

ESC Heart & Brain Workshop

Structural heart disease and stroke

P. Lanzer, Mitteldeutsches Herzzentrum, Standort Bitterfeld

Supported by Bayer, Bristol-Myers Squibb and Pfizer Alliance, Boehringer Ingelheim, Daiichi Sankyo Europe GmbH and Medtronic in the form of educational grants. The scientific programme has not been influenced in any way by its sponsors.



**Boehringer
Ingelheim**



Daiichi-Sankyo



Bristol-Myers Squibb



Medtronic
Further Together

Agenda

Stroke Facts

Struktural Heart Disease and Stroke

- **Congenital Heart Disease**
- **Heart Disease with Thromboembolic Potential**

Interventions and Stroke

Conclusions

Stroke Facts

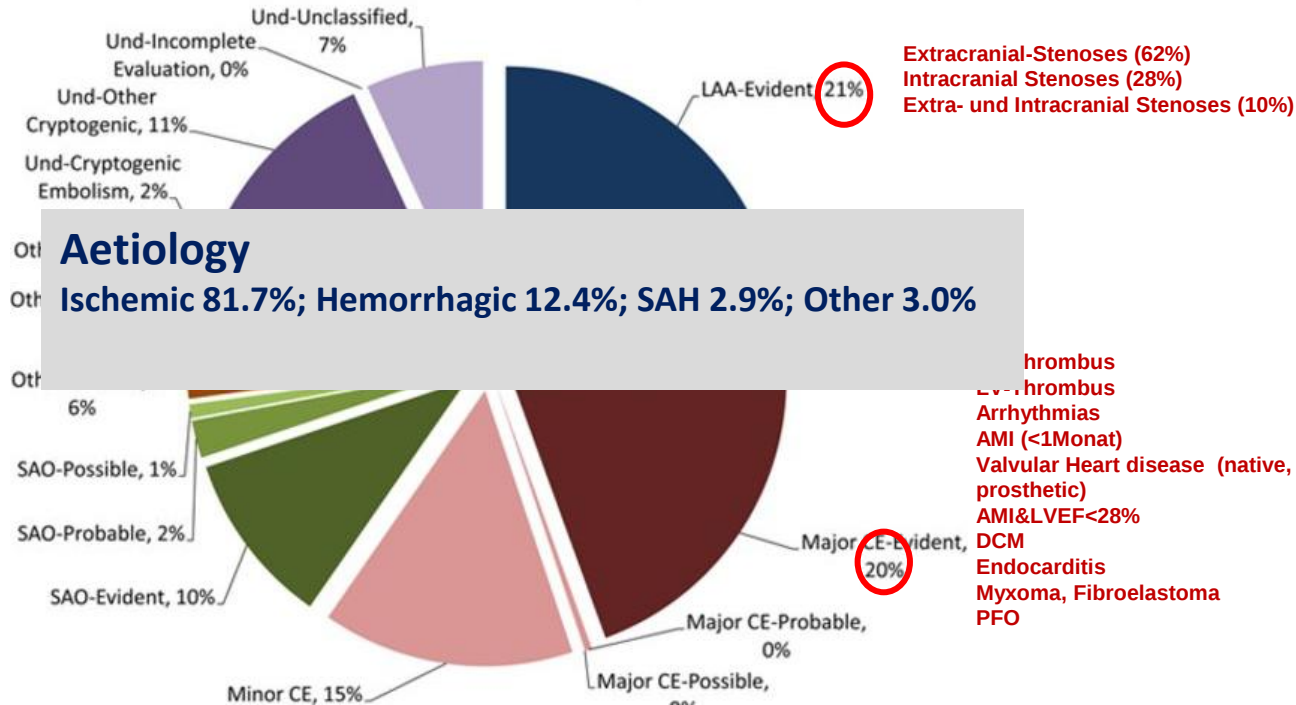
EU by Age (100.000/y)

	Austria		Belgium		Cyprus		Czech Republic		Denmark		Finland		France		Germany		Greece		Iceland		Ireland		Italy		Luxembourg		Malta				
Age	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women			
25-34	13	10	19	12	10				7	30	15	23	12	19	9	14	9	21	11	11			21	14	8	15	18	16	10		
35-44	26	20	37	23	20				14	60	30	46	24	37	18	28	17	42	21	23			42	27	16	31	36	32	20		
45-54	153	69	139	84	83				119	194	80	201	74	131	49	131	60	215	98	107			99	124	63	146	103	153	81		
55-64	324	172	312	186	229				347	351	184	384	191	253	109	316	152	533	288	212			92	295	154	366	231	381	203		
65-74	877	613	812	550	672				1140	882	580	987	653	630	364	899	588	1541	1316	600			647	877	673	818	585	988	721	1126	789
75-84	1631	1376									1708	1391	1105	837	1696	1395	31										852	1584	1870	1637	
85+	2005	1801									2009	1784	1325	1113	2096	1857	40										314	2087	2098	2021	
The Netherlands																															
	Men	Women										Switzerland	UK			Estonia															
												Men	Women	Men	Women	Men	Women	Men	Women	Men	Women						Men	Women	Men	Women	
25-34	11	12									8	6	16	9	27	12									7	4	21	11			
35-44	21	25	26	17	93	39	24	15	16		13	17	12	32	18	54	25	37	27	54	29	35	17	34	25	14	9	41	22		
45-54	119	93	123	69	362	149	132	57	122		65	58	49	129	94	367	133	455	205	367	141	268	138	250	103	156	58	194	139		
55-64	284	175	287	148	842	390	298	143	294		164	171	110	301	209	877	407	1155	587	877	332	670	332	613	289	469	183	612	296		
65-74	847	565	905	530	2299	1431	804	498	841		535	515	329	845	652	1858	1171	2563	1645	1824	907	1404	882	1255	800	1132	631	1467	858		
75-84	1567	1265	1796	1359	3769	3193	1413	1207	1579		1287	1074	822	1512	1453	2641	2473	3963	3539	2607	1680	2029	1659	1619	1459	1568	1102	2344	1754		
85+	1889	1657	2234	1887	4262	4153	1682	1647	1943		1767	1401	1158	1809	1925	2953	3284	4656	4757	2953	2070	2320	2081	1706	1792	1654	1251	2784	2244		

Truelsen T et al. Eur J Neurol 2006;13:581-59/The European Registers of stroke (EROS)
Investigators. Stroke 2009;40:1557-15638

Cardiovascular Diseases with Thromboembolic Potential

ESUS
ca. 35% Afib?



Structural Heart Disease

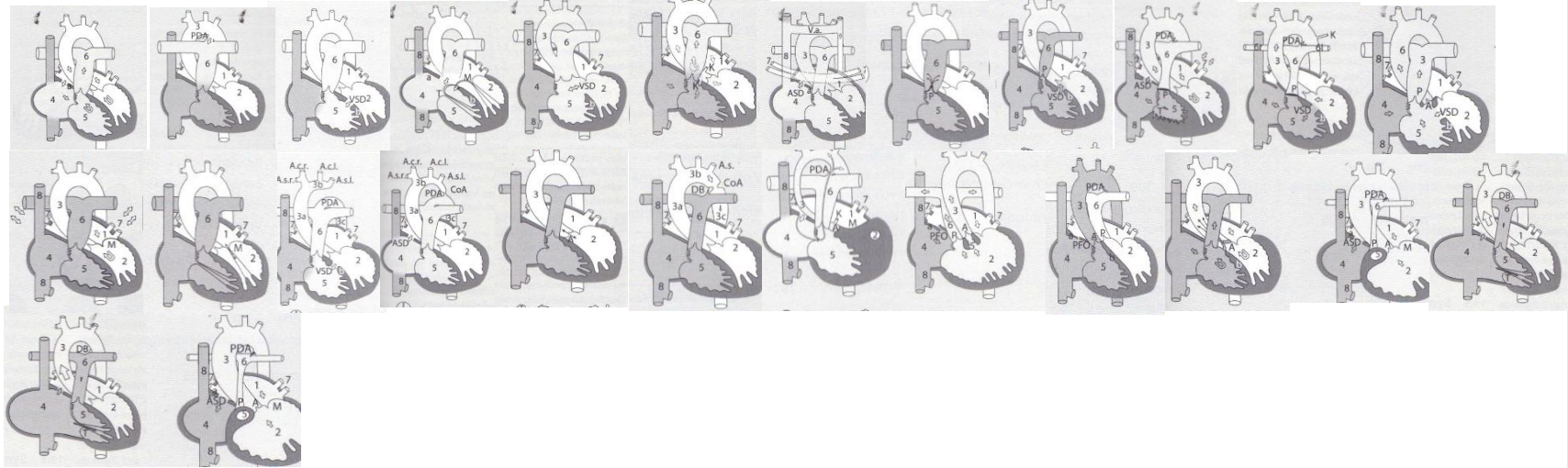
Definition

SHD refers to congenital or acquired cardiac defects affecting the non-coronary components of the heart.

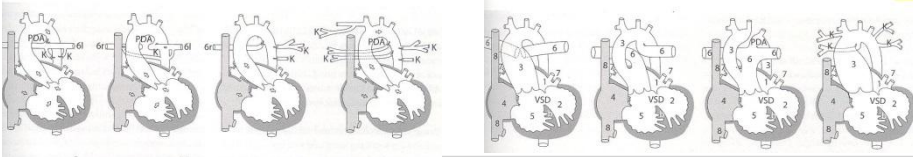
CHD



Main Defects



Individual Variants



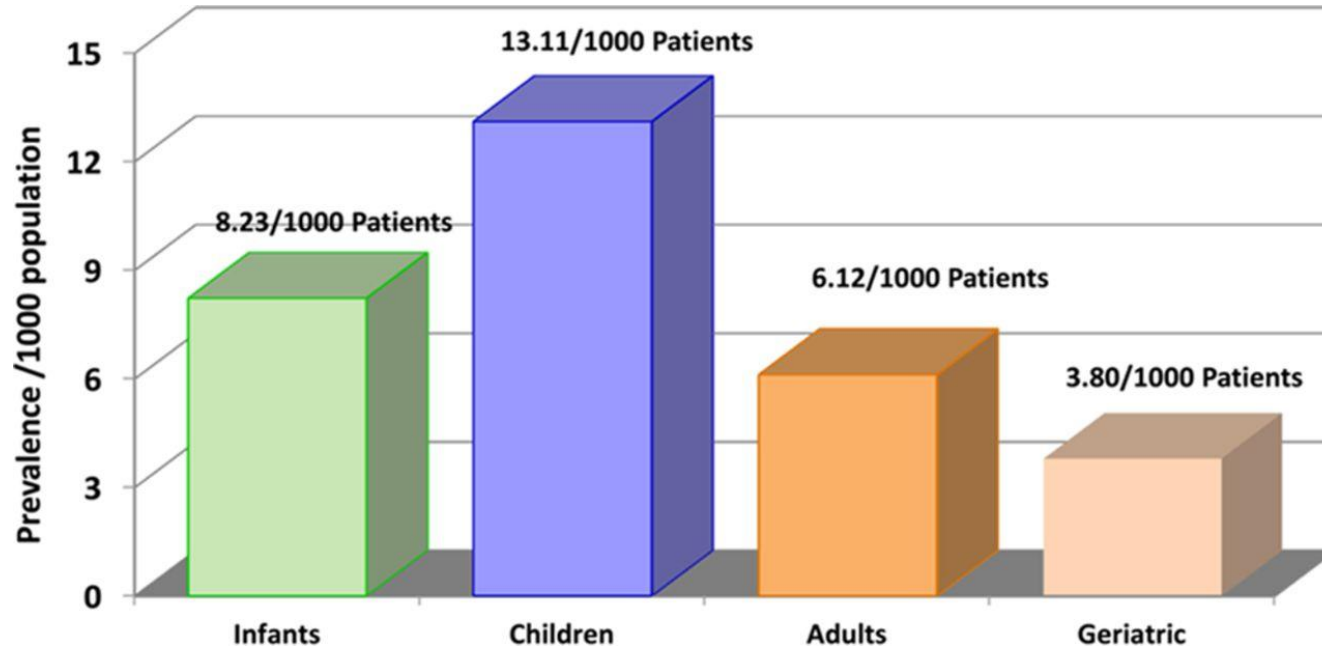
Blum et al. Springer, 2016

CHD - Incidence

≈1% of live birth; the most common congenital malformation

<u>Congenital defect</u>	<u>Incidence</u>
VSD	15-30%
Fallot Tetralogy	10-15%
ASD	7-10%
Patent Ductus arteriosus – Botalli	5-10%
Aortic isthmus stenosis	6%
Transposition of great vessels	6%
Pulmonal artery stenosis	6%
Aortic valve stenosis	4%
Tricuspid valve atresia	1-2%
Cor triatriatum	0,1-,04%

CHD - Incidence



Marelli A et al. Circulation 2016;133:1951-1962

CHD and Stroke Risk Factors

General

- Age
- Heart failure
- Myocardial infarction
- Diabetes mellitus
- Arterial hypertension
- Arrhythmias

CHD-related

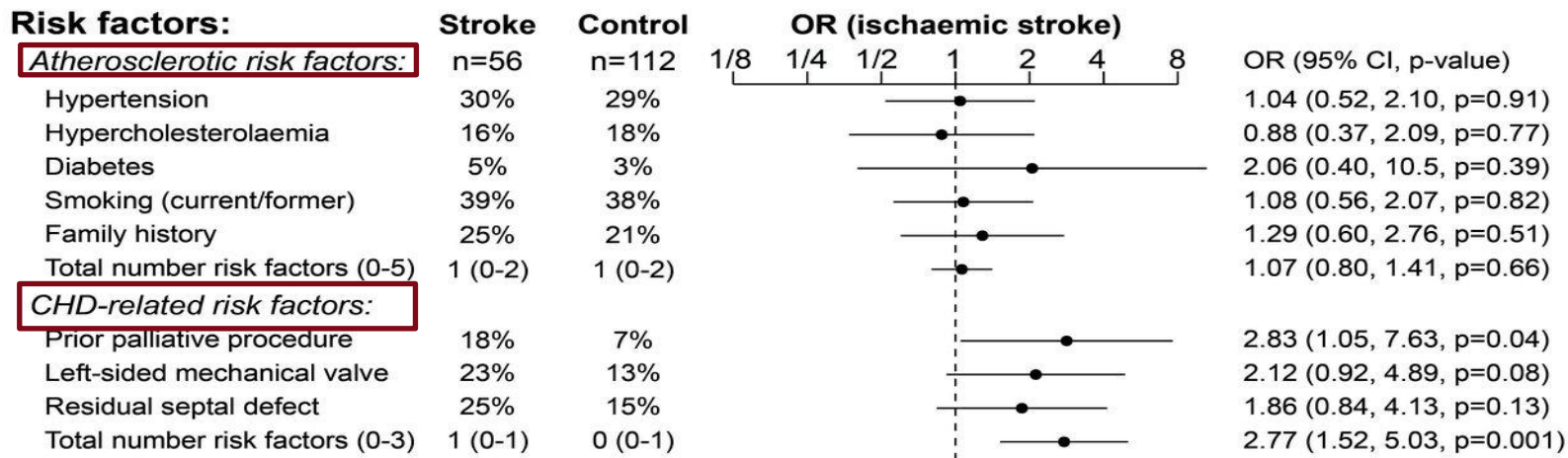
- Previous shunt operations
- Residual/unclosed septal defects
- Left-sided mechanical valves
- Arrhythmias
- Endocarditis
- Hypoxaemia
- Secondary erythrocytosis
- Iron deficiency
- Associated syndromes
- Heart failure

Pathophysiology

Embolic (Surgery, Procedures, Prosthetic valves, Foreign bodies, Endocarditis); Paradoxical embolism (Pulmonary AVMs, Veno-venous collaterals, CHD with r-l shunt, Septal defects)

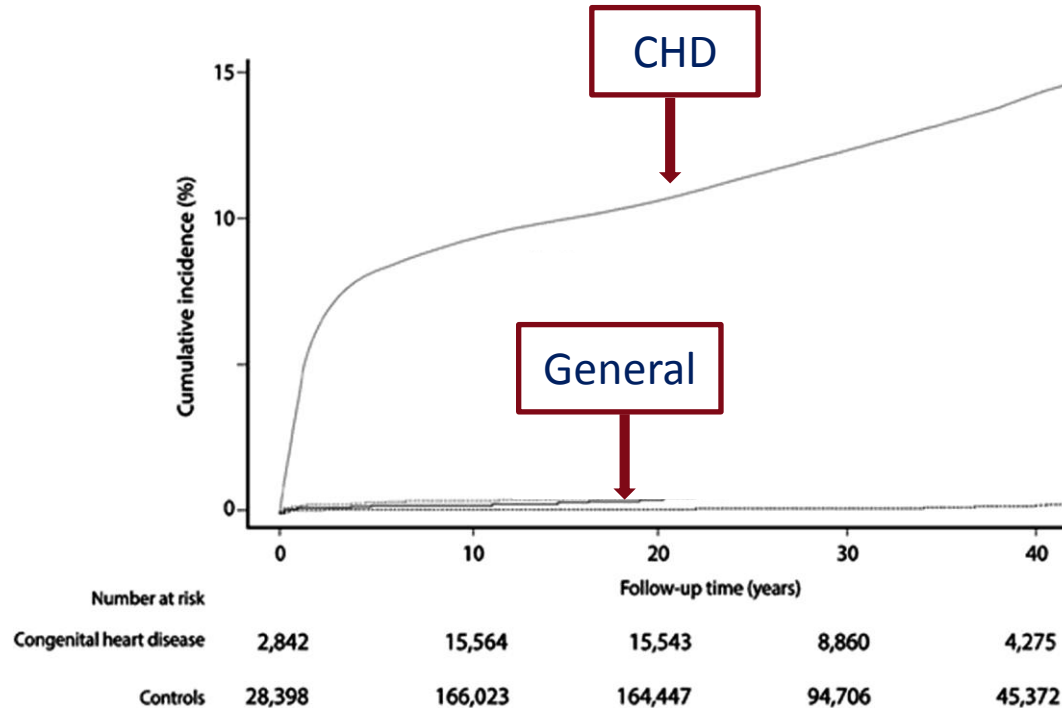
Hemorrhagic (Hypertension, NOAC, Aneurysms, intracranial AVMs)

CHD and Stroke Risk Factors



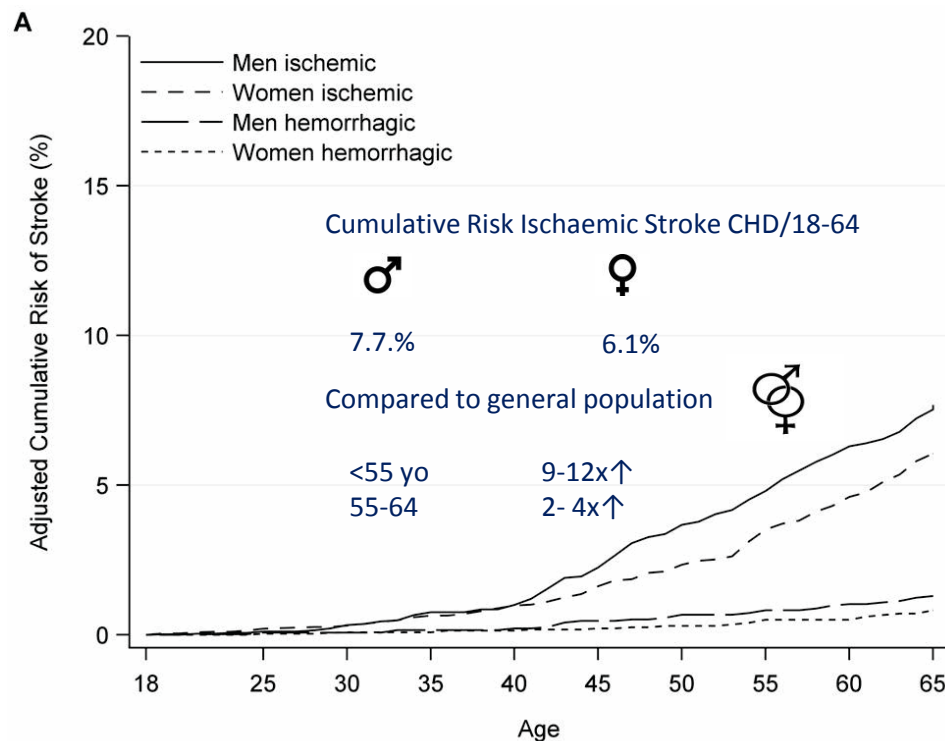
Jouke P Bokma et al. Heart doi:10.1136/heartjnl-2017-311620

CHD - Cumulative Stroke Incidence by Age (Young Adults)



Mandalenakis Z et al. JAHA 2016;5:e003071

CHD and Stroke Incidence by Adults



Lanz J et al. Circulation 2015;132f:2385-94

CHD – Classification (Marelli)

Marelli 1

AVCD, TOF, Univentricular Heart, Transposition complex, , Truncus arteriosus, Hypoplastic heart syndrome

Marelli 2

ASD, VSD, PDA, Aortic coarctation, Ebstein's anomaly

Marelli 3

Unspecified defect of septal closure

Marelli 4

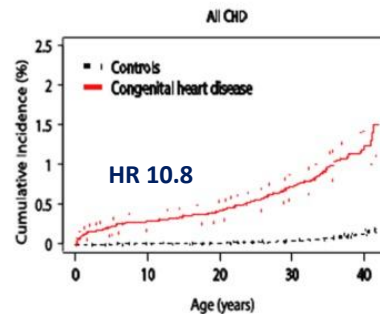
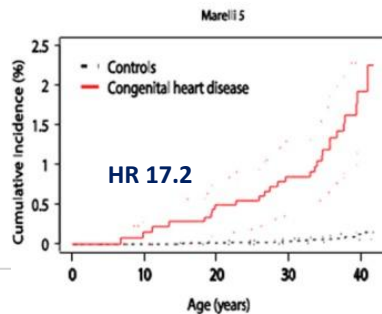
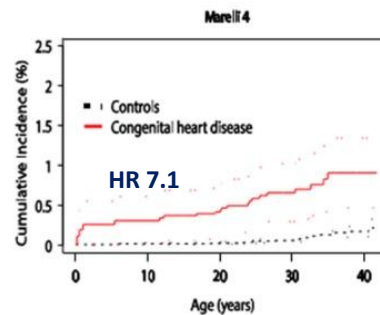
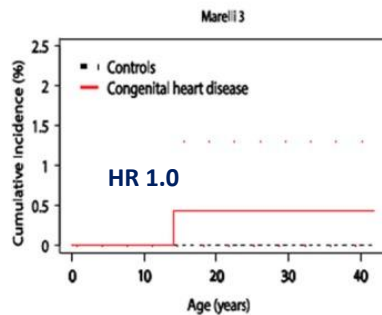
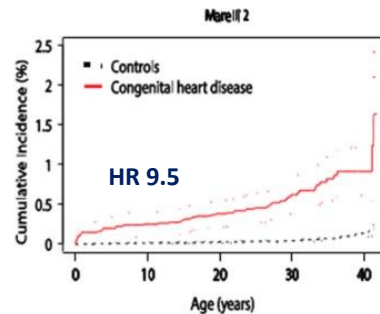
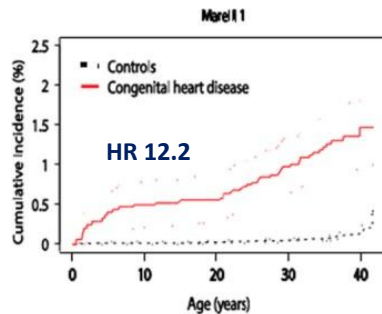
Anomalies pulmonary artery/valve, Congenital tricuspid disease, Congenital AS/AI, Congenital MS/MI, Anomalies great veins

Marelli 5

Other unspecified anomalies of the heart/aorta/circulation

Marelli et al. Circulation, 2007;115:163-172

CHD and Stroke Incidence by Marelli Class



Mandelenakis et al. J Am Heart Assoc 2016 Feb; 5(2): e003071

CHD and Stroke Incidence by Defect

CHD Diagnosis	Ischemic Stroke in CHD Patients/Total CHD Patients	Ischemic Stroke in Controls/Tot al Controls	HR (95% CI)	P Value
Total CHD	140/25 985	137/259750	10.76 (8.49–13.63)	<0.001
Atrial septal defect or patent foramen ovale	3/879	3/8790	10.00 (2.02–49.55)	0.004
Ventricular septal defect	5/2924	20/29 215	2.50 (0.94–6.65)	0.068
Tetralogy of Fallot	2/699	9/6687	2.20 (0.47–10.16)	0.315
Atrioventricular septal defect	0/162	0/1619	—	—
Common arterial trunk	1/200	4/2000	3.33 (0.35–32.05)	0.297
Ebstein's anomaly	0/108	0/1079	—	—
Transposition of great vesselsc	1/238	2/2379	4.85 (0.14–11.87)	0.997
Double inlet ventricle	5/1326	11/13 258	4.49 (1.56–12.93)	<0.001
Patent ductus arteriosus	1/2377	11/23 766	0.93 (0.17–7.23)	0.947
Hypoplastic left heart syndrome	0/54	0/540	—	—
Coarctation of aorta	9/1823	6/18 204	12.86 (4.79–34.56)	<0.001

Mandalenakis Z et al.
JAH 2016;5:e003071



ESC
Council
Stroke

CHD and Personalized Stroke Risk



Hauptdiagnose:

Q27.8

Aortopulmonale Kollateralen (MAPCA) bds.

geb.:

30.12.2011

Nebendiagnosen:

Q20.8

Funktionell univentrikuläres Herz bei Mitralatresie, Rechter Doppelausstromventrikel (DORV), Aortenisthmusstenose (ISTA), Malposition der grossen Gefässe (MGA)

Z95.88

Z.n. PDA-Ligatur und -Resektion, ISTA-Resektion, Rekonstruktion des Aortenbogens (End-zu-Seit-Anastomose), Verschluss der Pulmonalarterie unterhalb der Bifurkation und Anlage eines mBT-Shunts (3,5 mm GoreTex) rechts am 06.01.2012

-

Z.n. sekundärem Thoraxverschluss am 08.01.2012

-

Z.n. Re-OP mit Resektion einer hochgradigen Subaortenstenose und Erweiterung (Rinderperikardpatch) des rechtsventrikulären Ausflusstraktes am 18.01.2012

I44.2

Post-OP AV-Block III°

Z95.0

Z.n. Implantation eines VVI-Schrittmachers (St. Jude Medical Micron II SR+, Ser-Nr. 4125-33846), Anlage epikardialer Ventrikel Elektroden und sekundärer Thoraxverschluss am 20.01.2012

Z92.8

Z.n. Herzkatheteruntersuchung mit Ballonangioplastie der linken Pulmonalarterie und des Aortenisthmus am 23.05.2012

Z92.4

Z.n. Resektion des mBT Shunts, Anlage einer bidirektionalen Glennanastomose und Wechsel des Schrittmacheraggregates (VVI->DDD) am 28.06.2012

-

Z.n. Herzkatheteruntersuchung am 16.02.2015

I80.88

Verschluss der V. jugularis interna rechts (Dg. 02/2015)

-

Z.n. Abbruch der geplanten Komplettierung der univentrikulären Palliation am 28.05.2015

-

Z.n. Herzkatheteruntersuchung mit Stentimplantation im Bereich der linken Pulmonalarterie, Verschluss der großen venovenösen Kollaterale links (Amplatzer Vascular Plug, 12mm, 2 Stck.) am 24.09.2015

E83.58

Nephrocalcinose

-

Strabismus convergens

-

aktuell:

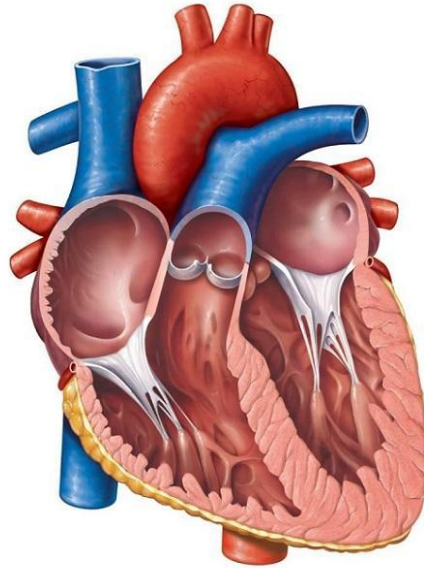
-

Herzkatheteruntersuchung mit Coilembolisation von aortopulmonalen Kollateralen bds. am 22.05.2017

HD with Thromboembolic Potential

Valvular HD

Regurgitation
Stenosis



Cardiomyopathy

Dilatative
Hyperthrophic

Arrhythmogenic Disease

HD with Thromboembolic Potential

n total = 402

Cardiac Source of Embolism	Total Patients	
<u>Arrhythmia without</u> structural heart disease	89 (22.1%)	
Atrial fibrillation		88
Atrial flutter		1
<u>Isolated structural</u> heart disease	81 (20.1%)	
Ischaemic heart disease		35
Acute myocardial infarction		3 (thrombus 2)
Left ventricular aneurysm		7 (thrombus 3)
Left ventricular ejection fraction < 40%		12
Akinesia/dyskinesia ≥ two segments		13 (thrombus 3)
Dilated cardiomyopathy		24 (thrombus 5)
Mitral annular calcification		14*
Cardiac tumour		4
Aortic prosthetic valve		4
Endocarditis		2
Atrial septal aneurysm with patent foramen ovale		2
Rheumatic mitral valve disease		1
Mitral valve prolapse		1
Calcified aortic stenosis		1
Moderate mitral valve regurgitation		1

Arboix A, Alio J. Curr Cardiol Rev 2010;6:150-161

HD with Thromboembolic Potential

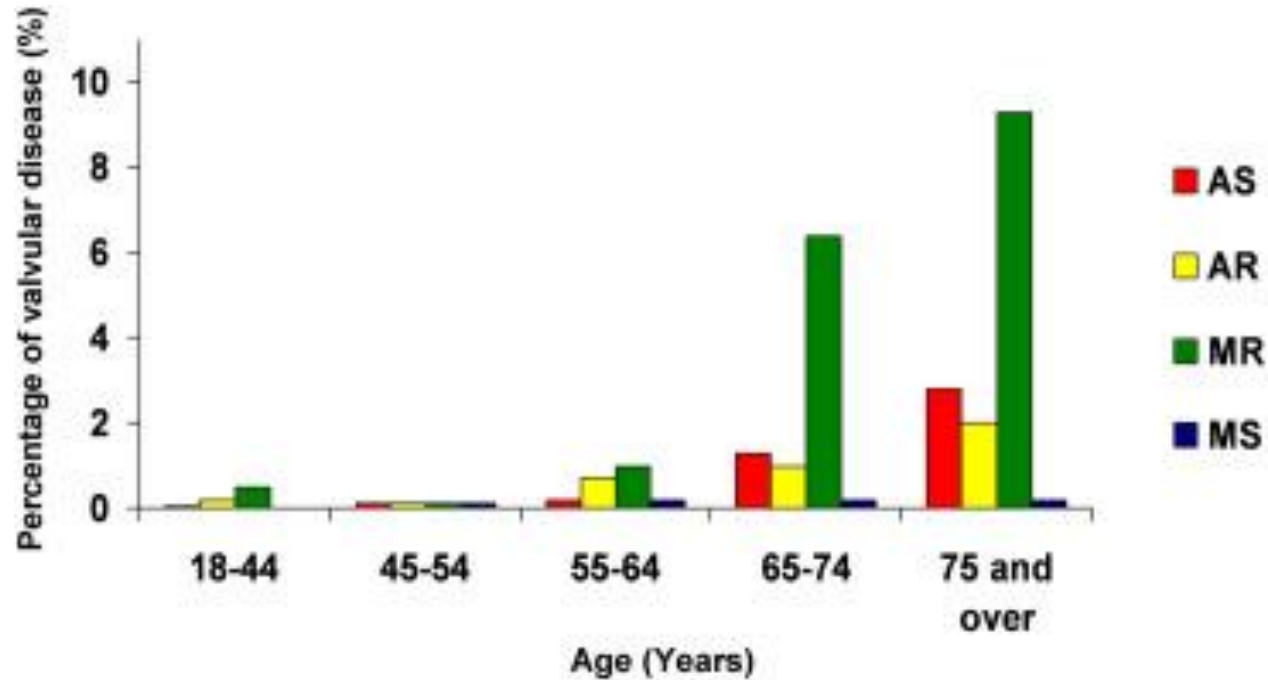
Structural heart disease and atrial arrhythmia	232 (57.7%)	
Atrial fibrillation		230
Atrial flutter		2
Hypertrophic hypertensive cardiac disease		120
Rheumatic mitral valve disease		49 (thrombus 7)
Ischaemic heart disease		19
Left ventricular aneurysm		3 (thrombus 1)
Left ventricular ejection fraction < 40%		9
Akinesia/dyskinesia ≥ two segments		7 (thrombus 1)
Mitral annular calcification		26 [†]
Dilated cardiomyopathy		13 (thrombus 2)
Mitral valve prolapse		4
Mitral prosthetic valve		3 (thrombus 2)
Lipomatous hypertrophy of the atrial septum		2
Hypertrophic cardiomyopathy		2
Atrial septal aneurysm and patent foramen ovale		2
Severe mitral regurgitation		2

HD with Thromboembolic Potential

Cardiac Source of Embolism	Total Patients	
Atrial fibrillation	318 (79.1%)	
Lone atrial fibrillation		88
Associated with structural cardiac disease		230
Hypertensive left ventricular hypertrophy	120 (29.8%)	
Associated with atrial fibrillation		118
Associated with atrial flutter		2
Left ventricular systolic dysfunction	91 (22.6%)	
Sinus rhythm		59
Atrial fibrillation		32
Rheumatic mitral valve disease	50 (12.4%)	
Mitral annular calcification	40 (9.9%)	
Mitral valve prolapse	5 (1.2%)	
Atrial septal aneurysm with patent foramen ovale	4 (1%)	
Degenerative heart valve disease	4 (1%)	

Arboix A, Alio J. Curr Cardiol Rev 2010;6:150-161

Valvular HD – Incidence (EU)



Iung B, Vahanian A. Can J Cardiol 2014 Sep;30(9):962-70

Valvular HD and Stroke Risk

VHD plus Other Stroke Risk Factor

Patients n =729

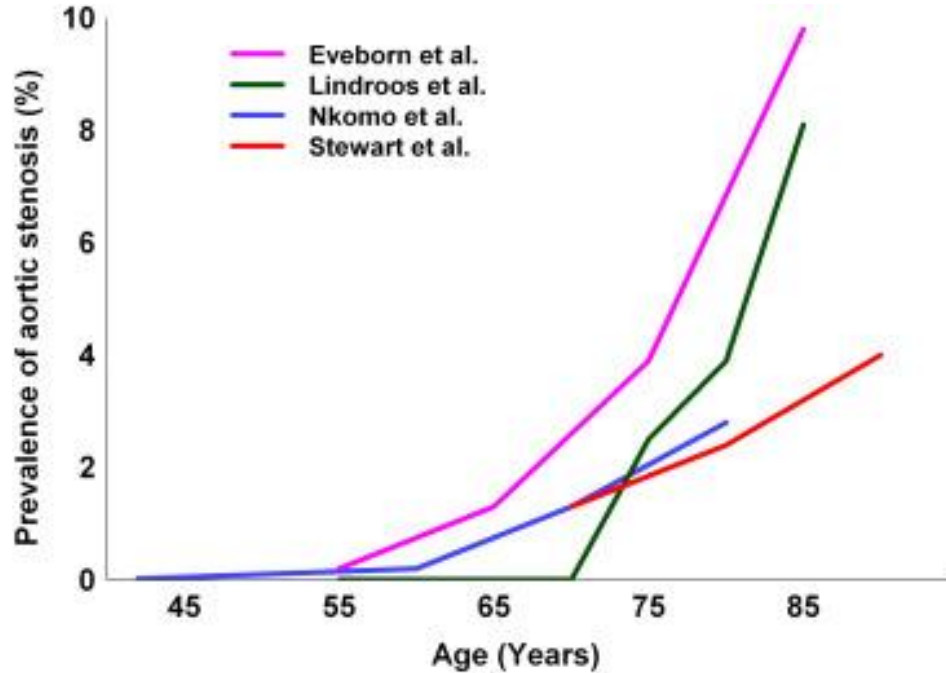
	No. %
Hypertension	509 (69.8)
Congestive heart failure	335 (46.0)
Intermittent atrial fibrillation	179 (24.6)
Persistent atrial fibrillation	145 (19.9)
Angina pectoris	280 (38.4)
Myocardial infarction	178 (24.4)

Time After Diagnosis VHD

CVE

	<u>%</u>	<u>95% CI</u>
6 mo	2.9	1.6–4.1
1 y	4.9	3.3–6.6
2 y	8.0	5.9–10.1
3 y	11.2	8.7–13.8
5 y	17.5	13.9–21.3
7 y	23.1	18.2–28.7

AS - Prevalence



AS – Stroke Risk Factors

Table 3. Hazard Ratios for First-Ever Ischemic Stroke in Nonoperated Patients During 4.3 Years of Follow-Up

Nonoperated				
Characteristic	HR Univariate (95% CI)	P Value	HR Adjusted (95% CI)	P Value
CHA ₂ DS ₂ -VASc (per 1 increase)	1.3 (1.0–1.8)	0.099	...	...
Baseline hypertension	1.1 (0.5–2.3)	0.835	...	...
Age 65–74 y	1.4 (0.4–4.3)	0.584	...	...
Age ≥75 y	4.0 (1.4–11.1)	0.008	4.5 (1.6–12.6)	0.004*
Female sex	0.8 (0.6–2.8)	0.610	...	...
Clinical covariates				
Body mass index (per 1 kg/m ²)	1.1 (1.0–1.2)	0.027	1.1 (1.0–1.2)	0.009*
Diastolic BP (per 10 mm Hg)	1.3 (0.9–1.9)	0.116	...	...
Atrial fibrillation*	2.7 (0.9–7.8)	0.069	...	...
Simvastatin/ezetimibe vs placebo	0.7 (0.3–1.6)	0.436	...	...
Medicine				
Diuretics	1.8 (0.8–3.9)	0.148	...	...
β-Blockade	1.5 (0.7–3.3)	0.287	...	...
Echocardiographic parameters				
LA systolic volume (per doubling)	2.2 (1.0–4.9)	0.046	1.8 (0.8–4.2)	0.152†
LA diastolic volume (per doubling)	1.8 (1.0–3.3)	0.038	1.6 (0.9–2.8)	0.133†
LV ejection fraction (per 10% increase)	1.1 (0.7–1.8)	0.737	...	...
Aortic valve area index (per 1 cm ² /m ²)	0.1 (0.01–1.2)	0.066	...	...

AS/AVR – Stroke Risk Factors

Table 4. Hazard Ratios for First-Ever Stroke in Patients After AVR: During 4.3 Years of Follow-Up

Characteristic	Post-AVR			
	HR Univariate Stroke (95% CI)	P Value	HR Univariate Stroke/Death (95% CI)*	P Value
CHA ₂ DS ₂ -VASC (per 1 increase)	1.5 (1.0–2.2)	0.078	1.4 (1.1–1.9)	0.014
Baseline hypertension	2.5 (0.9–7.1)	0.096	1.9 (1.0–3.7)	0.050
Age 65–74 y	11.6 (1.5–90.0)	0.019	2.2 (0.9–5.5)	0.076
Age ≥75 y	7.9 (0.9–70.4)	0.065	4.8 (2.0–11.6)	<0.001
Female sex	0.8 (0.3–2.2)	0.645	1.9 (0.9–4.0)	0.100
Clinical covariates				
Body mass index (per 1 kg/m ²)	1.1 (1.0–1.2)	0.277	1.1 (1.0–1.1)	0.169
Diastolic BP (per 10 mm Hg)	1.1 (1.0–1.1)	0.158	1.0 (1.0–1.0)	0.707
Atrial fibrillation	1.8 (0.4–8.1)	0.422	2.1 (0.8–5.4)	0.126
Simvastatin/ezetimibe vs placebo	0.6 (0.2–1.7)	0.326	0.5 (0.2–0.9)	0.030
Medicine				
Diuretics	1.8 (0.6–5.6)	0.310	1.3 (0.7–2.6)	0.432
β-Blockade	0.2 (0.1–1.3)	0.089	1.2 (0.6–2.4)	0.618
Echocardiographic parameters				
LA systolic volume (per doubling)	1.5 (0.6–4.3)	0.411	1.8 (1.0–3.5)	0.067
LA diastolic volume (per doubling)	1.1 (0.6–2.3)	0.701	1.3 (0.8–2.0)	0.278
LV ejection fraction (per 10% increase)	1.1 (1.0–1.2)	0.031	1.0 (1.0–1.0)	0.606
Aortic valve area index (per 1 cm ² /m ²)	2.1 (0.1–35.3)	0.601	1.3 (0.2–9.4)	0.774

Greve AM et al. Stroke 2014;45:1939-1946

Aortic VHD and Stroke

BASE-LINE CHARACTERISTICS OF THE SUBJECTS WITH NORMAL AORTIC VALVES, THOSE WITH SCLEROTIC VALVES, AND THOSE WITH STENOTIC VALVES.

CHARACTERISTIC	NORMAL AORTIC VALVES (N=3919)	AORTIC SCLEROSIS (N=1610)	AORTIC STENOSIS (N=92)	P VALUE FOR TREND
Mean $\pm$ SD age — yr	72.1 $\pm$ 5.2	74.7 $\pm$ 6.0	75.8 $\pm$ 6.1	<0.001
Sex — no. (%)				
Female	2372 (60.5)	818 (50.8)	45 (48.9)	<0.001
Male	1547 (39.5)	792 (49.2)	47 (51.1)	
Current smoking — no. (%)	452 (11.6)	191 (11.9)	13 (14.1)	0.43
History of hypertension — no. (%)	1724 (44.0)	833 (51.7)	47 (51.1)	<0.001
History of diabetes — no. (%)	446 (11.4)	211 (13.1)	6 (6.5)	0.90
Coronary heart disease — no. (%)	673 (17.2)	383 (23.8)	22 (23.9)	<0.001
Renal insufficiency — no. (%) [*]	182 (4.8)	123 (8.1)	16 (17.8)	<0.001
Impaired ability to perform activities of daily living — no. (%) [†]	1039 (26.6)	526 (32.8)	28 (30.8)	<0.001

^{*}Data were missing for 131 patients with normal aortic valves, 88 patients with aortic sclerosis, and 2 patients with aortic stenosis.

[†]Data were missing for 7 patients with normal aortic valves, 4 patients with aortic sclerosis, and 1 patient with aortic stenosis.

Age - >65y, n total – 5621 both sexes

. EVENT RATES IN THE THREE GROUPS.

EVENT	NORMAL AORTIC VALVES (N=3919)	AORTIC SCLEROSIS (N=1610)	AORTIC STENOSIS (N=92)	P VALUE FOR TREND
	number (percent)			
Death from any cause	583 (14.9)	353 (21.9)*	38 (41.3)*	<0.001
Death from cardiovascular causes	238 (6.1)	162 (10.1)*	18 (19.6)*	<0.001
Myocardial infarction [†]	217 (6.0)	123 (8.6) [‡]	9 (11.3) [‡]	<0.001
Angina [†]	358 (11.0)	160 (13.0)	17 (24.3)*	0.001
Congestive heart failure [†]	337 (8.9)	192 (12.6)*	21 (24.7)*	<0.001
Stroke [†]	238 (6.3)	122 (8.0) [§]	10 (11.6) [§]	0.003

*P<0.001 for the comparison with the group with normal aortic valves.

[†]The rates were calculated for subjects at risk for new events.

[‡]P<0.01 for the comparison with the group with normal aortic valves.

[§]P=0.02 for the comparison with the group with normal aortic valves.

Mitral Stenosis and Stroke

Age distribution in 82 patients with mitral stenosis

Age(yr)	Cerebral embolism		Total	AF*
	Present	Absent		
10~19	0	3	3	0
20~29	1	7	8	4
30~39	0	15	15	4
40~49	5	19	24	16
50~59	5	12	17	13
60~69	5	3	8	8
70~79	3	3	6	5
80~89	0	1	1	1
Total	19	63	82	51

n = 23%

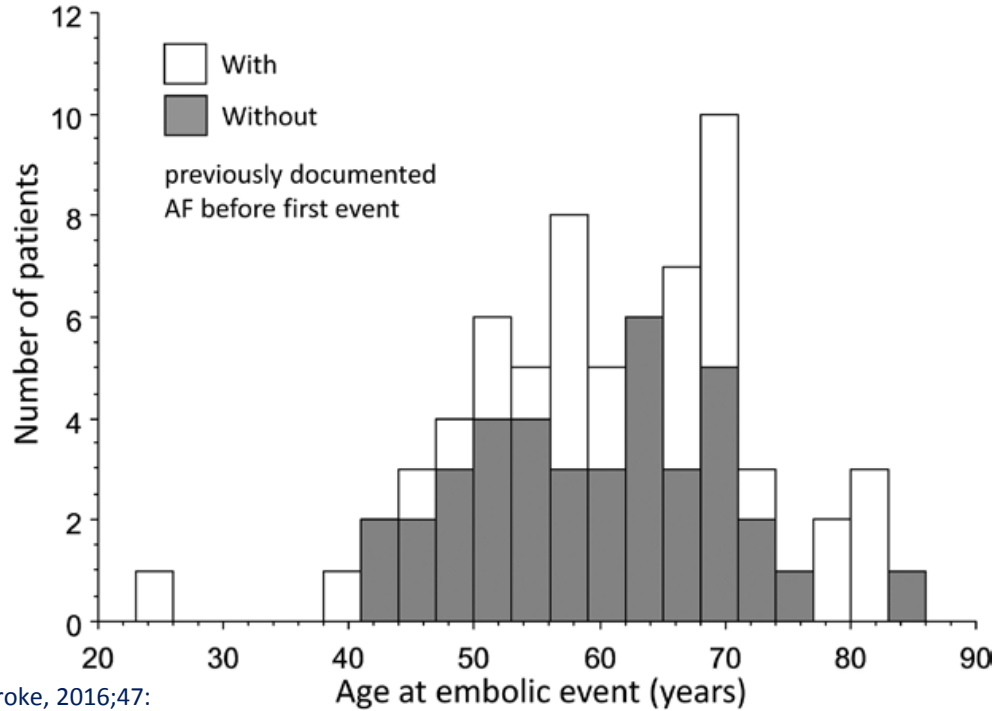
AFib = 62%

Correlation between atrial fibrillation and cerebral embolism in mitral stenosis

	Cerebral embolism		Total
	Present	Absent	
AF*	16(34.0)#	31(66.0)	47(100)
NSR**	3(8.6)#	32(91.4)	35(100)
Total	19(23.2)	63(76.8)	82(100)

AFib = 84%

HCMP and Stroke



Haruki S et al. Stroke, 2016;47:

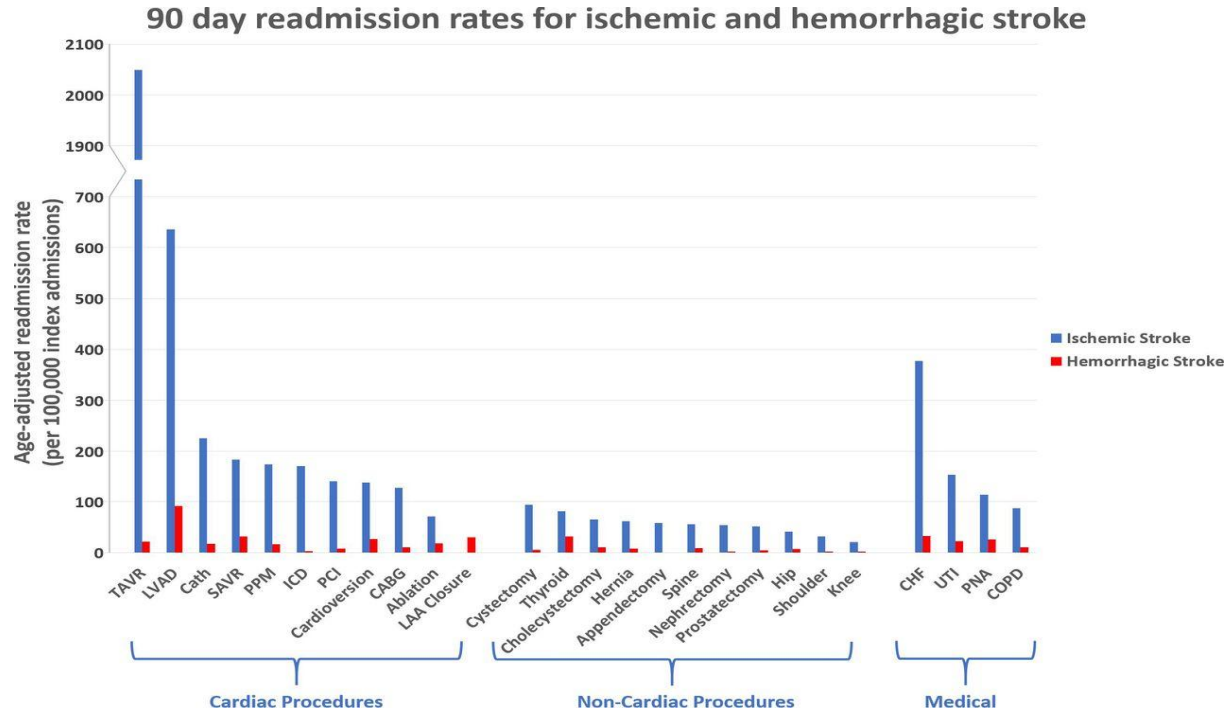
HCMP and Stroke

Patient Characteristics of Studied Patients With Hypertrophic Cardiomyopathy Without Documented Atrial Fibrillation According to the Presence or Absence of Embolic Events

Characteristic	Patients With Embolic Events (n=39)	Patients Without Embolic Events (n=392)	P Value
Female sex	23 (59.0)	145 (37.0)	0.012
Age at diagnosis, y	55.8±11.2	49.5±16.6	0.022
Family history of sudden death	5 (12.8)	44 (11.2)	0.791
Left ventricular outflow tract obstruction	12 (30.8)	84 (21.4)	0.256
Left ventricular midcavitary obstruction	6 (15.4)	39 (9.9)	0.276
Apical hypertrophy	4 (10.3)	133 (33.9)	0.004
Apical aneurysm	1 (2.6)	20 (5.1)	0.709
Left atrial dimension	41.6±7.5	36.5±6.8	<0.001
Maximum left ventricular wall thickness	18.9±3.6	19.9±4.7	0.215
Unexplained syncope	9 (23.1)	48 (12.2)	0.098
Nonsustained ventricular tachycardia	14 (35.9)	129 (32.9)	0.841
Follow-up duration, y	10.4±8.7	10.2±7.3	0.859

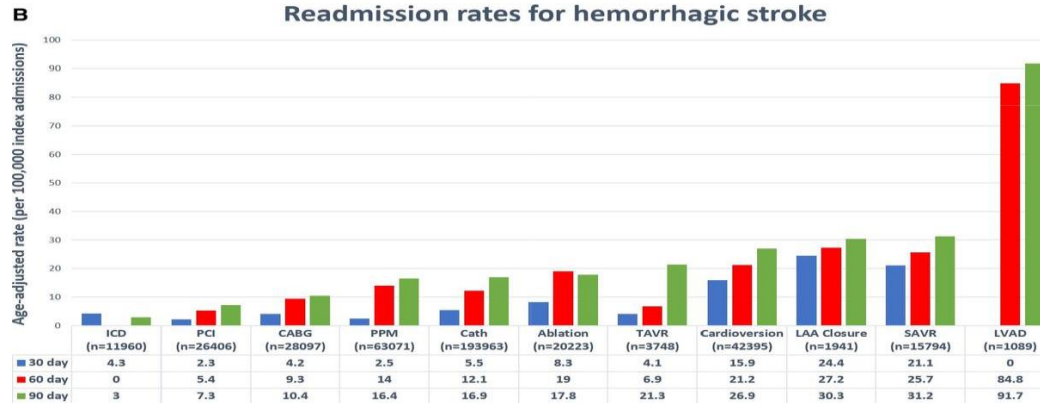
Results are given as the mean±SD or number (%).

Assorted Interventions and Stroke



Stein L et al. J Am Heart Assoc 2017;6:e006900

Cardiovascular Intervention and Stroke



Stein L et al. J Am Heart Assoc 2017;6:e006900

CAS and Stroke

Trial	Overall randomized patients, n	Any stroke/death, %	Any stroke, %	Disabling/major stroke, %	Non-disabling/minor stroke, %
ACT-I	1,453	2.9	2.8	0.5	2.4
CAVATAS	504	10.0	7.2	3.6	N/R
CREST	2,502	4.4	4.1	0.9	3.2
EVA-3S	527	9.4	9.1	2.6	6.0
ICSS	1,713	8.4	7.6	2.0	4.6
SAPPHIRE	334	N/R	3.6	1.2	3.0
SPACE	1,200	7.4	7.2	4.1	N/R
SPACE 2	513	2.5	N/R	N/R	N/R

Cassese et al. in Lanzer P, Springer, 2018

TAVR/SAVR and Stroke

Stroke at 30 days (no. of patients (%))									
	Overall Stroke			Major Disabling Stroke			Minor Non-Disabling Stroke		
	TAVR	SAVR	p	TAVR	SAVR	p	TAVR	SAVR	p
PARTNER 1B (n=358)	12 (6.7)	-	-	9 (5.0)	-	-	3 (1.7)	-	-
PARTNER 1A (n=699)	19 (5.5)	8 (2.4)	0.04	13 (3.8)	7 (2.1)	0.20	3 (0.9)	1 (0.3)	0.34
PARTNER 2B (n=560)	25 (4.5)	-	-	17 (3.0)	-	-	6 (1.1)	-	-
PARTNER 2A (n=2032)	64 (6.4)	65 (6.5)	0.94	32 (3.2)	43 (4.3)	0.20	23 (2.3)	18 (1.8)	0.43
US CoreValve (n=747)	19 (4.9)	22 (6.2)	0.46	15 (3.9)	11 (3.1)	0.55	4 (1.0)	12 (3.4)	0.03
NOTION (n=280)	4 (2.8)	4 (3.0)	0.94	1.4	3.0	0.37	2 (1.4)	0 (0)	0.17
SAPIEN 3i (n=1077)	29 (2.7)	57 (6.1)	-	11 (1.0)	41 (4.4)	-	18 (1.7)	16 (1.7)	-
SAPIEN 3HR (n=583)	8 (1.4)	-	-	5 (0.9)	-	-	-	-	-

Endris, Tuzcu in Lanzer P, Springer, 2018

Conclusions

CHD is a major lifelong independent stroke predictor

HD with thromboembolic potential is variable dependent stroke predictor ; Atrial fibrillation is an overriding major risk factor

Stroke is a relevant complication of some cardiovascular interventions;

Prioritize prevention and on-site management!

Stroke management is the next frontier in cardiology