

Epidemiology of valvular heart disease in a Swedish nationwide hospital-based register study

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Supplementary materials

Table of contents

eTable 1. Definitions for valvular heart diseases	3
eTable 2. Definitions for comorbidities	5
eTable 3. Validation of aortic regurgitation cases from the Malmö Diet and Cancer Study	12
eTable 4. Validation of mitral stenosis cases from the Malmö Diet and Cancer Study	13
eTable 5. Validation of mitral regurgitation cases from the Malmö Diet and Cancer Study	14
eTable 6. Validation of tricuspid regurgitation cases from the Malmö Diet and Cancer Study	15
eTable 7a-b. Age and sex-adjusted odds ratios for comorbidities in VHD diagnoses	16
eTable 8. Individual components of non-valvular congenital heart disease	18
eTable 9. Individual components of autoimmune disorders	19
eTable 10. Individual components of heritable connective tissue disorders	20
eTable 11. Individual components of prolapse/hernia.	21
eTable 12. Individual components of non-valvular cardiothoracic surgical procedures	22
eFigure 1a-b. Severity rating and etiologies of validated aortic regurgitation cases	23
eFigure 2a-b. Severity rating and etiologies of validated mitral stenosis cases	24
eFigure 3a-b. Severity rating and etiologies of validated mitral regurgitation cases	25
eFigure 4a-b. Severity rating and etiologies of validated tricuspid regurgitation cases	26

eTable 1. Definitions for valvular heart diseases

Aortic stenosis

I35.0	Aortic stenosis
I35.2	Aortic stenosis with insufficiency
I06.0	Rheumatic aortic stenosis
I06.2	Rheumatic aortic stenosis with insufficiency
Q23.0	Congenital stenosis of aortic valve

Aortic regurgitation

I35.1	Aortic insufficiency
I06.1	Rheumatic aortic insufficiency
Q23.1	Congenital insufficiency of aortic valve

Mitral stenosis

I34.2	Nonrheumatic mitral stenosis
I05.0	Mitral stenosis
I05.2	Mitral stenosis with insufficiency
Q23.2	Congenital mitral stenosis

Mitral regurgitation

I34.0	Mitral insufficiency
I05.1	Rheumatic mitral insufficiency
Q23.3	Congenital mitral insufficiency

Pulmonary stenosis

I37.0	Pulmonary valve stenosis
I37.2	Pulmonary valve stenosis with insufficiency
Q22.0	Pulmonary valve atresia
Q22.1	Congenital pulmonary valve stenosis
Q24.3	Pulmonary infundibular stenosis

Pulmonary regurgitation

I37.1	Pulmonary valve insufficiency
Q22.2	Congenital pulmonary valve insufficiency

Tricuspid stenosis

I36.0	Nonrheumatic tricuspid stenosis
I36.2	Nonrheumatic tricuspid stenosis with insufficiency
I07.0	Tricuspid stenosis

I07.2 Tricuspid stenosis with insufficiency
Q22.4 Congenital tricuspid stenosis

Tricuspid regurgitation

I36.1 Nonrheumatic tricuspid insufficiency
I07.1 Tricuspid insufficiency

eTable 2. Definitions for comorbidities

Non-valvular congenital heart disease

ICD-10

Q20	Congenital malformations of cardiac chambers and connections
Q21	Congenital malformations of cardiac septa
Q22.5	Ebstein anomaly
Q22.6	Hypoplastic right heart syndrome
Q23.4	Hypoplastic left heart syndrome
Q24	Other congenital malformations of heart
Q25	Congenital malformations of great arteries
Q26.1	Persistent left superior vena cava
Q26.2	Total anomalous pulmonary venous connection
Q26.3	Partial anomalous pulmonary venous connection
Q26.4	Anomalous pulmonary venous connection, unspecified

ICD-9

745	Bulbus cordis anomalies and anomalies of cardiac septal closure
746	Other congenital anomalies of heart
747.1(A)	Coarctation of aorta
747.2(B)	Other congenital anomalies of aorta
747.3(C)	Congenital anomalies of pulmonary artery
747.4(D)	Congenital anomalies of great veins

ICD-8

746	Congenital anomalies of heart
747.0 (09)	Patent ductus arteriosus
747.1 (19)	Coarctation of aorta
747.2 (24, 29)	Tetralogy of Fallot
747.3 (34, 39)	Stenosis or atresia of pulmonary artery

Rheumatic fever

ICD-10

I00-I02	Acute rheumatic fever
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ICD-9

390	Rheumatic fever without mention of heart involvement
391	Rheumatic fever with heart involvement

ICD-8

390	Rheumatic fever without mention of heart involvement
391	Rheumatic fever with heart involvement

Endocarditis

I33	Acute and subacute endocarditis
I38	Endocarditis, valve unspecified
I39	Endocarditis and heart valve disorders in diseases classified elsewhere

Atherosclerotic vascular disease

I70	Atherosclerosis
I71.3	Abdominal aortic aneurysm, ruptured
I71.4	Abdominal aortic aneurysm, without mention of rupture
I71.8	Aortic aneurysm of unspecified site, ruptured
I71.9	Aortic aneurysm of unspecified site, without mention of rupture
I72	Other aneurysm and dissection
I73.9	Peripheral vascular disease, unspecified
I73.9B	Intermittent claudication
I73.9X	Peripheral vascular disease, unspecified
I74	Arterial embolism and thrombosis
I20	Angina pectoris
I21	Acute myocardial infarction
I22	Subsequent myocardial infarction
I24	Other acute ischaemic heart diseases
I25	Chronic ischaemic heart disease
I63.0	Cerebral infarction due to thrombosis of precerebral arteries
I63.2	Cerebral infarction due to unspecified occlusion or stenosis of precerebral arteries
I63.3	Cerebral infarction due to thrombosis of cerebral arteries
I63.5	Cerebral infarction due to unspecified occlusion or stenosis of cerebral arteries
I63.8	Other cerebral infarction
I63.9	Cerebral infarction, unspecified
I64.9	Stroke, not specified as haemorrhage or infarction
I65	Occlusion and stenosis of precerebral arteries, not resulting in cerebral infarction
I66	Occlusion and stenosis of cerebral arteries, not resulting in cerebral infarction
I67.2	Cerebral atherosclerosis
I67.9	Cerebrovascular disease, unspecified

Cancer

C00-C97	Malignant neoplasms
D00-D09	In situ neoplasms

Infections

A00-A09	Intestinal infectious diseases
A15-A19	Tuberculosis
A20-A28	Certain zoonotic bacterial diseases
A30-A49	Other bacterial diseases
A50-A64	Infections with a predominantly sexual mode of transmission
A65-A69	Other spirochaetal diseases
A70-A74	Other diseases caused by chlamydiae
A75-A79	Rickettsioses
A80-A89	Viral infections of the central nervous system
A90-A99	Arthropod-borne viral fevers and viral haemorrhagic fevers
B00-B09	Viral infections characterized by skin and mucous membrane lesions
B15-B19	Viral hepatitis
B20-B24	Human immunodeficiency virus [HIV] disease
B25-B34	Other viral diseases
B35-B49	Mycoses
B50-B64	Protozoal diseases
B65-B83	Helminthiases
B85-B89	Pediculosis, acariasis and other infestations
B90-B94	Sequelae of infectious and parasitic diseases
B95-B98	Bacterial, viral and other infectious agents
B99-B99	Other infectious diseases

Pericarditis

I30	Acute pericarditis
I32	Pericarditis in diseases classified elsewhere

Myocarditis

I40	Acute myocarditis
I41	Myocarditis in diseases classified elsewhere

Meningitis/encephalitis

G00	Bacterial meningitis, not elsewhere classified
G01	Meningitis in bacterial diseases classified elsewhere
G02	Meningitis in other infectious and parasitic diseases classified elsewhere
G03	Meningitis due to other and unspecified causes

G04	Encephalitis, myelitis and encephalomyelitis
G05	Encephalitis, myelitis and encephalomyelitis in diseases classified elsewhere
G06	Intracranial and intraspinal abscess and granuloma
G07	Intracranial and intraspinal abscess and granuloma in diseases classified elsewhere

Otitis media

H66	Suppurative and unspecified otitis media
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Tonsillitis, sinusitis and other upper airway infections

J00-J06	Acute upper respiratory infections
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Pneumonia and influenza

J09-J18	Influenza and pneumonia
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Bronchitis

J20-J22	Other acute lower respiratory infections
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Lung abscess, empyema

J85-J86	Suppurative and necrotic conditions of lower respiratory tract
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Dental infections

K02	Dental caries
K04	Diseases of pulp and periapical tissues
K05	Gingivitis and periodontal diseases

Skin infections

L00-L08	Infections of the skin and subcutaneous tissue
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Joint infections

M00	Pyogenic arthritis
M01	Direct infections of joint in infectious and parasitic diseases classified elsewhere

Skeletal infections

M86	Osteomyelitis
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Pyelonephritis, cystitis

N10	Acute tubulo-interstitial nephritis
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N11	Chronic tubulo-interstitial nephritis
N12	Tubulo-interstitial nephritis, not specified as acute or chronic
N30.0	Acute cystitis

Autoimmune disorders

E27.1, E27.2	Addison's disease
G12.2	Amyotrophic lateral sclerosis
M45, M08.1	Ankylosing spondylitis
D59.0	Autoimmune hemolytic anemia
M35.2	Behcet's disease
K90.0	Celiac disease
I02.9	Chorea minor
K50	Crohn's disease
E10	Diabetes mellitus type I
L93.0	Discoid lupus erythematosus
E05	Graves' disease
E00-E03, E06.3	Hashimoto's thyroiditis
D69.3	Immune thrombocytopenic purpura
L94.0	Localized scleroderma
K75.4	Lupoid hepatitis
G35	Multiple sclerosis
G70.0	Myasthenia gravis
D51.0	Pernicious anemia
M30.0	Polyarteritis nodosa
M31.5, M35.3	Polymyalgia rheumatica
M33	Polymyositis/dermatomyositis
K74.3	Primary biliary cirrhosis
L40	Psoriasis
M02.3	Reiter's disease
M05-06, M08.0, M08.2	Rheumatoid arthritis
D86	Sarcoidosis
M35.0	Sjögren's syndrome
M32	Systemic lupus erythematosus
M34	Systemic sclerosis
K51	Ulcerative colitis
M31.3	Wegener's granulomatosis

Heritable connective tissue disorders

Q79.6	Ehlers-Danlos syndrome
Q87.4	Marfan syndrome

Q78.0 Osteogenesis imperfecta

Abdominal hernia and prolapse

K40 Inguinal hernia
K41 Femoral hernia
K42 Umbilical hernia

Diaphragmatic hernia

Q79.0 Congenital diaphragmatic hernia
Q79.1 Other congenital malformations of diaphragm
Q40.1 Congenital hiatus hernia
K44 Diaphragmatic hernia

Pelvic organ prolapse

N81 Female genital prolapse
N83.4 Prolapse and hernia of ovary and fallopian tube
K62.2 Anal prolapse
K62.3 Rectal prolapse
N36.3 Prolapsed urethral mucosa

Carcinoid

E34.0 Carcinoid syndrome

Pulmonary hypertension

I27.0 Primary pulmonary hypertension
I27.2 Other secondary pulmonary hypertension

Ascending aortic aneurysm or dissection

I71.0 Dissection of aorta
I71.1 Thoracic aortic aneurysm, ruptured
I71.2 Thoracic aortic aneurysm, without mention of rupture
I71.5 Thoracoabdominal aortic aneurysm, ruptured
I71.6 Thoracoabdominal aortic aneurysm, without mention of rupture

Atrial fibrillation

I48 Atrial fibrillation and flutter

Heart failure

I50 Heart failure
I11.0 Hypertensive heart disease with (congestive) heart failure

- I13.0 Hypertensive heart and renal disease with (congestive) heart failure
I13.2 Hypertensive heart and renal disease with both (congestive) heart failure
and renal failure

Non-valvular thoracic surgery

KKÅ97 classification

- FA Surgical procedure involving the intrathoracic great veins
FB Surgical procedure involving the pulmonary artery and its branches
FC Surgical procedure involving the thoracic aorta
FD Surgical procedure involving anomalies/defects of the thoracic aorta
FE Surgical procedure involving the pericardium
FF Surgical procedure involving the atrium, atrial septum and pulmonary
veins
FH Surgical procedure involving the septum of the ventricles (except FHE)
FJ Surgical procedure involving the right chamber and the pulmonary valve
(except FJD, FJE, FJF, FJW)
FL Surgical procedure involving the left chamber
FN Surgical procedure involving coronary arteries
FP Surgical procedure for arrhythmias and conduction disorders
FQ Surgical procedure involving heart and lung transplantation
FX Procedures related to extracorporeal or assisted circulation
FW Reoperations on the heart and large intrathoracic vessels

eTable 3. Validation of aortic regurgitation cases from the Malmö Diet and Cancer Study

Valid cases no./total (%) [95% CI]	93/99 (93.9) [88.9-99.0]
Age at diagnosis, median (IQR)	74 (54-88)
Female, no. (%)	41 (44.1)
≥ Moderate severity, no. (%)	51 (54.8)
<i>Diagnostic modality</i>	
TTE, no. (%)	78 (83.9)
TOE, no. (%)	13 (14.0)
MRI, no. (%)	2 (2.2)
Left ventricular dysfunction, no. (%)	30 (32.3)
Concomitant other valve dysfunction, no. (%)	32 (34.4)
Acute presentation, no. (%)	7 (7.5)
Chronic presentation, no. (%)	83 (89.2)
Aortic aneurysm/root dilatation, no. (%)	30 (32.3)
Aortic dissection, no. (%)	4 (4.3)
Combined aortic defect, no. (%)	11 (11.8)
Bicuspid aortic valve, no. (%)	3 (3.2)

Validity of randomly selected aortic regurgitation cases (100 from a total of 279) from the Malmö Diet and Cancer Study with 95% confidence intervals (CI). Patient characteristics from review of individual patient medical records. One case had unavailable medical records. IQR, interquartile range. MRI, magnetic resonance imaging. TOE, transoesophageal echocardiography. TTE, transthoracic echocardiography.

eTable 4. Validation of mitral stenosis cases from the Malmö Diet and Cancer Study

Valid cases no./total (%) [95% CI]	21/24 (87.0) [70.8-100]
Age at diagnosis, median (IQR)	69 (64-76)
Female, no. (%)	19 (90.5)
≥ Moderate severity, no. (%)	14 (66.7)
<i>Diagnostic modality</i>	
TTE, no. (%)	15 (71.4)
TOE, no. (%)	5 (23.8)
MRI, no. (%)	0 (0.0)
Left ventricular dysfunction, no. (%)	5 (23.8)
Valve area, mean (±SD)	1.7 (±0.7)
Pulmonary artery pressure, mean (±SD)	53 (±15)
Right ventricular dysfunction, no. (%)	2 (9.5)
Concomitant other valve dysfunction, no. (%)	14 (66.7)
Acute presentation, no. (%)	1 (4.8)
Chronic presentation, no. (%)	19 (90.5)
Mitral calcification, no. (%)	13 (61.9)
Combined mitral defect, no. (%)	11 (52.4)
Past commissurotomy, no. (%)	2 (9.5)
Concomitant atrial fibrillation, no. (%)	6 (28.6)

Validity of all mitral stenosis cases from the Malmö Diet and Cancer Study with 95% confidence intervals (CI). Patient characteristics from review of individual patient medical records. IQR, interquartile range. MRI, magnetic resonance imaging. SD, standard deviation. TOE, transoesophageal echocardiography. TTE, transthoracic echocardiography.

eTable 5. Validation of mitral regurgitation cases from the Malmö Diet and Cancer Study

Valid cases no./total (%) [95% CI]	92/100 (92.0) [86.0-97.0]
Age at diagnosis, median (IQR)	75 (68-79)
Female, no. (%)	55 (59.8)
≥ Moderate severity, no. (%)	70 (76.1)
<i>Diagnostic modality</i>	
TTE, no. (%)	68 (73.9)
TOE, no. (%)	21 (22.8)
MRI, no. (%)	1 (1.1)
Left ventricular dysfunction, no. (%)	27 (29.3)
Concomitant other valve dysfunction, no. (%)	42 (45.7)
Acute presentation, no. (%)	12 (13.0)
Chronic presentation, no. (%)	78 (84.8)
Primary (organic), no. (%)	67 (72.8)
Secondary (functional), no. (%)	19 (20.7)
Concomitant atrial fibrillation, no. (%)	40 (43.5)

Validity of randomly selected mitral regurgitation cases (100 from a total of 369) from the Malmö Diet and Cancer Study with 95% confidence intervals (CI). Patient characteristics from review of individual patient medical records. IQR, interquartile range. MRI, magnetic resonance imaging. TOE, transoesophageal echocardiography. TTE, transthoracic echocardiography.

eTable 6. Validation of tricuspid regurgitation cases from the Malmö Diet and Cancer Study

Valid cases no./total (%) [95% CI]	66/68 (97.1) [92.6-100]
Age at diagnosis, median (IQR)	76 (70-82)
Female, no. (%)	20 (30.3)
≥ Moderate severity, no. (%)	57 (86.4)
<i>Diagnostic modality</i>	
TTE, no. (%)	57 (86.4)
TOE, no. (%)	8 (12.1)
MRI, no. (%)	0 (0.0)
Left ventricular dysfunction, no. (%)	27 (40.9)
Right ventricular dysfunction, no. (%)	31 (47.0)
Pulmonary artery pressure, mean (±SD)	48.0 (±18.6)
Concomitant other valve dysfunction, no. (%)	42 (63.6)
Acute presentation, no. (%)	3 (4.5)
Chronic presentation, no. (%)	63 (95.5)
Concomitant atrial fibrillation, no. (%)	29 (43.9)

Validity of all tricuspid regurgitation cases from the Malmö Diet and Cancer Study with 95% confidence intervals (CI). Patient characteristics from review of individual patient medical records. IQR, interquartile range. MRI, magnetic resonance imaging. SD, standard deviation. TOE, transoesophageal echocardiography. TTE, transthoracic echocardiography.

eTable 7a. Age and sex-adjusted odds ratios for comorbidities in left-sided VHD diagnoses

	AS			AR			MS			MR		
	OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI	
Non-valvular congenital heart disease	11.63	10.72	12.61	22.87	21.18	24.70	13.68	11.16	16.76	13.07	12.04	14.20
Rheumatic fever	1.23	0.86	1.75	2.28	1.44	3.62	3.54	1.35	9.30	1.83	1.19	2.81
Endocarditis	10.06	9.31	10.87	21.84	19.92	23.94	8.35	6.47	10.78	18.79	17.29	20.42
Atherosclerotic vascular disease	2.33	2.27	2.39	1.41	1.34	1.48	1.41	1.24	1.60	1.32	1.27	1.37
Cancer	1.12	1.09	1.15	1.08	1.03	1.14	0.93	0.81	1.07	1.18	1.14	1.23
Infections	1.17	1.14	1.20	1.22	1.17	1.27	1.51	1.36	1.67	1.10	1.07	1.14
Autoimmune disorders	1.52	1.48	1.56	1.29	1.23	1.36	1.51	1.34	1.70	1.19	1.14	1.24
Heritable connective tissue disorders	0.88	0.44	1.76	6.40	4.74	8.66	-			9.90	7.16	13.67
Herniation/Prolapse	1.26	1.21	1.30	1.53	1.44	1.63	1.13	0.95	1.35	1.58	1.50	1.66
Carcinoid	1.55	0.98	2.46	2.98	1.60	5.54	-			3.63	2.32	5.70
Pulmonary hypertension	1.34	1.10	1.63	0.84	0.57	1.22	3.62	2.43	5.39	2.31	1.91	2.79
Ascending aortic aneurysm or dissection	5.64	5.23	6.08	34.07	31.79	36.53	0.75	0.38	1.46	1.32	1.12	1.56
Atrial fibrillation	1.60	1.55	1.64	2.13	2.03	2.24	5.69	5.00	6.49	3.88	3.73	4.03
Heart failure	2.60	2.53	2.67	2.27	2.15	2.39	3.82	3.35	4.37	4.93	4.73	5.13
Non-valvular thoracic surgery	2.76	2.66	2.87	3.39	3.20	3.59	3.04	2.59	3.57	3.09	2.94	3.26

Adjusted for age and sex. Odds ratios are shown for cases with a VHD diagnosis compared to cases without a VHD diagnosis. AS, aortic stenosis. AR, aortic regurgitation. MS, mitral stenosis. MR, mitral regurgitation.

eTable 7b. Age and sex-adjusted odds ratios for comorbidities in left-sided VHD diagnoses

	PS			PR			TS			TR		
	OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI	
Non-valvular congenital heart disease	175.09	159.20	192.58	329.26	269.95	401.59	61.07	44.22	84.36	11.93	9.98	14.26
Rheumatic fever	1.19	0.15	9.27	-			4.20	0.51	34.59	0.75	0.17	3.31
Endocarditis	2.33	1.40	3.87	0.53	0.13	2.28	0.85	0.26	2.80	8.61	7.06	10.51
Atherosclerotic vascular disease	1.14	0.87	1.50	1.00	0.68	1.46	0.93	0.63	1.36	0.94	0.85	1.03
Cancer	1.48	1.14	1.92	0.97	0.62	1.49	0.86	0.55	1.34	1.26	1.14	1.39
Infections	1.38	1.26	1.51	1.26	1.05	1.52	2.03	1.56	2.63	1.18	1.08	1.28
Autoimmune disorders	1.16	0.97	1.39	1.37	1.01	1.86	1.11	0.77	1.60	1.18	1.07	1.30
Heritable connective tissue disorders	0.70	0.22	2.23	0.77	0.10	5.68	-			6.11	2.24	16.66
Herniation/Prolapse	1.15	0.91	1.45	1.31	0.89	1.93	1.44	0.92	2.26	1.47	1.30	1.67
Carcinoid	29.63	9.61	91.30	97.02	31.63	297.64	91.16	31.13	266.91	37.72	25.36	56.12
Pulmonary hypertension	1.23	0.66	2.32	0.97	0.29	3.26	2.56	0.98	6.66	9.22	7.40	11.48
Ascending aortic aneurysm or dissection	0.32	0.08	1.30	1.18	0.36	3.82	1.39	0.50	3.86	0.78	0.48	1.28
Atrial fibrillation	1.59	1.19	2.12	1.90	1.30	2.78	3.91	2.71	5.64	6.83	6.18	7.55
Heart failure	1.65	1.26	2.16	1.71	1.14	2.55	3.03	2.10	4.35	5.67	5.12	6.28
Non-valvular thoracic surgery	2.68	2.36	3.04	1.70	1.30	2.22	10.08	7.25	14.02	2.92	2.57	3.32

Adjusted for age and sex. Odds ratios are shown for cases with a VHD diagnosis compared to cases without a VHD diagnosis. PS, pulmonary stenosis. PR, pulmonary regurgitation. TS, tricuspid stenosis. TR, tricuspid regurgitation.

eTable 8. Individual components of non-valvular congenital heart disease

	Population		AS		AR		MS		MR		PS		PR		TS		TR	
	10164211	%	36319	%	13853	%	1917	%	18595	%	2460	%	637	%	302	%	2885	%
Congenital malformations of cardiac chambers and connections	810	0.0	26	0.1	42	0.3	15	0.8	25	0.1	108	4.4	19	3.0	13	4.3	2	0.1
Congenital malformations of cardiac septa	19822	0.2	187	0.5	342	2.5	34	1.8	393	2.1	636	25.9	106	16.6	29	9.6	80	2.8
Ebstein anomaly	147	0.0	1	0.0		0.0	1	0.1	2	0.0	8	0.3	1	0.2	4	1.3	13	0.5
Hypoplastic right heart syndrome	31	0.0		0.0		0.0		0.0		0.0	16	0.7	2	0.3	10	3.3		0.0
Hypoplastic left heart syndrome	104	0.0	11	0.0	3	0.0	10	0.5	2	0.0	1	0.0	1	0.2		0.0	2	0.1
Other congenital malformations of heart	1200	0.0	55	0.2	35	0.3	5	0.3	28	0.2	106	4.3	6	0.9	9	3.0	1	0.0
Congenital malformations of great arteries	4634	0.0	240	0.7	260	1.9	20	1.0	93	0.5	139	5.7	12	1.9	8	2.6	5	0.2
Persistent left superior vena cava	48	0.0	1	0.0	2	0.0		0.0	4	0.0		0.0		0.0		0.0		0.0
Total anomalous pulmonary venous connection	71	0.0		0.0		0.0	1	0.1	1	0.0		0.0		0.0		0.0		0.0
Partial anomalous pulmonary venous connection	71	0.0		0.0		0.0		0.0		0.0	3	0.1		0.0		0.0	1	0.0
Anomalous pulmonary venous connection, unspecified	27	0.0		0.0	1	0.0		0.0		0.0		0.0	1	0.2		0.0		0.0

For each valvular heart disease, numbers and percentages of cases with concomitant comorbidity diagnosis from ICD-10 codes are shown. The numbers and percentages in the total population are also shown for comparison. AS, aortic stenosis. AR, aortic regurgitation. MS, mitral stenosis. MR, mitral regurgitation. PS, pulmonary stenosis. PR, pulmonary regurgitation. TS, tricuspid stenosis. TR, tricuspid regurgitation.

eTable 9. Individual components of autoimmune disorders

	Population		AS		AR		MS		MR		PS		PR		TS		TR	
	10164211	%	36319	%	13853	%	1917	%	18595	%	2460	%	637	%	302	%	2885	%
Addison disease	1986	0.0	15	0.0	4	0.0	1	0.1	12	0.1	0.0	0.0	0.0	0.0	0.0	0.0		0.0
Amyotrophic lateral sclerosis	2867	0.0	23	0.1	5	0.0		0.0	10	0.1	0.0	0.0	0.0	0.0	0.0	0.0	1	0.0
Ankylosing spondylitis	10428	0.1	43	0.1	54	0.4	3	0.2	39	0.2	1	0.0	3	0.5	1	0.3	6	0.2
Autoimmune hemolytic anemia	138	0.0	2	0.0	1	0.0		0.0	1	0.0	0.0	0.0	0.0	0.0	0.0	0.0		0.0
Behcet disease	563	0.0	2	0.0	3	0.0		0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0		0.0
Celiac disease	26856	0.3	62	0.2	48	0.3	8	0.4	42	0.2	24	1.0	2	0.3	0.0	0.0	3	0.1
Chorea minor	36	0.0	1	0.0	1	0.0		0.0	2	0.0	0.0	0.0	0.0	0.0	0.0	0.0		0.0
Crohn disease	25310	0.2	86	0.2	47	0.3	9	0.5	61	0.3	7	0.3	2	0.3	0.0	0.0	11	0.4
Diabetes mellitus type I	118873	1.2	1455	4.0	182	1.3	83	4.3	474	2.5	21	0.9	6	0.9	6	2.0	87	3.0
Discoid lupus erythematosus	2228	0.0	14	0.0	4	0.0	2	0.1	6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1	0.0
Grave disease	36144	0.4	249	0.7	103	0.7	23	1.2	227	1.2	10	0.4	3	0.5	0.0	0.0	42	1.5
Hashimoto thyroiditis	65619	0.6	676	1.9	244	1.8	40	2.1	320	1.7	24	1.0	4	0.6	6	2.0	63	2.2
Immune thrombocytopenic purpura	4538	0.0	46	0.1	16	0.1	3	0.2	28	0.2	2	0.1	0.0	0.0	1	0.3	4	0.1
Localized scleroderma	1664	0.0	13	0.0	1	0.0	1	0.1	4	0.0	0.0	0.0	0.0	1	0.3	2	0.1	0.0
Lupoid hepatitis	1379	0.0	14	0.0	2	0.0	2	0.1	5	0.0	0.0	0.0	0.0	0.0	0.0	0.0		0.0
Multiple sclerosis	17136	0.2	35	0.1	20	0.1	2	0.1	27	0.1	2	0.1	2	0.3	0.0	0.0	4	0.1
Myasthenia gravis	2204	0.0	22	0.1	8	0.1		0.0	9	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1	0.0
Pernicious anemia	1050	0.0	14	0.0	3	0.0	3	0.2	7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2	0.1
Polyarteritis nodosa	500	0.0	5	0.0	1	0.0		0.0	4	0.0	0.0	0.0	0.0	0.0	0.0	0.0		0.0
Polymyalgia rheumatica	18737	0.2	447	1.2	108	0.8	13	0.7	144	0.8	0.0	0.0	1	0.2	0.0	0.0	22	0.8
Polymyositis/dermatomyositis	1443	0.0	22	0.1	2	0.0	2	0.1	5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1	0.0
Primary biliary cirrhosis	1980	0.0	32	0.1	4	0.0	2	0.1	10	0.1	0.0	0.0	0.0	0.0	0.0	0.0	3	0.1
Psoriasis	90685	0.9	509	1.4	188	1.4	20	1.0	212	1.1	17	0.7	5	0.8	1	0.3	37	1.3
Reiter disease	356	0.0	1	0.0	1	0.0		0.0	2	0.0	0.0	0.0	0.0	0.0	0.0	0.0		0.0
Rheumatic fever	160	0.0	2	0.0	4	0.0	1	0.1	9	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2	0.1
Rheumatoid arthritis	62914	0.6	674	1.9	239	1.7	42	2.2	345	1.9	5	0.2	7	1.1	3	1.0	54	1.9
Sarcoidosis	10514	0.1	75	0.2	35	0.3	9	0.5	42	0.2	4	0.2	1	0.2	2	0.7	9	0.3
Sjören syndrome	8348	0.1	78	0.2	39	0.3	8	0.4	29	0.2	1	0.0	0.0	0.0	0.0	0.0	5	0.2
Systemic lupus erythematosus	5740	0.1	81	0.2	41	0.3	7	0.4	69	0.4	0.0	0.0	0.0	1	0.3	8	0.3	0.0
Systemic sclerosis	1894	0.0	26	0.1	7	0.1	3	0.2	20	0.1	0.0	0.0	2	0.3	1	0.3	4	0.1
Ulcerative colitis	41128	0.4	159	0.4	68	0.5	10	0.5	116	0.6	2	0.1	3	0.5	0.0	0.0	14	0.5
Wegener granulomatosis	2032	0.0	26	0.1	10	0.1		0.0	16	0.1	1	0.0	1	0.2	0.0	0.0	1	0.0

For each valvular heart disease, numbers and percentages of cases with concomitant comorbidity diagnosis codes are shown. The numbers and percentages in the total population are also shown for comparison. AS, aortic stenosis. AR, aortic regurgitation. MS, mitral stenosis. MR, mitral regurgitation. PS, pulmonary stenosis. PR, pulmonary regurgitation. TS, tricuspid stenosis. TR, tricuspid regurgitation.

eTable 10. Individual components of heritable connective tissue disorders

	Population		AS		AR		MS		MR		PS		PR		TS		TR	
	10164211	%	36319	%	13853	%	1917	%	18595	%	2460	%	637	%	302	%	2885	%
Ehlers-Danlos syndrome	1553	0.0	2	0.0	4	0.0		0.0	3	0.0	1	0.0		0.0		0.0	3	0.1
Marfan syndrome	753	0.0	7	0.0	68	0.5		0.0	42	0.2	1	0.0	1	0.2		0.0	1	0.0
Osteogenesis imperfecta	479	0.0		0.0	9	0.1		0.0		0.0	1	0.0		0.0		0.0		0.0

For each valvular heart disease, numbers and percentages of cases with concomitant comorbidity diagnosis codes are shown. The numbers and percentages in the total population are also shown for comparison. AS, aortic stenosis. AR, aortic regurgitation. MS, mitral stenosis. MR, mitral regurgitation. PS, pulmonary stenosis. PR, pulmonary regurgitation. TS, tricuspid stenosis. TR, tricuspid regurgitation.

eTable 11. Individual components of abdominal hernia and prolapse

	Population		AS		AR		MS		MR		PS		PR		TS		TR	
	10164211	%	36319	%	13853	%	1917	%	18595	%	2460	%	637	%	302	%	2885	%
Diaphragmatic herniation	103465	1.0	1055	2.9	370	2.7	49	2.6	557	3.0	7	0.3	5	0.8	5	1.7	85	2.9
Inguinal herniation	151378	1.5	1380	3.8	615	4.4	35	1.8	936	5.0	57	2.3	18	2.8	10	3.3	127	4.4
Femoral herniation	3174	0.0	39	0.1	13	0.1		0.0	21	0.1		0.0		0.0	1	0.3	2	0.1
Umbilical herniation	25872	0.3	147	0.4	57	0.4	10	0.5	81	0.4	5	0.2	1	0.2	1	0.3	17	0.6
Pelvic organ prolapse	98395	1.0	820	2.3	264	1.9	43	2.2	383	2.1	5	0.2	4	0.6	5	1.7	66	2.3

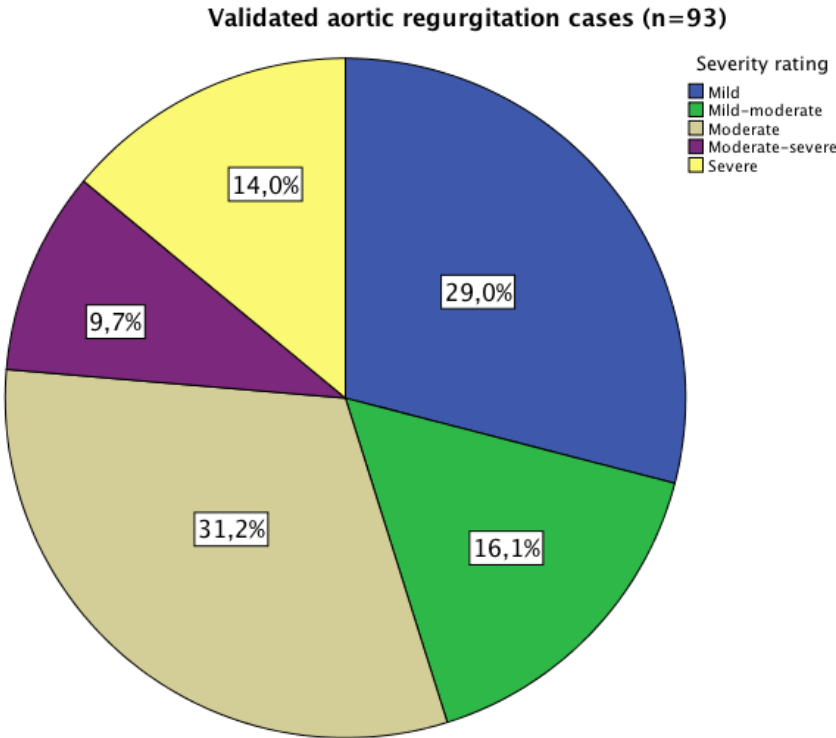
For each valvular heart disease, numbers and percentages of cases with concomitant comorbidity diagnosis codes are shown. The numbers and percentages in the total population are also shown for comparison. AS, aortic stenosis. AR, aortic regurgitation. MS, mitral stenosis. MR, mitral regurgitation. PS, pulmonary stenosis. PR, pulmonary regurgitation. TS, tricuspid stenosis. TR, tricuspid regurgitation.

eTable 12. Individual components of non-valvular cardiothoracic surgical procedures

	Population		AS		AR		MS		MR		PS		PR		TS		TR	
	10164211	%	36319	%	13853	%	1917	%	18595	%	2460	%	637	%	302	%	2885	%
Large intrathoracic veins	180	0.0	2	0.0	1	0.0	2	0.1	3	0.0	24	1.0	0.0	17	5.6			0.0
Pulmonary artery and its branches	427	0.0	5	0.0	22	0.2	8	0.4	9	0.0	128	5.2	23	3.6	27	8.9	6	0.2
Thoracic aorta	2719	0.0	542	1.5	832	6.0	3	0.2	80	0.4	1	0.0	3	0.5	2	0.7	7	0.2
Thoracic aortic anomalies or defects	1029	0.0	60	0.2	62	0.4	27	1.4	29	0.2	44	1.8	7	1.1	6	2.0	2	0.1
Pericardial	597	0.0	103	0.3	44	0.3	4	0.2	54	0.3	4	0.2	1	0.2	2	0.7	6	0.2
Atrium, atrial septum and pulmonary veins	1394	0.0	38	0.1	23	0.2	13	0.7	127	0.7	62	2.5	3	0.5	7	2.3	33	1.1
Ventricle septum	803	0.0	14	0.0	49	0.4	8	0.4	53	0.3	92	3.7	11	1.7	5	1.7	6	0.2
Right ventricle	330	0.0	7	0.0	4	0.0	1	0.1	11	0.1	1	0.0	0.0	0.0	0.0	0.0	3	0.1
Left ventricle	238	0.0	38	0.1	27	0.2	1	0.1	23	0.1	2	0.1	0.0	0.0	3	1.0	1	0.0
Coronary arteries	56402	0.6	1567	4.3	408	2.9	46	2.4	827	4.4	6	0.2	3	0.5	5	1.7	106	3.7
Conduction disorders and arrhythmias	59615	0.6	1879	5.2	584	4.2	136	7.1	1253	6.7	31	1.3	17	2.7	23	7.6	268	9.3
Heart and/or lung transplantations	103	0.0	2	0.0	2	0.0		0.0	9	0.0		0.0	1	0.2	1	0.3	2	0.1
Extracorporeal or assisted circulation	7792	0.1	1594	4.4	512	3.7	64	3.3	705	3.8	12	0.5	7	1.1	4	1.3	82	2.8
Reoperations on the heart and large intrathoracic vessels	467	0.0	154	0.4	44	0.3	10	0.5	62	0.3	2	0.1	4	0.6	1	0.3	11	0.4

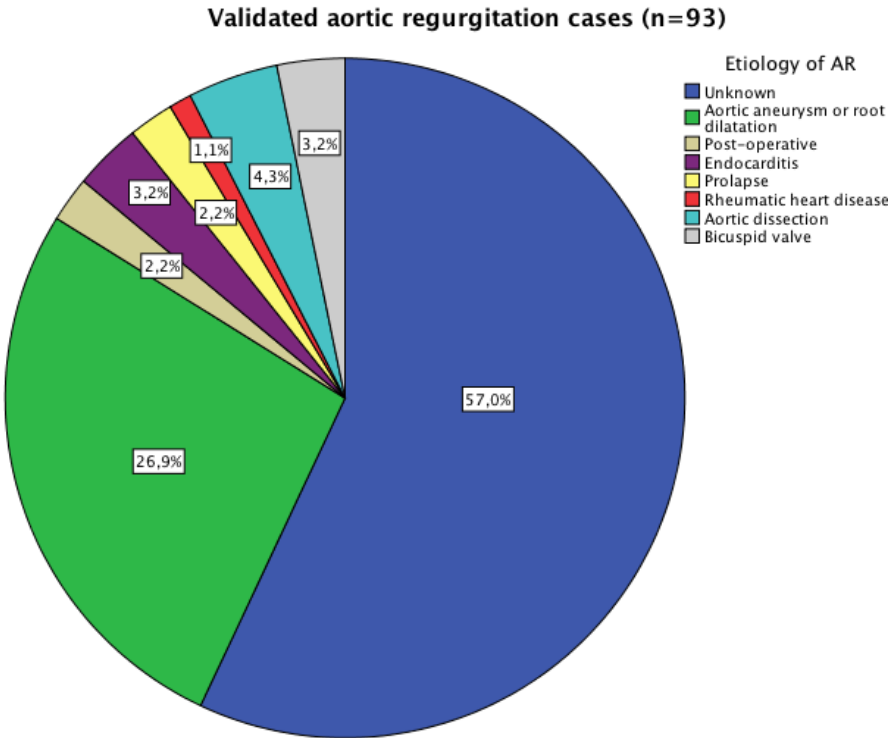
For each valvular heart disease, numbers and percentages of cases with concomitant surgical procedure codes are shown. The numbers and percentages in the total population are also shown for comparison. AS, aortic stenosis. AR, aortic regurgitation. MS, mitral stenosis. MR, mitral regurgitation. PS, pulmonary stenosis. PR, pulmonary regurgitation. TS, tricuspid stenosis. TR, tricuspid regurgitation.

eFigure 1a. Severity rating in validated aortic regurgitation cases



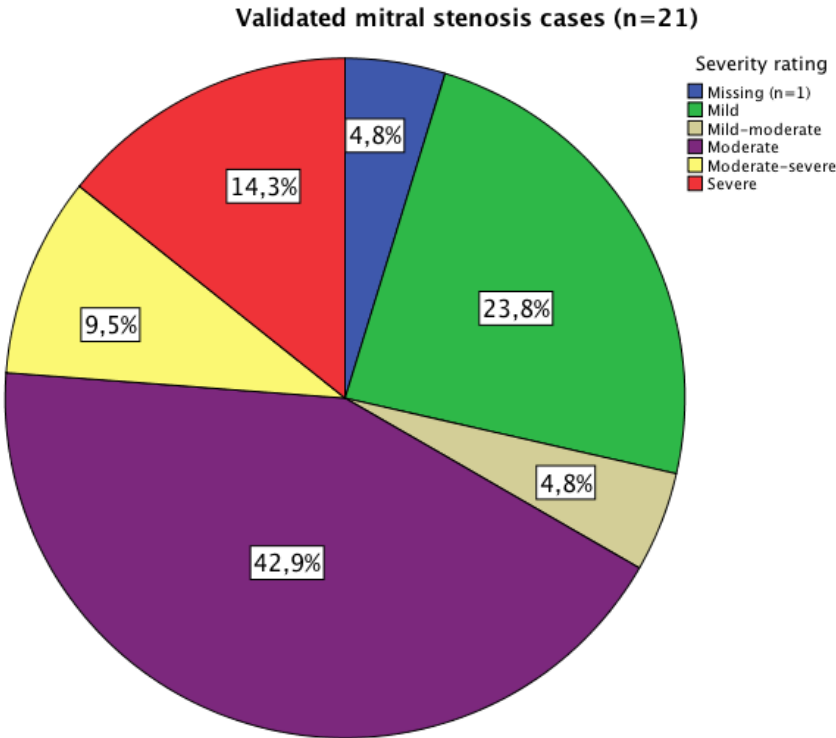
Severity ratings according to echocardiographic or magnetic resonance imaging summaries.

eFigure 1b. Etiology of validated aortic regurgitation cases



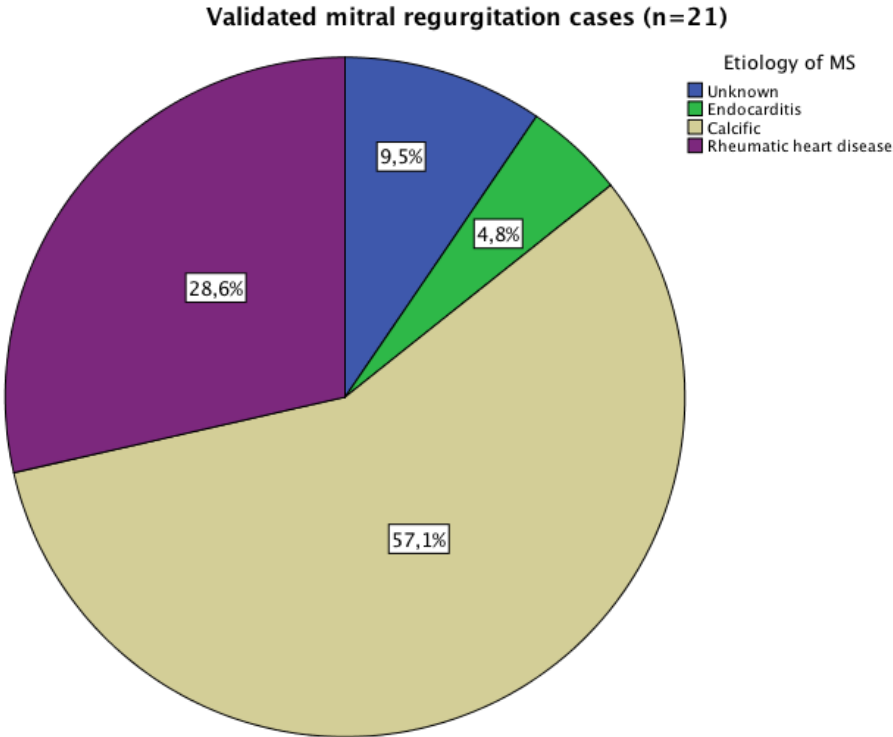
Etiologies based on imaging and medical record summaries. AR, aortic regurgitation.

eFigure 2a. Severity rating in validated mitral stenosis cases



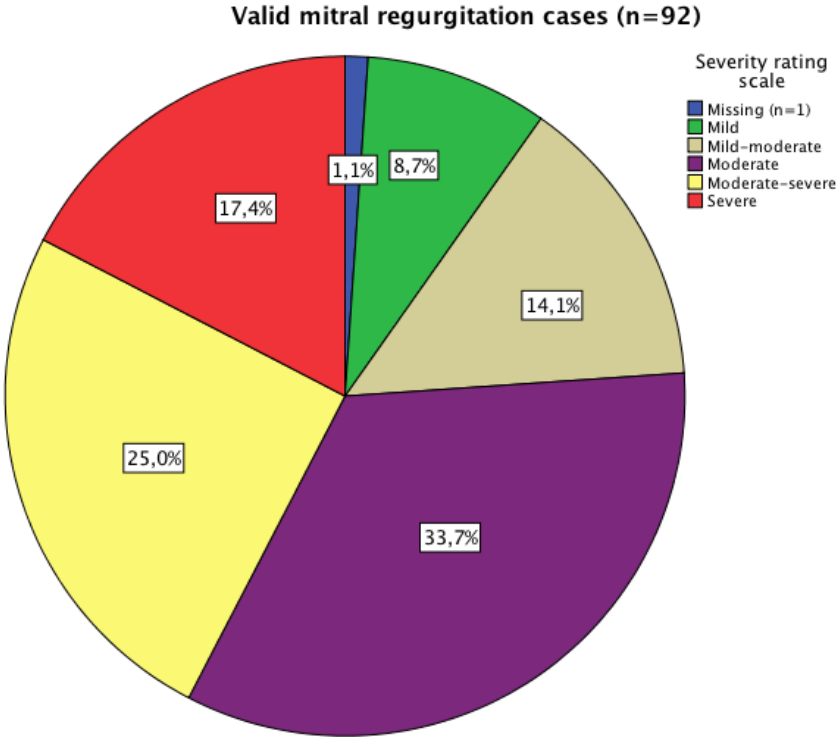
Severity ratings according to echocardiographic summaries.

eFigure 2b. Etiology in validated mitral stenosis cases



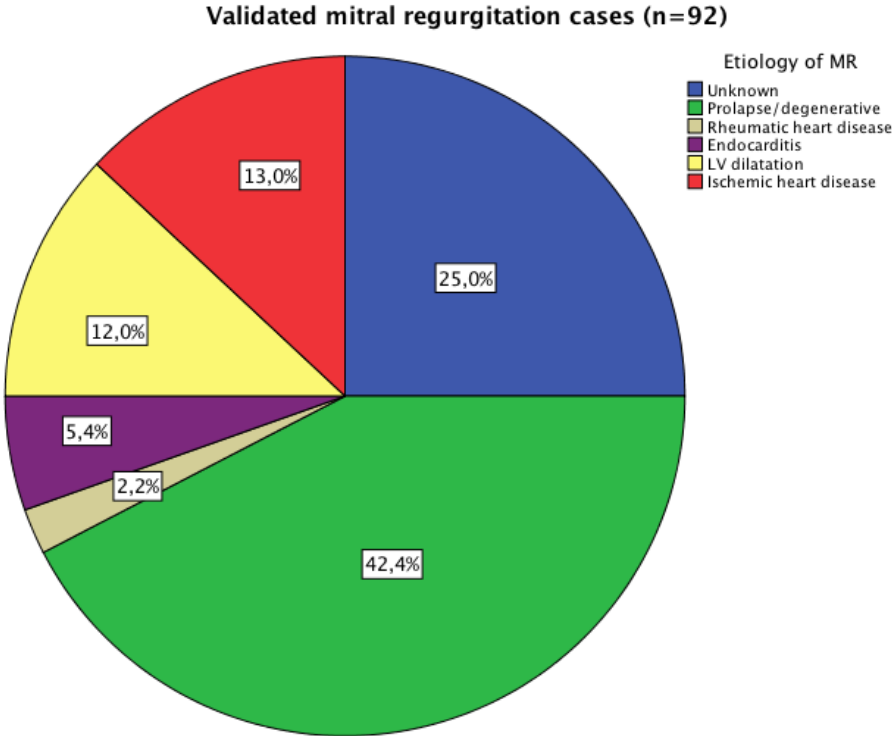
Etiologies based on imaging and medical record summaries. MS, mitral stenosis.

eFigure 3a. Severity rating in validated mitral regurgitation cases



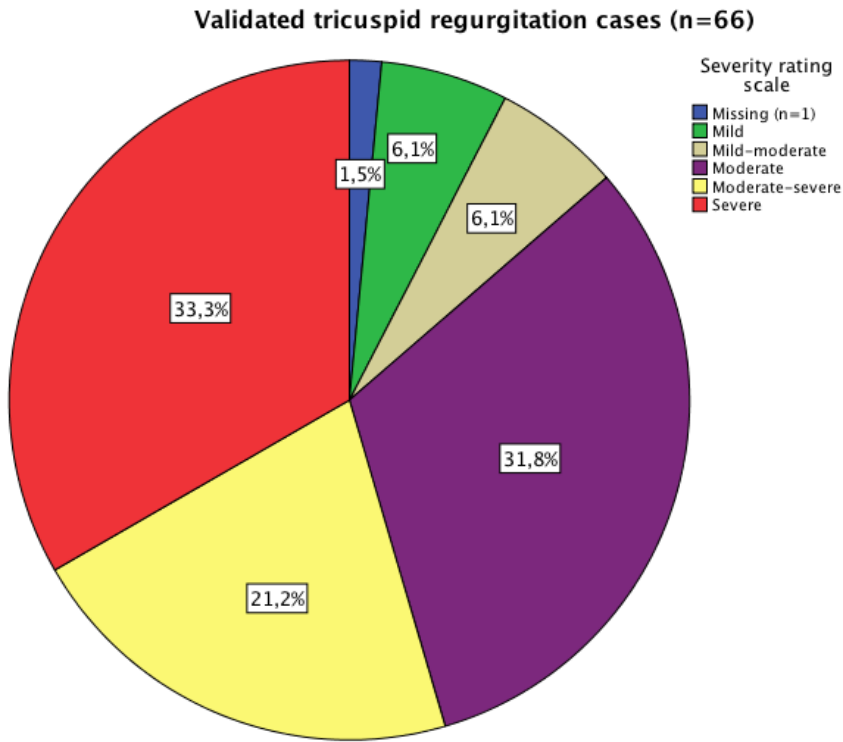
Severity ratings according to echocardiographic or magnetic resonance imaging summaries.

eFigure 3b. Etiology in validated mitral regurgitation cases



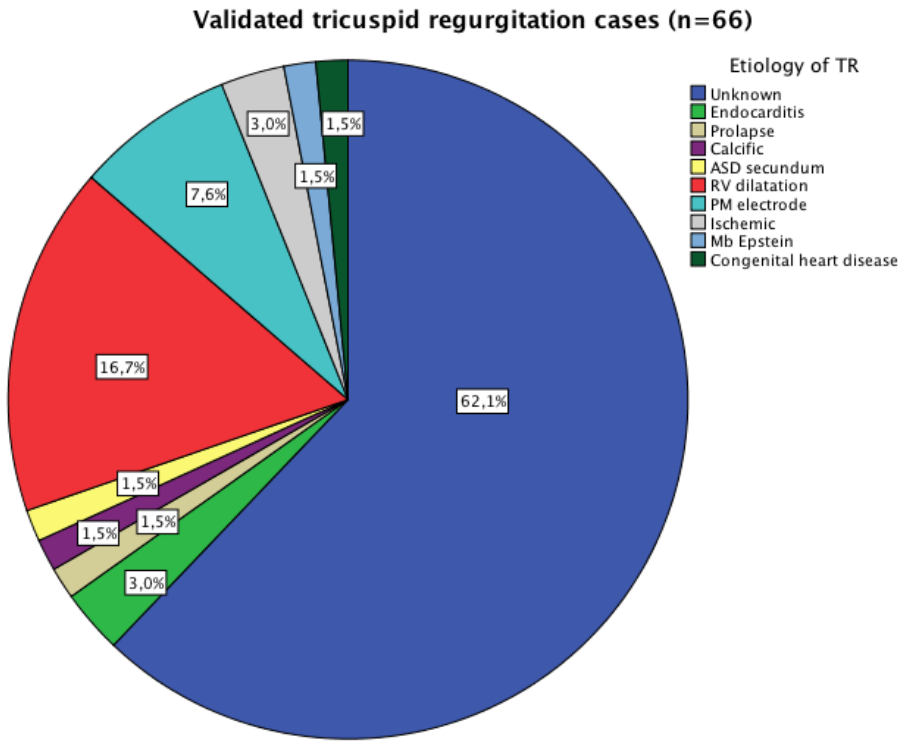
Etiologies based on imaging and medical record summaries. LV, left ventricular. MR, mitral regurgitation.

eFigure 4a. Severity rating in validated tricuspid regurgitation cases



Severity ratings according to echocardiographic summaries.

eFigure 4b. Etiology in validated tricuspid regurgitation cases



Etiologies based on imaging and medical record summaries. ASD, atrial septal defect. PM, pacemaker. RV, right ventricular.