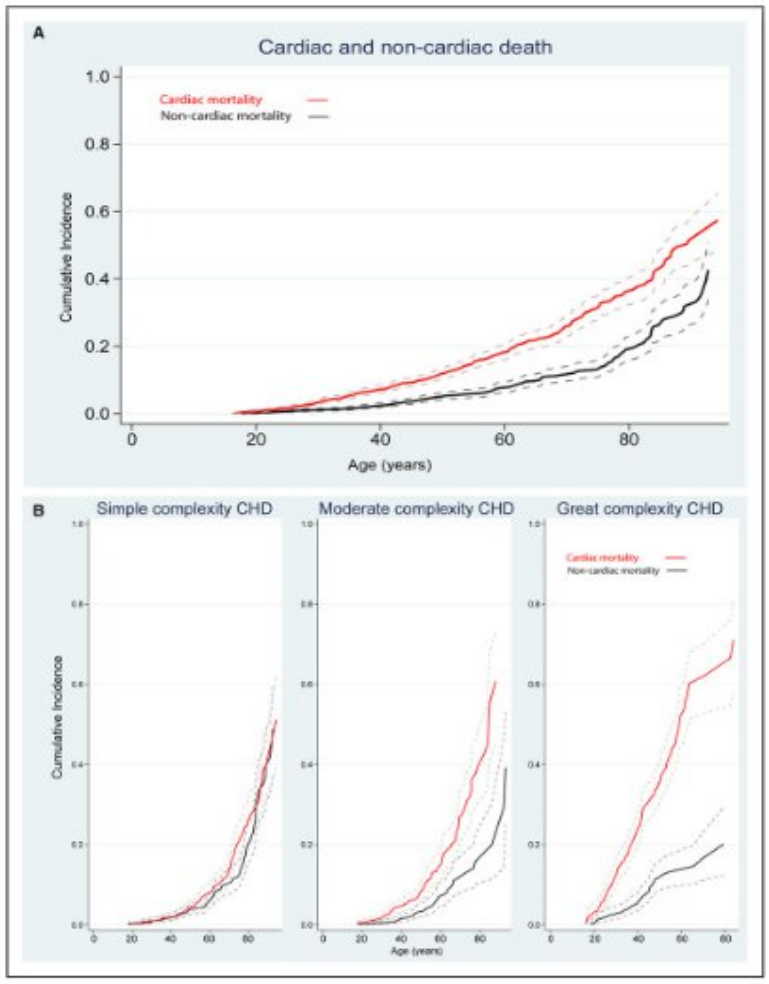
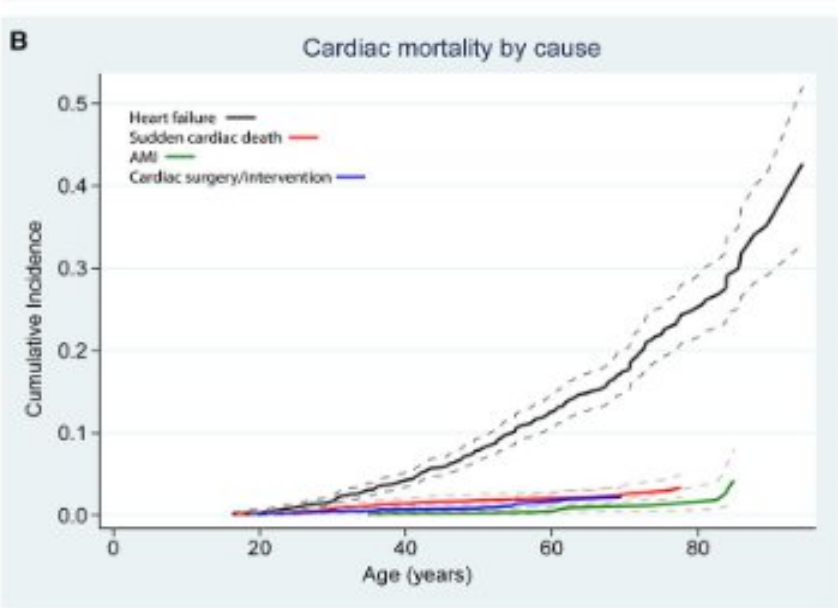
ACHD Prognosis



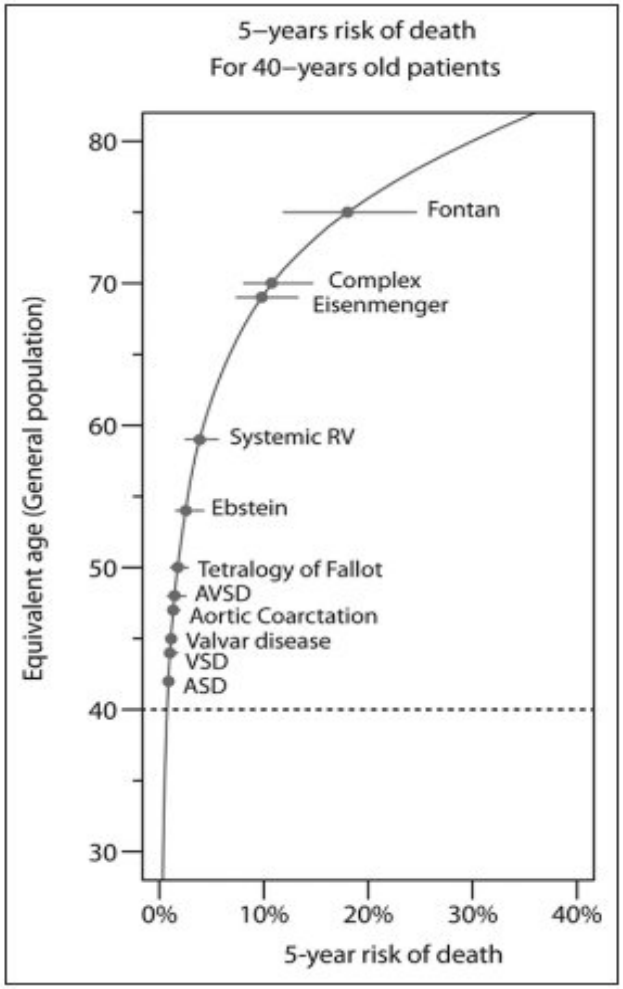
Heart Failure and Arrhythmias are the major determinant of mortality & hospitalization



Diller et al., Circulation, 2015

ACHD Prognosis

Still significantly lower compared to age-matched population



	Patient's age (years)								
	20	25	30	35	40	45	50	55	60
ASD	25	26	32	38	42	47	52	57	61
Valvar disease	29	31	36	40	45	49	54	59	63
VSD	28	30	36	40	44	49	53	59	63
Aortic Coarctation	32	33	38	43	47	52	56	62	66
AVSD	33	34	39	44	48	52	57	62	66
Marfan syndrome	37	38	42	46	50	54	59	64	68
Tetralogy of Fallot	37	38	42	47	50	54	60	65	69
Ebstein anomaly	42	43	47	51	54	59	63	68	72
Systemic RV	46	48	51	55	59	63	67	72	76
Eisenmenger syndrome	57	58	62	65	69	73	77	81	84
Complex CHD	58	59	63	67	70	74	78	82	85
Fontan	64	65	68	72	75	78	82	86	91

Age difference:
>40
30-40
20-30
10-20
5-10
2-5
<2

Diller et al., Circulation, 2015

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ACHD-Corrected but not Cured

Clinical Cardiology: New Frontiers

Challenges Posed by Adults With Repaired Congenital Heart Disease

Joseph K. Perloff, MD; Carole A. Warnes, MD

TABLE 1. Residua After Reparative Surgery for Congenital Heart Disease

- Electrophysiological
- Valvular
- Ventricular
  - Chamber morphology
  - Chamber mass
  - Chamber function
- Vascular
  - Anatomic anomalies or defects
  - Elevated systemic/pulmonary arterial pressure/resistance
- Noncardiovascular
  - Development abnormalities
    - Mental retardation
    - Physical retardation (dwarfism)
    - Somatic abnormalities (facial, musculoskeletal)
  - Central nervous system abnormalities
    - Focal neurological deficits
    - Seizures
  - Senses
    - Visual abnormalities
    - Auditory abnormalities
  - Dental abnormalities
  - Medical disorders

TABLE 2. Sequelae After Reparative Surgery for Congenital Heart Disease

- Electrophysiological
  - Atriotomy
    - Intra-atrial repair
    - Intraventricular repair
  - Ventriculotomy
    - Incision site
    - Intracardiac repair
- Valvular
  - Left ventricular or right ventricular outflow repair
  - Left ventricular or right ventricular inflow repair
- Prosthetic materials
  - Patches
  - Valves
  - Conduits
- Myocardial and endocardial
- Vascular
- Neurological

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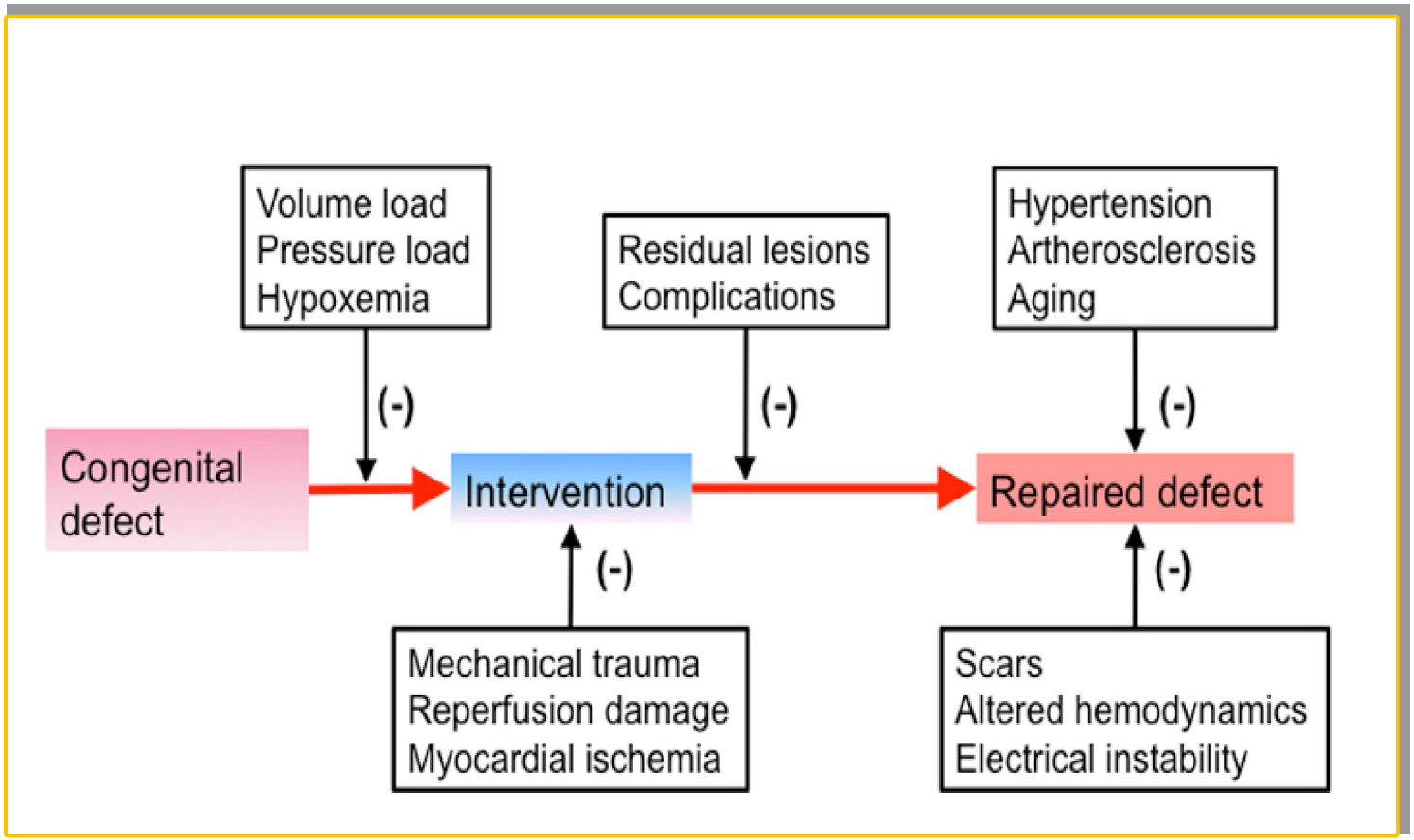
Factors contributing to the CV burden over their lifetime



Residual haemodynamic lesions

- The presence of significant residual haemodynamic lesions has been linked with worse outcomes

- The associated increase in mortality/morbidity may be acute or longer-term, and related to the residual lesion itself and its effect on the heart, and/or the requirement for further intervention

Examples of important residual lesion

- Systemic AV valve regurgitation, particularly when affecting a morphological systemic right ventricle
- Pulmonary regurgitation in ToF
- Significant residual shunts conferring ongoing volume overload
- Obstruction in any venous pathway
- Obstruction and/or regurgitation anywhere in a Univentricular circulation
- Significant peripheral pulmonary stenosis
- Residual straddling tissue post AVSD repair associated with LVOTO and AV valve regurgitation

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ACHD-The Population

- Patients with prior repair and residual or new haemodynamic complications

- Patients with conditions not diagnosed or not considered severe enough to require surgery in childhood

- Patients with prior palliation

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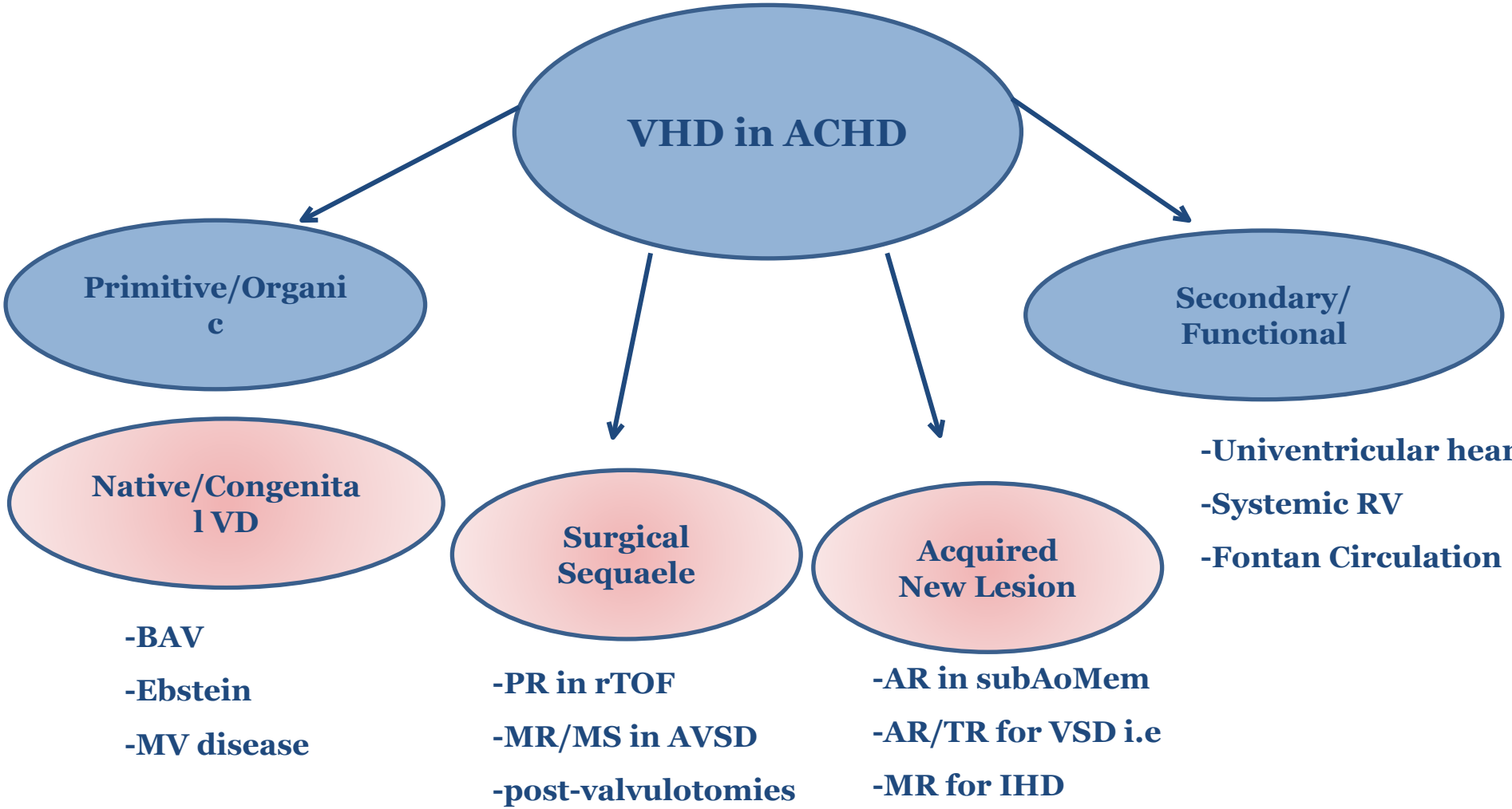
VHD in ACHD patients



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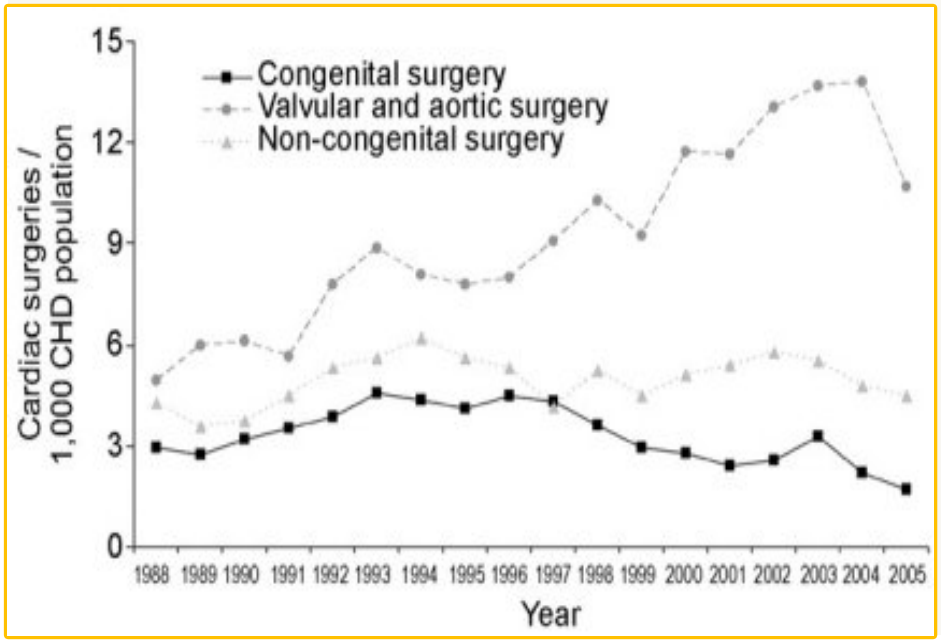
VHD in ACHD patients

VHD are the *main* cause of intervention/reintervention in ACHD

Diagnosis	No. (%)
Conotruncal anomalies[a]	361 (36.7)
Ebstein/tricuspid valve disease	174 (17.7)
Pulmonary stenosis, RVOTO	92 (9.4)
Single ventricle	71 (7.2)
Atrioventricular septal defect	64 (6.5)
Subaortic stenosis, HCM	62 (6.3)
Coarctation, interrupted arch	23 (2.3)
Anomalous pulmonary vein	21 (2.1)
Marfan syndrome	14 (1.4)
Other	102 (10.4)
Total	984 (100)

Holst et al., Ann Thorac Surg 2011



Ionescu-Ittu et al., Ann Thorac Surg 2010

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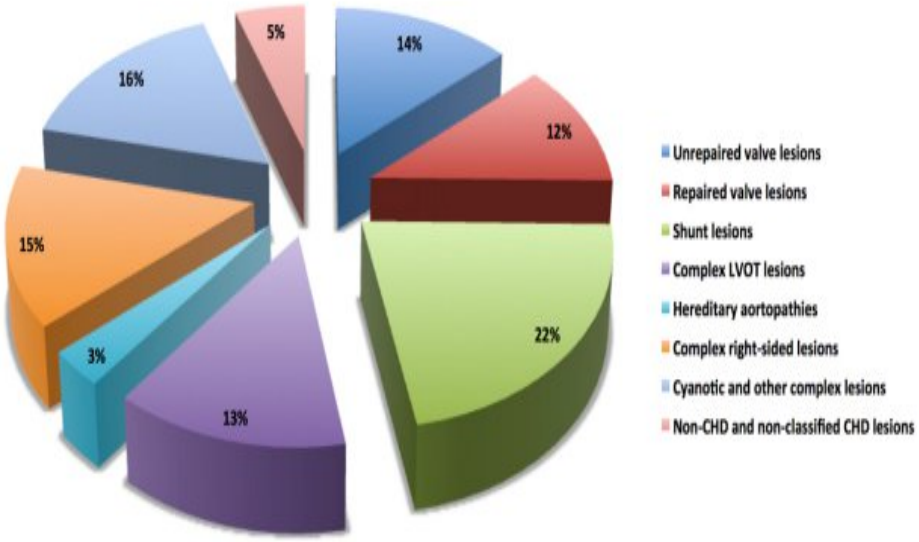
VHD in ACHD patients

› Swiss Med Wkly. 2017 Oct 27;147:w14519. doi: 10.4414/smw.2017.14519. eCollection 2017.

Swiss Adult Congenital HEart disease Registry (SACHER) – rationale, design and first results

Daniel Tobler [1], Markus Schwerzmann [2], Judith Bouchardy [3], Reto Engel [4], Dominik Stambach [4], Christine Attenhofer Jost [5], Kerstin Wustmann [2], Fabienne Schwitz [2], Tobias Rutz [6], Harald Gabriel [7], Hans Peter Kuen [8], Christoph Auf der Maur [8], Angela Oxenius [9], Theresa Seeliger [9], Bruno Santos Lopes [9], Francesca Bonassin [9], Matthias Greutmann [9], On Behalf Of Sacher



› BMC Cardiovasc Disord. 2014 Mar 21;14:38. doi: 10.1186/1471-2261-14-38.

Major adverse cardiovascular events in adult congenital heart disease: a population-based follow-up study from Taiwan

Yu-Sheng Lin, Pi-Hua Liu, Lung-Sheng Wu, Yu-Ming Chen, Chee-Jen Chang [1], Pao-Hsien Chu

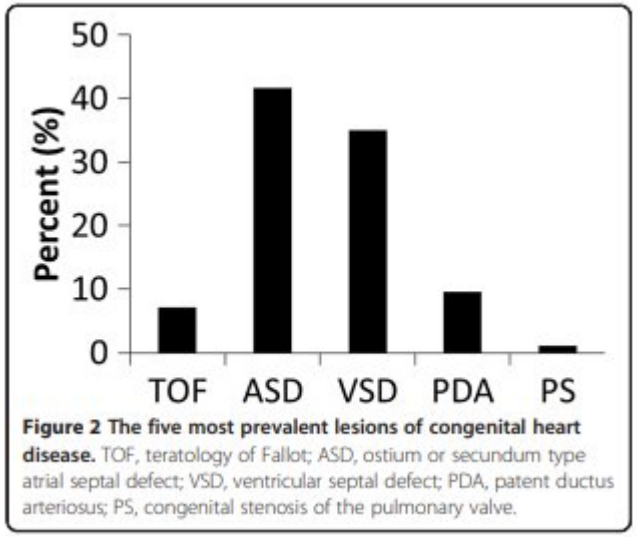


Figure 2 The five most prevalent lesions of congenital heart disease. TOF, teratology of Fallot; ASD, ostium or secundum type atrial septal defect; VSD, ventricular septal defect; PDA, patent ductus arteriosus; PS, congenital stenosis of the pulmonary valve.

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VHD in ACHD patients

Does the presence of severe VHD (S-VHD) impact prognosis in ACHD patients?

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Methods

- ✓ Single center observational clinical study
- ✓ Data have been prospectively collected within the framework of clinical pathway dedicated to ACHD patients at our Institution
- ✓ All patients evaluated in our ACHD outpatient clinic from Sep 2014 to Feb 2021 were screened

Exclusion criteria:

- ***Patent foramen ovale, mild CHD***
- ***Cardiomyopathies***
- ***Congenital arrhythmias without any structural abnormalities***
- ***Fup <12 months***

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Methods

Clinical, imaging and operation details were obtained from the report of the ***first*** clinical outpatient evaluation:

- ***Clinical findings***: age, gender, CHD diagnosis at birth, number of cardiac interventions performed before our first evaluation, age at cardiac intervention(s), presence of genetic syndrome, severity of the CHD lesion (, previous PM/ICD implantation, %Sat O_2, NYHA functional class, complained symptoms.
- ***ECG findings***: rhythm; PR interval; presence of right or left bundle branch block; QRS interval.
- ***Echocardiographic findings***: left ventricle ejection fraction (LVEF), right ventricle systolic function expressed by tricuspid annular plane systolic excursion (TAPSE), parameters of diastolic function (E/A; E/e', left atrium volume index, LAVi), right ventricle systolic pressure (RVSP), degree of valvular stenosis or regurgitation

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Study Endpoints

Primary Endpoint

*Composite of cardiac death and/or cardiac hospitalization**

Cardiac hospitalization ☾ heart failure and/or arrhythmias

excluded hospitalizations for planned or urgent procedures

Secondary Analysis

CV mortality and hospitalization under medical management

(censoring patients at the time of interventions)

We also recorded:

- major arrhythmias not requiring hospitalization
- the rate of cardiac interventions (percutaneous or surgical)

Definitions

Table 4 Classification of congenital heart disease complexity

MILD:
- Isolated congenital aortic valve disease and bicuspid aortic disease
- Isolated congenital mitral valve disease (except parachute valve, cleft leaflet)
- Mild isolated pulmonary stenosis (infundibular, valvular, supravalvular)
- Isolated small ASD, VSD, or PDA
- Repaired secundum ASD, sinus venosus defect, VSD, or PDA without residuae or sequellae, such as chamber enlargement, ventricular dysfunction, or elevated PAP.

MODERATE: (Repaired or unrepaired where not specified; alphabetical order)
- Anomalous pulmonary venous connection (partial or total)
- Anomalous coronary artery arising from the PA
- Anomalous coronary artery arising from the opposite sinus
- Aortic stenosis - subvalvular or supravalvular
- AVSD, partial or complete, including primum ASD (excluding pulmonary vascular disease)
- ASD secundum, moderate or large unrepaired (excluding pulmonary vascular disease)
- Coarctation of the aorta
- Double chambered right ventricle
- Ebstein anomaly
- Marfan syndrome and related HTAD, Turner Syndrome
- PDA, moderate or large unrepaired (excluding pulmonary vascular disease)
- Peripheral pulmonary stenosis
- Pulmonary stenosis (infundibular, valvular, supravalvular), moderate or severe
- Sinus of Valsalva aneurysm/fistula
- Sinus venosus defect
- Tetralogy of Fallot – repaired
- Transposition of the great arteries after arterial switch operation
- VSD with associated abnormalities (excluding pulmonary vascular disease) and/or moderate or greater shunt.

SEVERE: (Repaired or unrepaired where not specified; alphabetical order)
- Any CHD (repaired or unrepaired) associated with pulmonary vascular disease (including Eisenmenger syndrome)
- Any cyanotic CHD (unoperated or palliated)
- Double-outlet ventricle
- Fontan circulation
- Interrupted aortic arch
- Pulmonary atresia (all forms)
- Transposition of the great arteries (except for patients with arterial switch operation)
- Univentricular heart (including double inlet left/right ventricle, tricuspid/mitral atresia, hypoplastic left heart syndrome, any other anatomic abnorm with a functionally single ventricle)
- Truncus arteriosus
- Other complex abnormalities of AV and ventriculoarterial connection (i.e. crisscross heart, heterotaxy syndromes, ventricular inversion).

ACHD ESC Guidelines 2022

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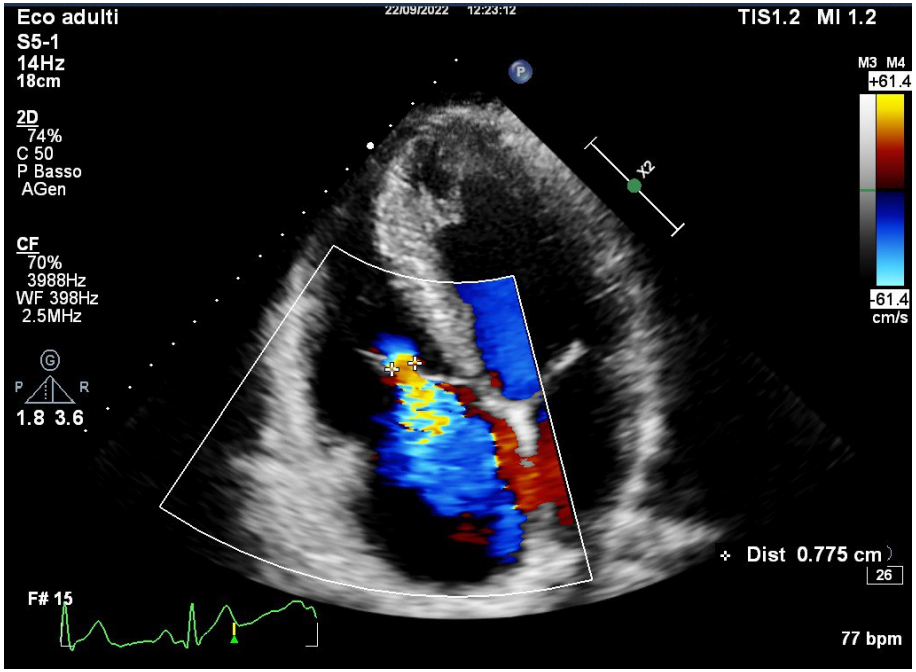
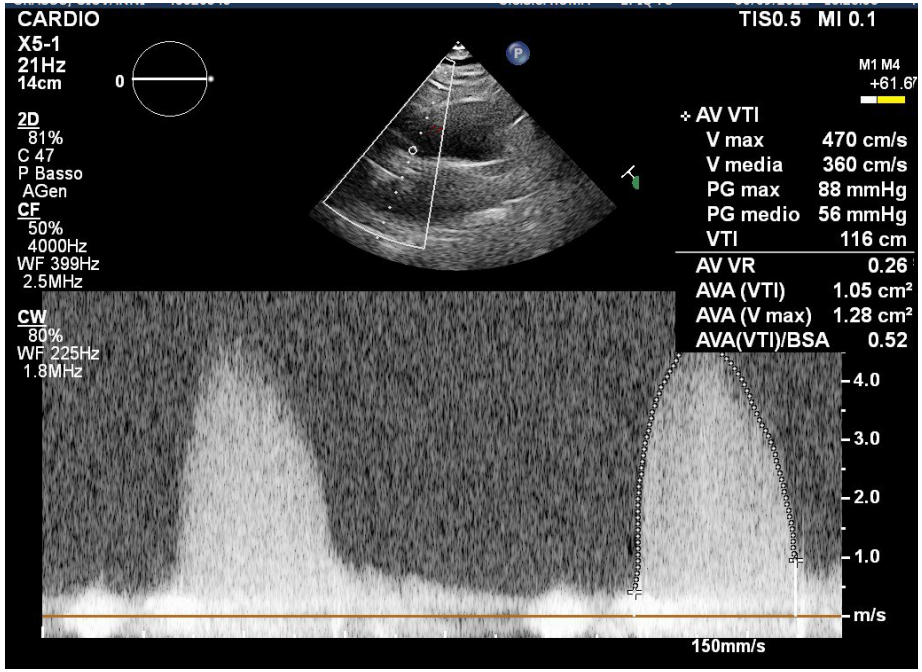
Definitions





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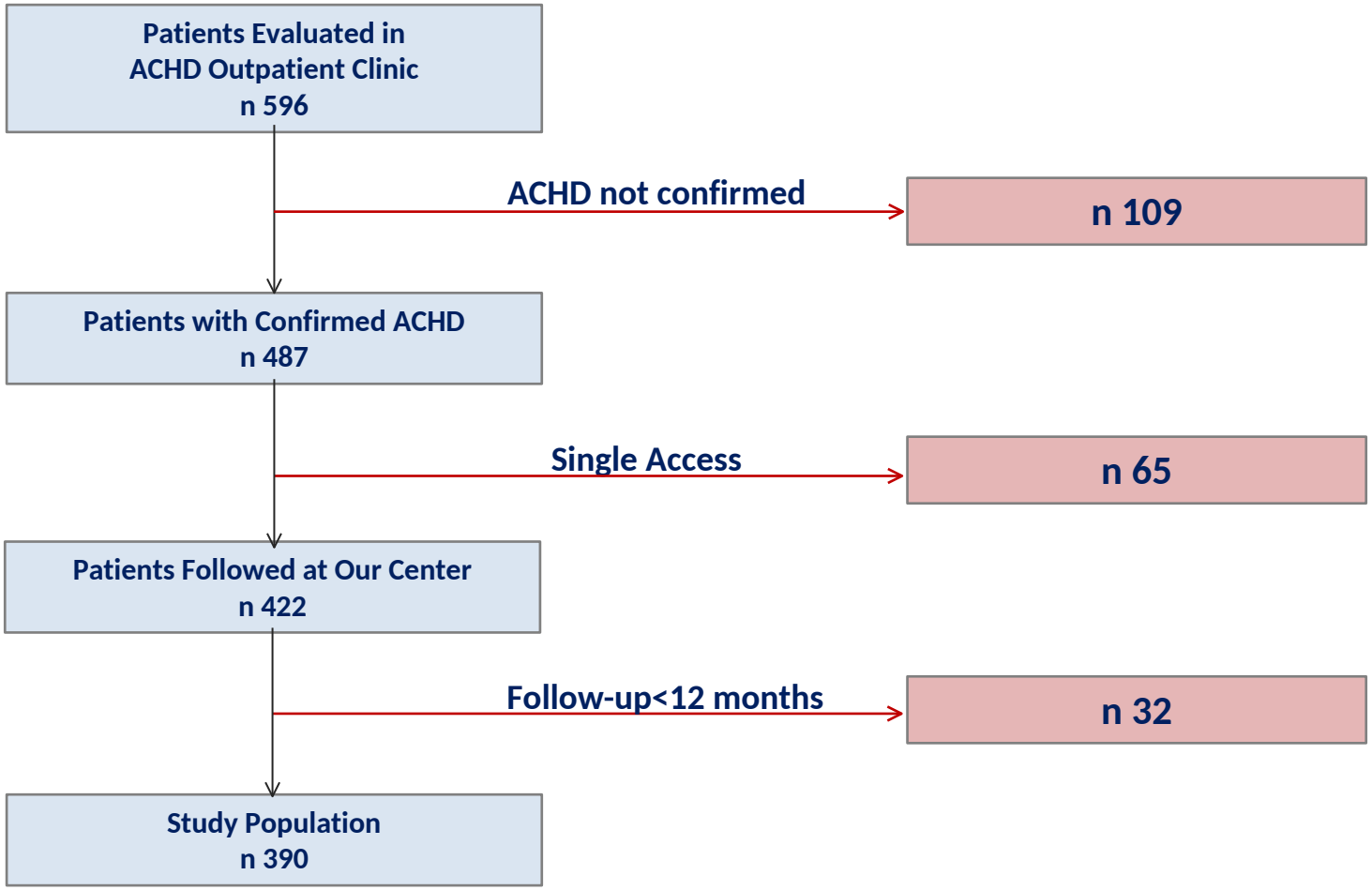
Study flow-chart



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Baseline characteristics

Variables	Total (n=390)
Age (years)	34 (26-46)
Male (n,%)	189 (49)
Complexity of CHD (n,%)	
Mild	159 (41)
Moderate	191 (49)
Severe	40 (10)
Surgery in pediatric age (n,%)	
None	184 (47)
Corrective surgery	179 (46)
Palliative surgery	27 (7)
Previous implantation of PM/ICD (n,%)	30 (8)
Af/Afib (n,%)	22 (6)
HR (bpm)	73 ± 13
QRS (ms)	105 (94-126)
Sat O_2(%)	98 (97-98)
NYHA class II-IV	146 (37)
LVEF (%)	61 ± 7
LAVi (ml/m2)	31 (24-43)
E/E' ratio	7 (5-8)
S-VHD (n,%)	101 (26)
TAPSE (mm)	22 ± 5
RVSP (mmHg)	30 (25-40)
RVSP>45 mmHg (n,%)	29 (7)

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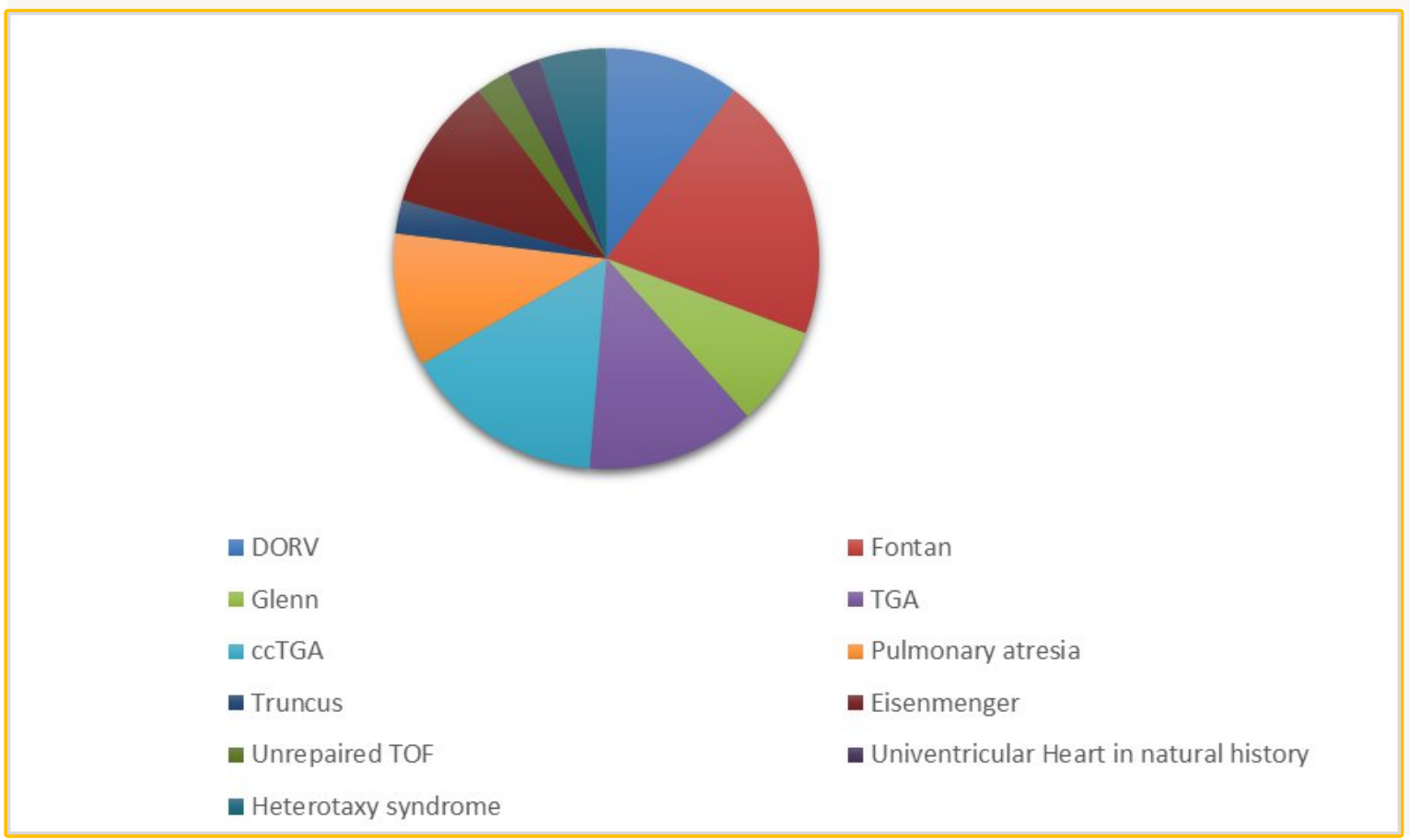
Baseline characteristics

Distribution of Severe CHD



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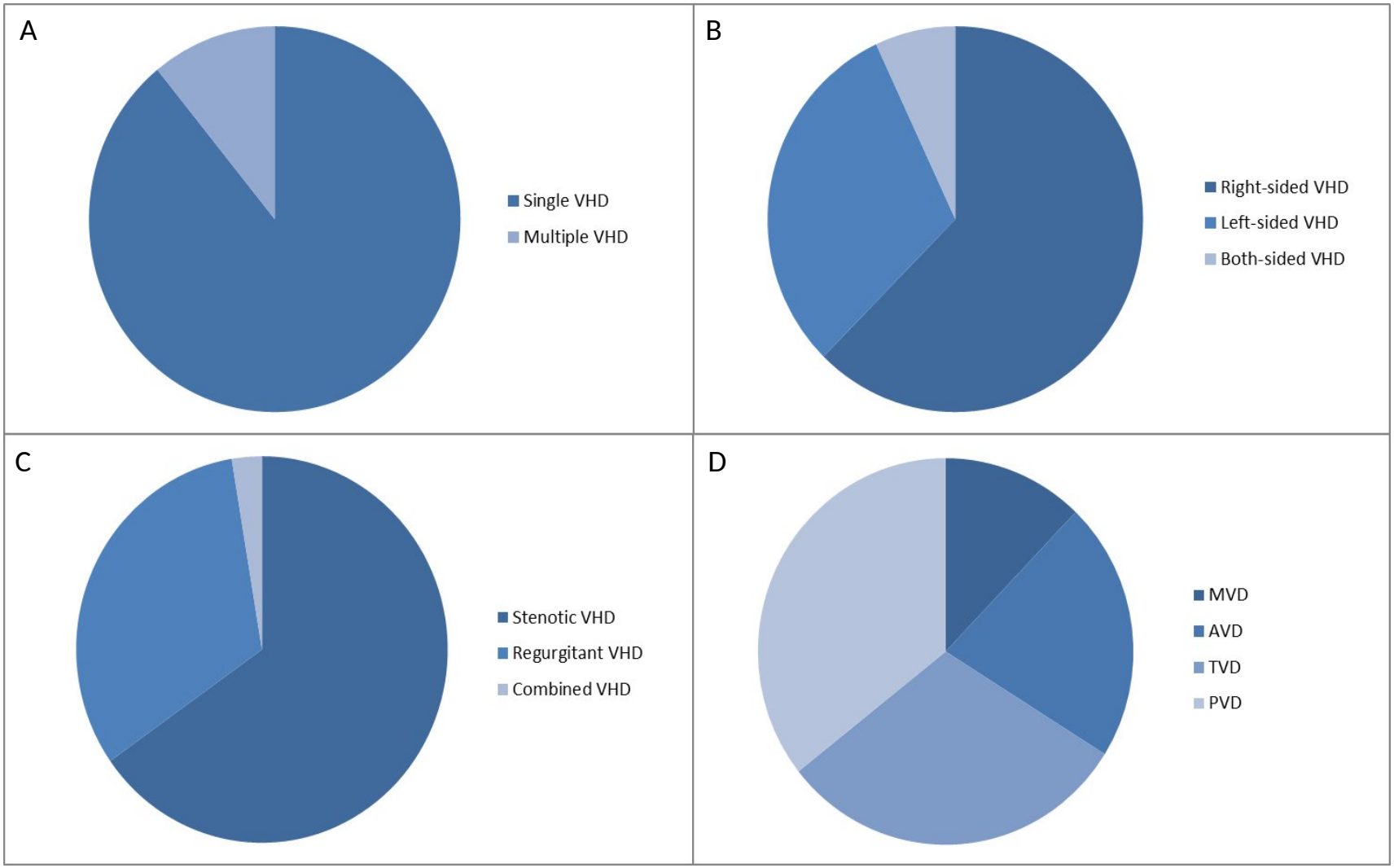
S-VHD distribution



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Results

Variables	S-VHD (n=101)	NS-VHD (n=289)	p-value
Age (years)	40 (30-54)	33 (24-44)	<0.001
Male (n,%)	49 (49)	140 (48)	0.990
Complexity of CHD (n,%)			
Mild	23 (23)	136 (47)	<0.001
Moderate	63 (62)	128 (44)	
Severe	15 (15)	25 (9)	
Surgery in pediatric age (n,%)			
None	37 (37)	147 (51)	0.0014
Corrective surgery	53 (53)	127 (44)	
Palliative surgery	11 (10)	15 (5)	
Previous implantation of PM/ICD (n,%)	10 (10)	20 (7)	0.343
Af/Afib (n,%)	15 (15)	7 (3)	<0.001
HR (bpm)	73 ± 15	72 ± 12	0.49
QRS (ms)	117 (101-149)	103 (93-119)	<0.001
Sat O_2(%)	97 (95-98)	98 (97-99)	<0.001
NYHA class II-IV (n,%)	57 (57)	89 (31)	<0.001
LVEF (%)	60 ± 6	62 ± 7	0.027
LAVi (ml/m2)	41 (27-61)	29 (23-40)	<0.001
E/E' ratio	7 (5-10)	6 (5-8)	0.344
TAPSE (mm)	20 ± 6	22 ± 5	0.006
RVSP (mmHg)	40 (30-55)	30 (25-35)	<0.001
RVSP>45 mmHg (n,%)	17 (17)	12 (4)	<0.001

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Results

To further confirm the prognostic value of S-VHD on the clinical evolution, the occurrence of cardiac mortality or cardiac hospitalization without cardiac operations was examined.
After a median follow-up of 23 months (range: 9-44), 68 events occurred. At univariable Cox regression analysis, S-VHD was significantly associated with outcomes in patients medically treated (HR: 3.473 (2.144-5.627); $p<0.001$). The adjustment for significant clinical and echocardiographic variables (age, severe CHD, Af/Afib, NYHA class ≥II, LVEF and increased RVSP) did not affect the powerful association of S-VHD with the occurrence of the composite endpoint under medical management (HR: 1.920 (1.093-3.373); $p=0.023$).

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Results

Over a median follow-up time of 26 months (range:12-48)
the ***primary endpoint*** occurred in a total of 76 patients (19.5%)

A ***cardiac intervention*** was performed in 78 patients

Patients with S-VHD

- more frequently *percutaneous or surgical intervention* (41.6% vs 12.5%, p<0.001)

- more *arrhythmias* occurred in patients with S-VHD (32.7% vs 15.2%, p<0.001)

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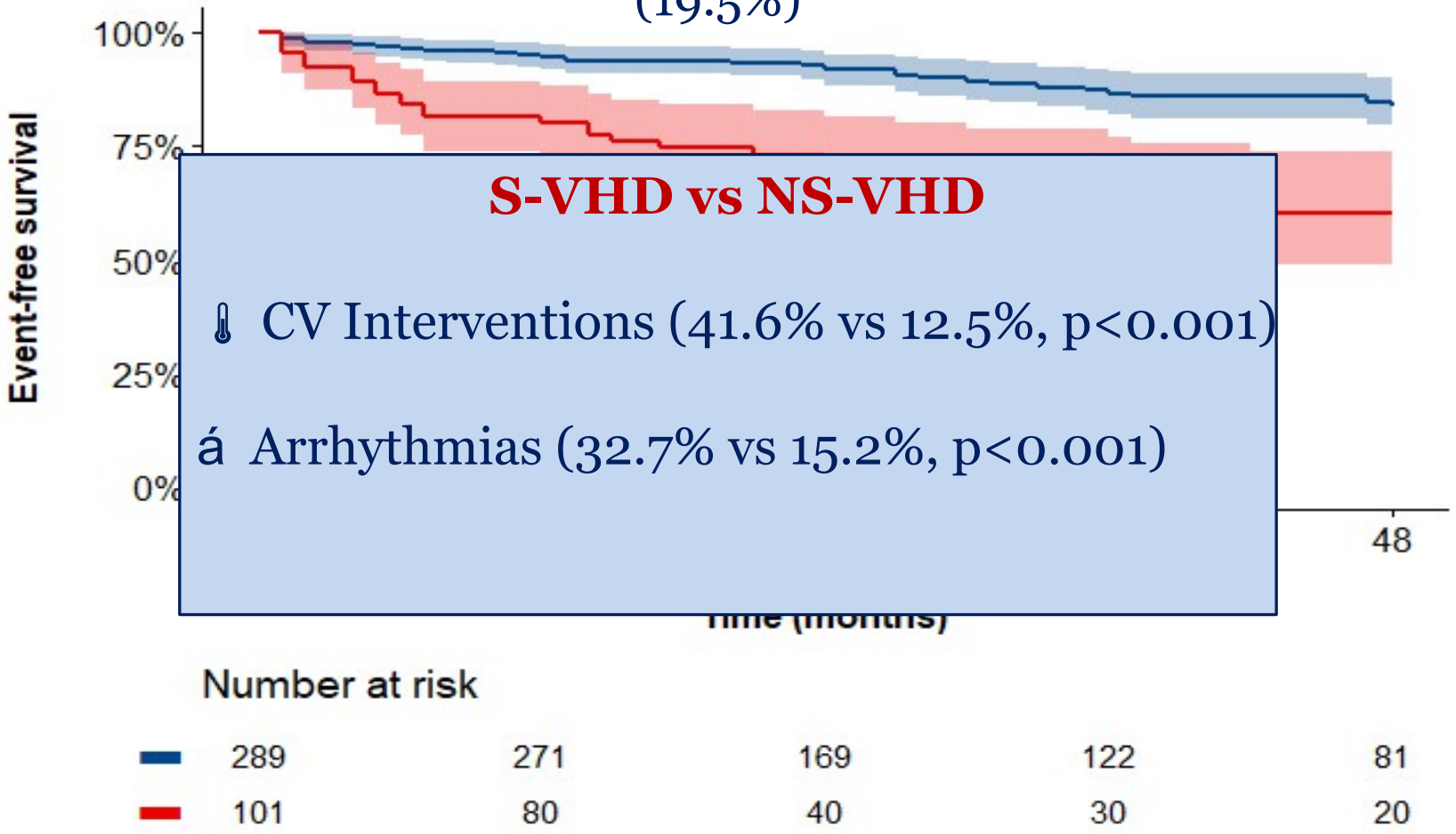
Results

Median FUP: 26 months (IQR:12-48): Primary Endpoint ☾ 76 pts (19.5%)



S-VHD vs NS-VHD

- ↓ CV Interventions (41.6% vs 12.5%, p<0.001)
- ↑ Arrhythmias (32.7% vs 15.2%, p<0.001)

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Results

	Univariable analysis		Multivariable analysis	
Variables	OR (95% CI)	p-value	OR (95% CI)	p-value
Age (years)	1.037 (1.020-1.054)	<0.001	1.022 (1.002-1.041)	**0.029**
Male	0.981 (0.623-1.546)	0.935		
Severe CHD	3.483 (2.086-5.816)	<0.001	1.332 (0.663-2.673)	0.421
Surgery in pediatric age	1.376 (0.865-2.186)	0.177		
Af/Afib	6.444 (3.224-12.877)	<0.001	3.214 (1.408-7.333)	**0.006**
HR (bpm)	1.011 (0.994-1.029)	0.209		
QRS duration (ms)	1.007 (0.999-1.014)	0.075		
Sat O_2 (%)	0.934 (0.914-0.955)	<0.001	0.956 (0.926-0.986)	**0.005**
NYHA class II-IV	4.224 (2.613-6.827)	<0.001	2.246 (1.270-3.974)	**0.005**
Surgical or percutaneous intervention (time-dependent)	1.503 (0.745-3.031)	0.255		
LVEF (%)	0.922 (0.896-0.948)	<0.001	0.952 (0.918-0.987)	**0.008**
LAVi (ml/m2)	1.000 (0.998-1.003)	0.657		
E/E' ratio	1.049 (0.932-1.181)	0.426		
S-VHD	3.258 (2.073-5.121)	<0.001	1.925 (1.133-3.271)	**0.015**
TAPSE (mm)	0.901 (0.856-0.949)	<0.001		
RVSP >45 mmHg	1.029 (1.017-1.040)	<0.001	2.023 (0.955-4.286)	**0.066**

CV mortality or hospitalization without cardiac operations: 1.920 (1.093-3.373); p=0.023

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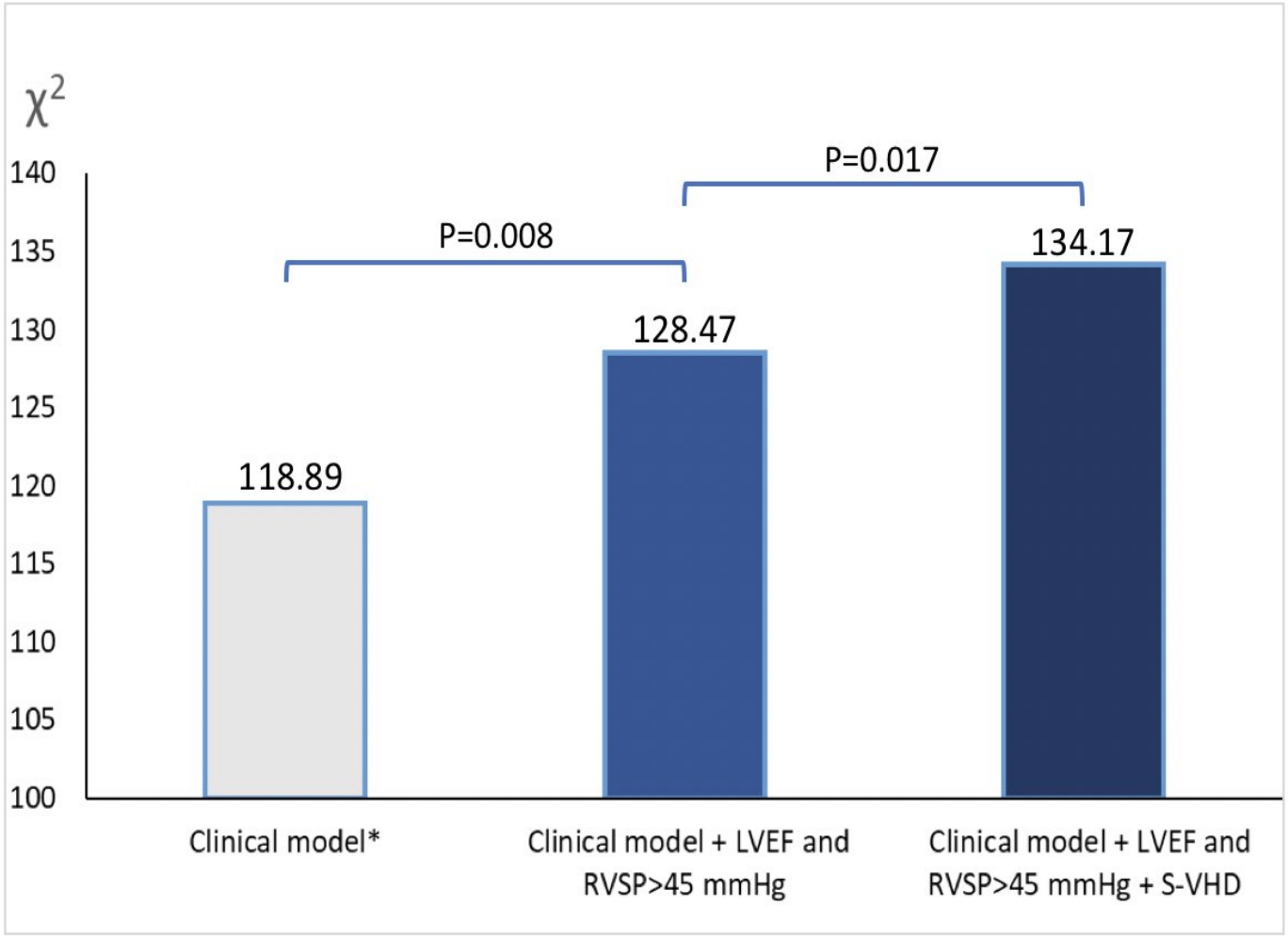
Results



** Clinical model: Age, severe CHD, Af/Afib, Sat O_2 (%), NYHA class ≥II*

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Results

Total number of events in the overall population and two sub-groups

Outcome	Total population (n=390)	S-VHD (n=101)	NS-VHD (n=289)	p-value
Cardiac hospitalization (n,%)	74 (19.0)	36 (35.6)	38 (13.1)	<0.001
Cardiac death (n,%)	8 (2.1)	6 (6.1)	2 (0.7)	0.001

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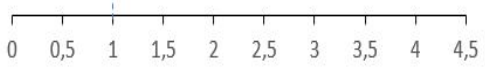
Results

Association between each subtype of S-VHD and the primary endpoint

Type of S-VHD	Unadjusted HR (95% CI)	P-value	Adjusted HR (95% CI)	P-value
Isolated S-VHD	2.606 (1.645-4.129)	**<0.001**	1.672 (1.002-2.790)	**0.049**
Multiple S-VHD	5.038 (2.177-11.658)	**<0.001**	1.557 (0.631-3.642)	0.336
Left-sided S-VHD	2.383 (1.344-4.225)	**0.003**	2.338 (1.263-4.230)	**0.007**
Right-sided S-VHD	3.314 (2.065-5.321)	**<0.001**	1.435 (0.827-2.489)	0.199
Stenotic S-VHD	2.575 (1.485-4.464)	**0.001**	1.663 (0.889-3.113)	0.240
Regurgitant S-VHD	3.203 (1.970-5.208)	**<0.001**	1.987 (1.134-3.483)	**0.016**
AV S-VHD	3.353 (1.946-5.774)	**<0.001**	1.674 (0.898-3.122)	0.105
VA S-VHD	2.399 (1.474-3.906)	**<0.001**	1.506 (0.881-2.575)	0.134



After adjustment for: age, severe CHD, Af/Afib, NYHA ≥II, Sat O_2, LVEF, RVSP>45mmHg

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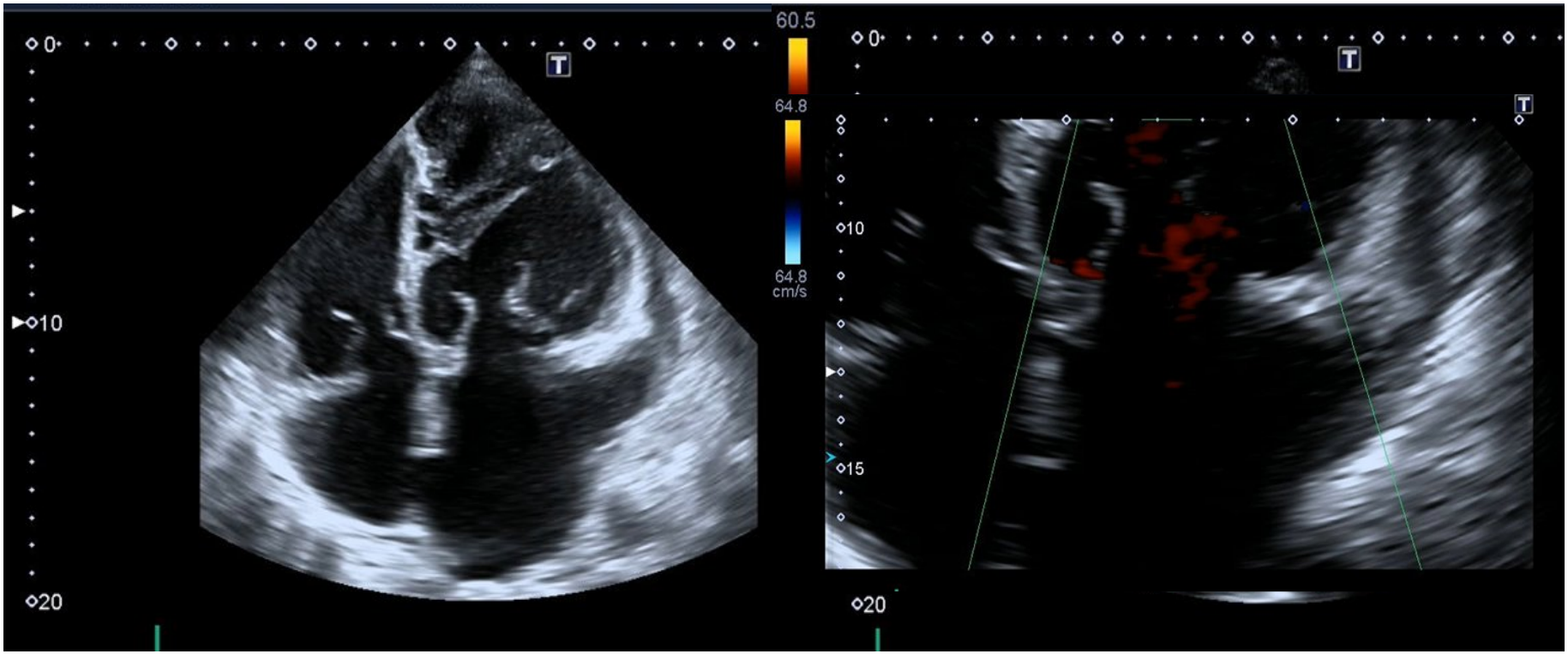
ccTGA, systemic RV systolic dysfunction



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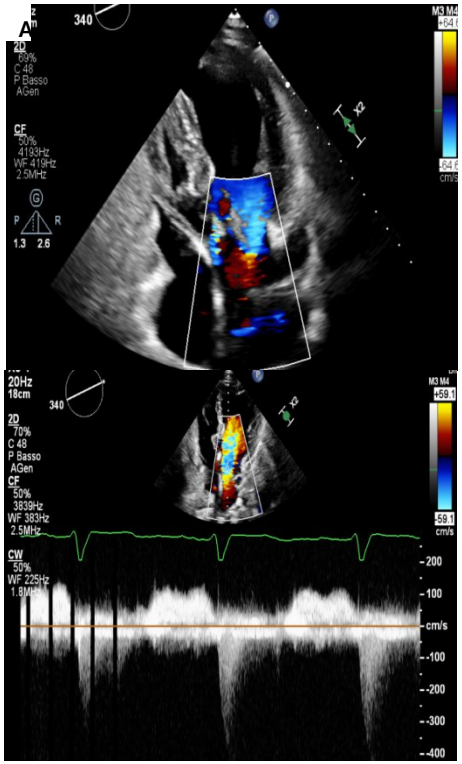
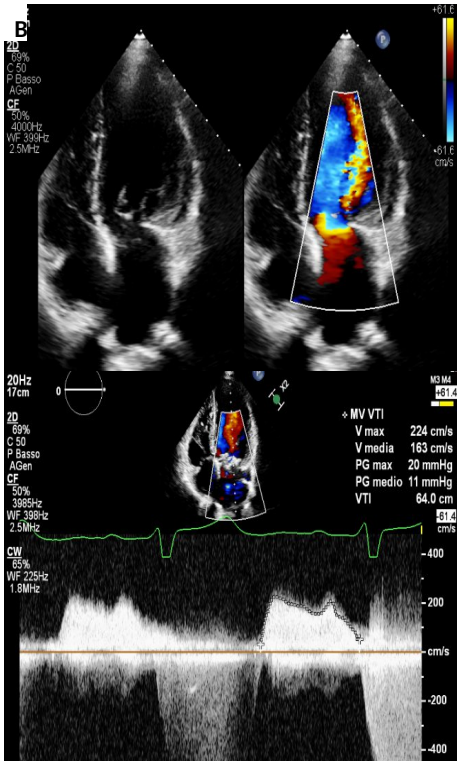
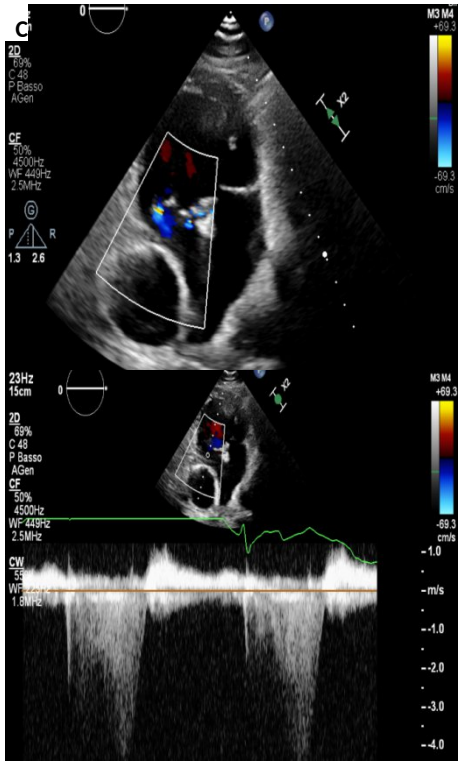
Examples



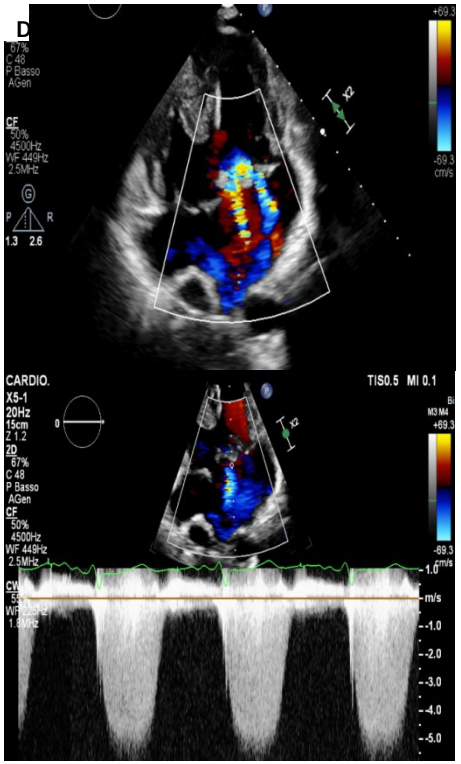
S/P AVSD repair, no S-VHD
MACE-



S/P AVSD repair, S-VHD
MACE+



Fontan, normal EF, no S-VHD
MACE-



Fontan, normal EF, S-VHD
MACE+

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Conclusions

✓ The occurrence of ***severe*** VHD in ACHD patients is a significant independent predictor of CV hospitalization or death

✓ The prognostic value of severe valve dysfunction is ***incremental*** above other established prognostic markers and consistent ***independently*** from CHD severity

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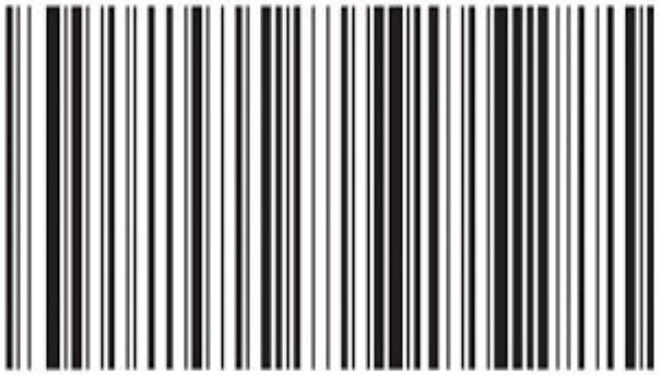
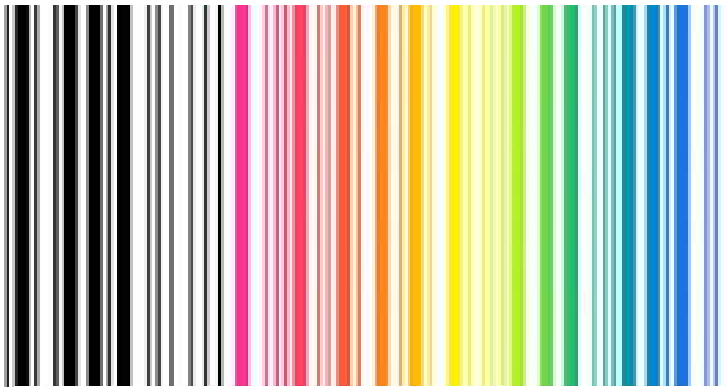
Insights

- Mean age 34 ☾ >50% moderate or severe VHD
- Difficult to dissect the individual burden of each VHD subtype



DISEASE 1 2 3 4 5



WIDE VARIETY OF DISEASE

VHD in ACHD patients

The Individual Patient Can Fit Multiple Different Classification

Systemic AV valve
- *functional*
- *primitive-organic*
- *sequela*

AVSD
- *primitive -CH*
- *sequela*

BAV → *CoA*

Ebstein → *ASD, PFO, WPW*

Parachute MV → *Shone Complex*

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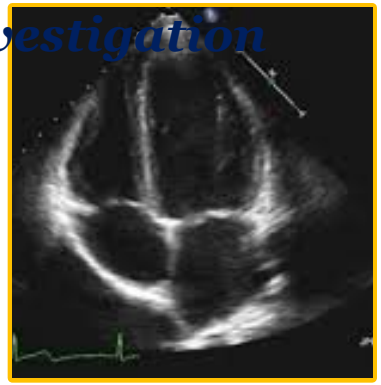
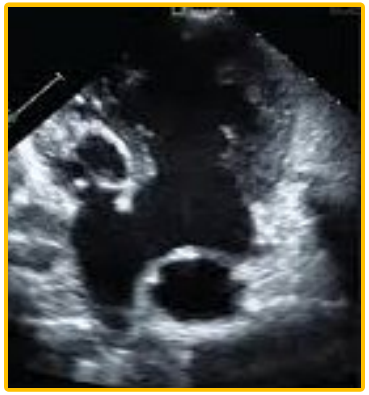
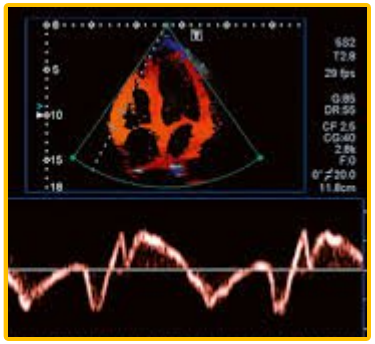
Insights-Echocardiography

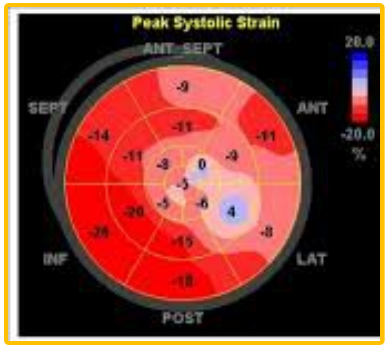
First-line investigation

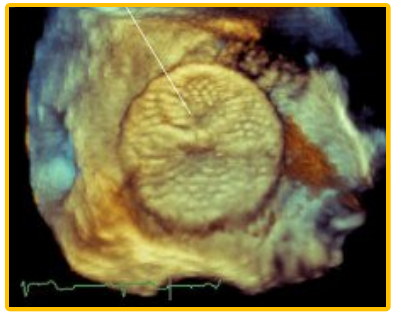




Evolution of standard echocardiography







Basic cardiac anatomy

Technical Difficulties

- Abnormal segmental and regional incoordination ☾ **systemic RV and UVH**
- Misleading Doppler gradients ☾ **RVOTO, CoA, Stenosis in series**
- Venous return and great arteries difficult to image

- Position of the heart
- Connection of the atria and ventricles
- Origin of the great arteries

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TAKE HOME MESSAGES

- ✓ ACHD patients retain a life-long risk for CV complications (never cured)
- ✓ Main causes of death: heart failure/arrythmias
- ✓ VHD are the main cause of intervention/reintervention in adulthood
- ✓ S-VHD is independently associated to the risk of CV death and hospitalization
- ✓ Strict follow-up, dedicated multidisciplinary care team

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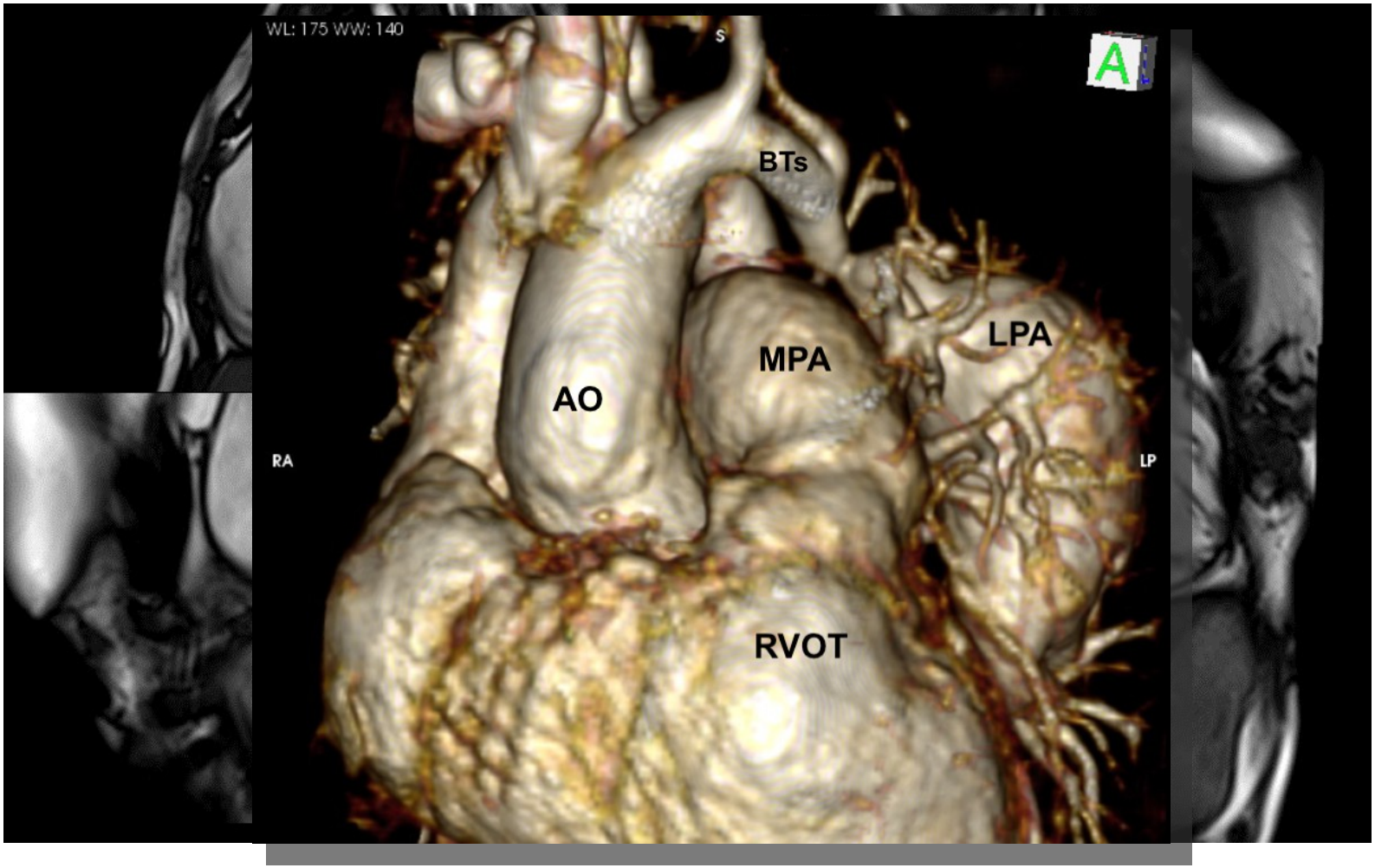
Residual haemodynamic lesions- Case



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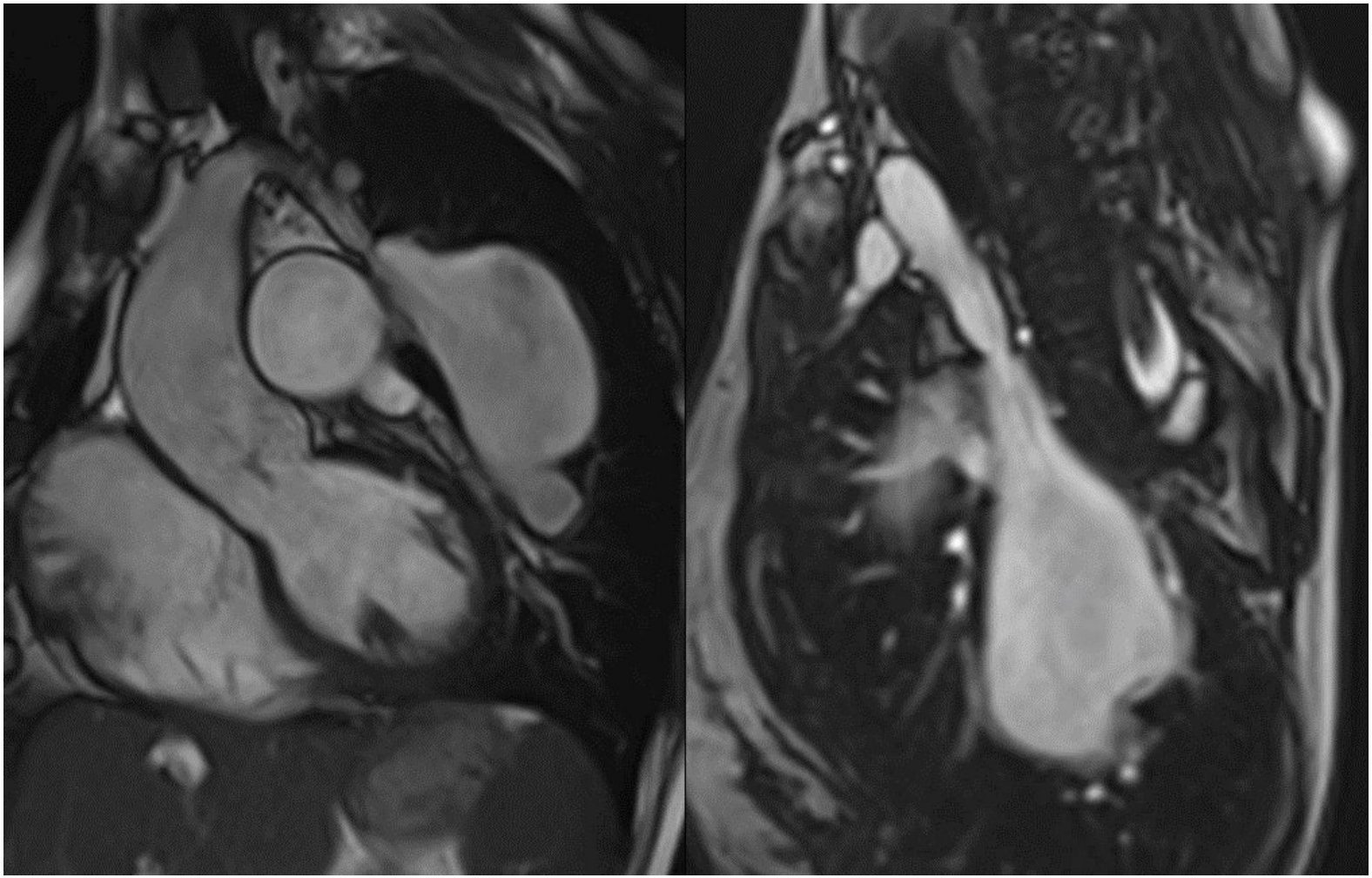
Residual haemodynamic lesions- Case



Grazie