Patients with age-related macular degeneration have increased susceptibility to valvular heart disease

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Introduction:

- 2.5% of the population (13% if age>75y) has moderate-severe Valvular heart disease (VHD).
- Aortic valve stenosis is the third most common cardiovascular disease in the Western world.
- Recent studies have reported an association between VHD and the presence of subretinal drusenoid deposits (SDDs), a distinct manifestation of age-related macular degeneration (AMD).

Methods:

- Retrospective case-control study.
- 945 patients with AMD and 8275 control patients without AMD from a single tertiary center were included in this study.
- All patients with AMD underwent spectral-domain optical coherence tomography (SD-OCT). The SD-OCT scans were annotated by two, experienced graders.
- Among the patients with AMD, 547 had drusen and SDDs, and 398 had drusen only with no SDDs. We also extracted data from all 9220 patients' electronic medical records, including demographics and previous heart valve procedures based on ICD-9 codes.

Results:

	Non-AMD (N = 8725)	AMD		
		All AMD (N = 945)	Non-exudative AMD (N = 314)	Exudative AMD (N = 631)
Age, years	79.3 ± 10.31	82.97 ± 6.95	81.85 ± 7.33	83.52 ± 6.7
Female	4810 (55.13%)	557 (58.94%)	201 (64.01%)	356 (56.42%)
Hypertension	4276 (49.01%)	529 (56.34%)	184 (58.6%)	345 (55.2%)
Hyperlipidaemia	2540 (29.11%)	343 (36.53%)	127 (40.45%)	216 (34.56%)
Hypercholesterolemia	1052 (12.06%)	106 (11.29%)	38 (12.1%)	68 (10.88%)
Diabetes	2051 (23.51%)	215 (22.9%)	77 (24.52%)	138 (22.08%)

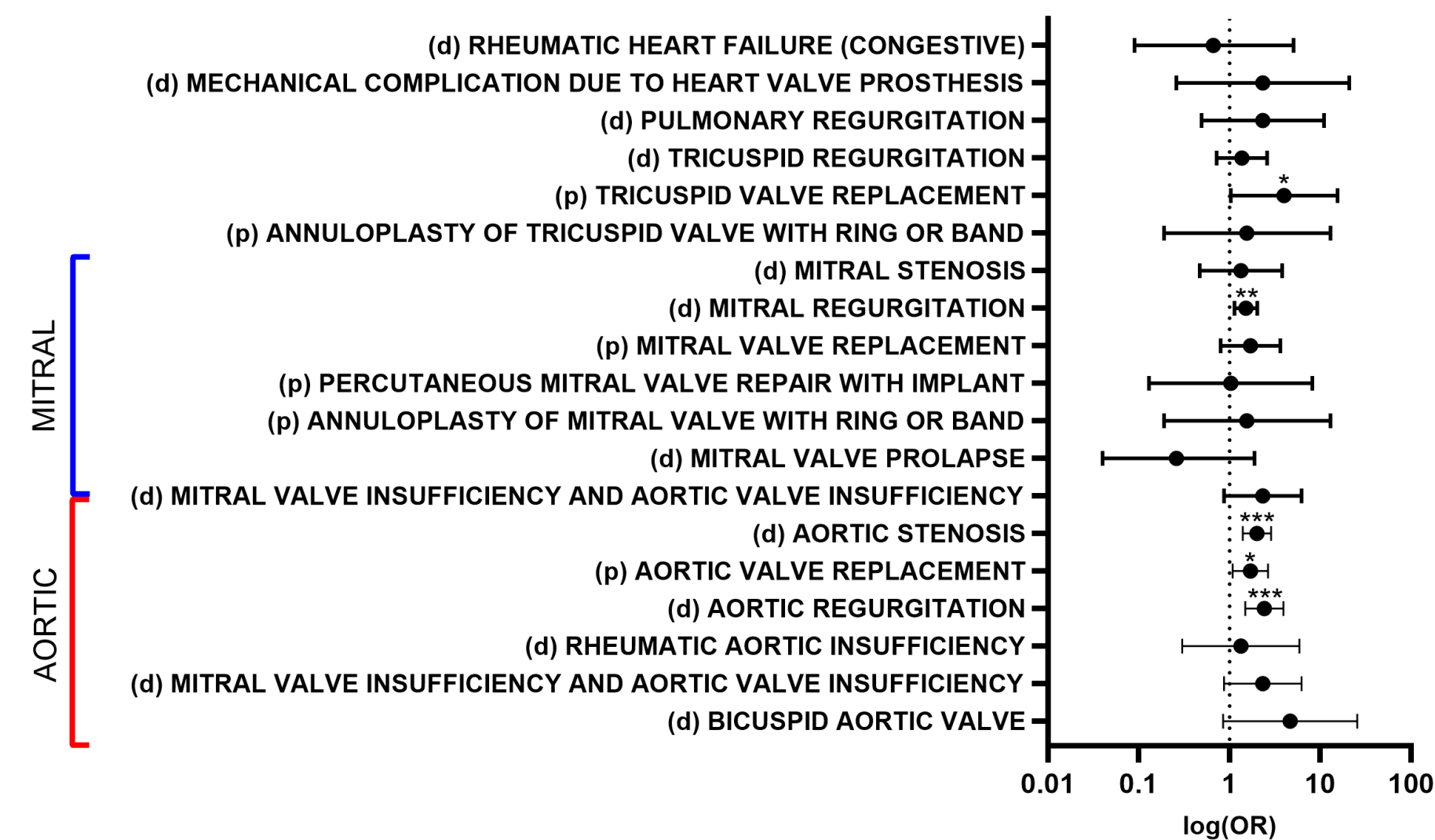**Table 1:** Summary of the general characteristics of the study cohort.

Figure 1: Forest plot summarizing the odds ratio (OR) for the prevalence of valve-related diagnoses and procedures in patients with AMD vs. patients without AMD. Note that the x-axis is a log scale. *$p<0.05$, **$p<0.01$, and ***$p<0.001$. d, diagnosis; p, procedure.
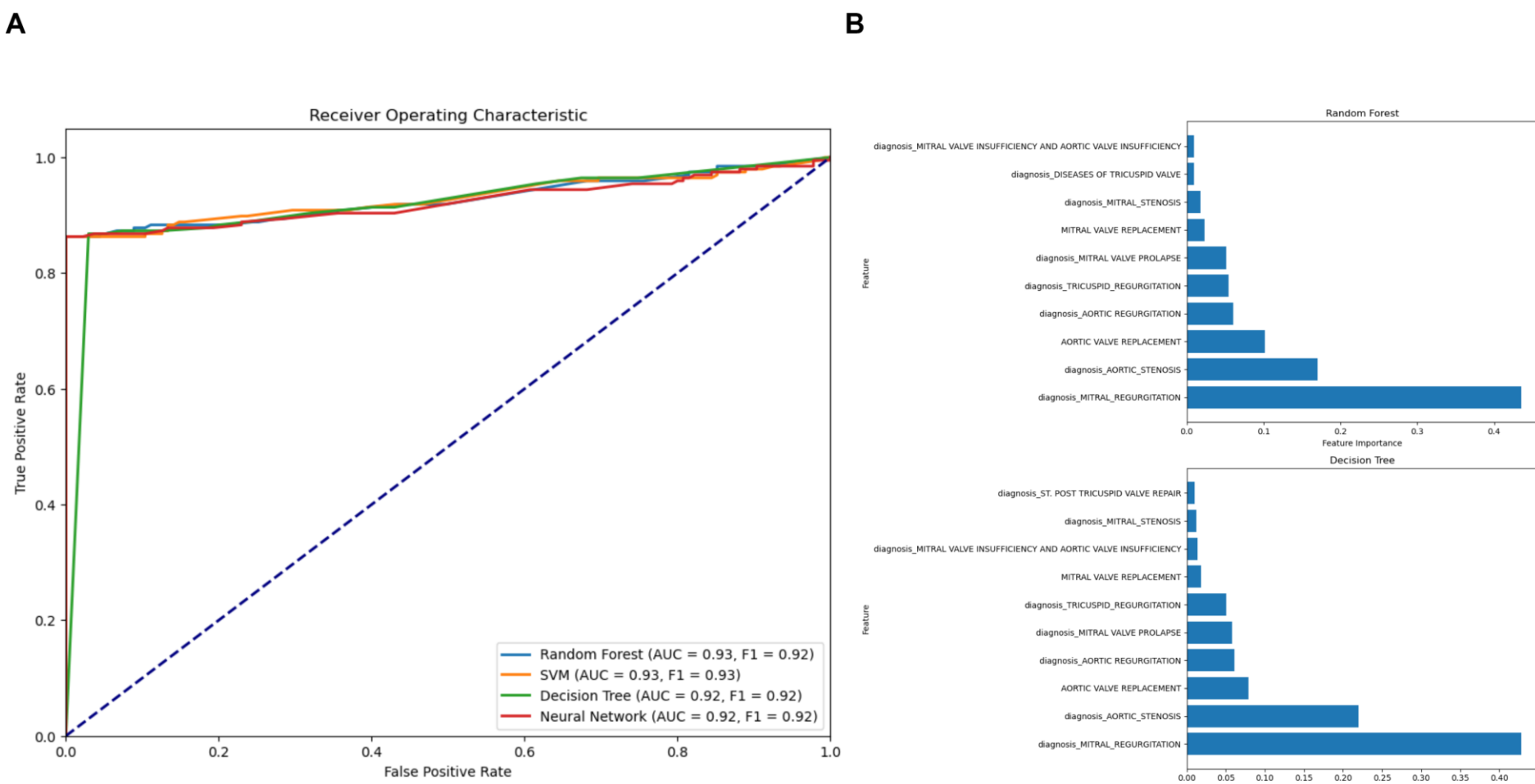

Figure 2: (A) True positive rate plotted against false positive rate for predicting AMD based on a patient's valvular history. The corresponding receiver operation characteristic (ROC) curves were analyzed using the random forest classifier, support vector machine (SVM), decision tree classifier, and neural network models. (B) Summary of the relative importance of the indicated valve-related diagnoses and procedures in the random forest and decision tree classifier models.

Diagnosis/Procedure	No SDDs (N = 396)	SDDs (N = 543)	OR	95% CI	p-value
(d) Bicuspid aortic valve	0 (0.0%)	2 (0.37%)	0.5	[0.03, 8.05]	0.62
(d) Mitral valve insufficiency and/or aortic valve insufficiency	2 (0.51%)	3 (0.55%)	2.02	[0.22, 18.11]	0.52
(d) Rheumatic aortic insufficiency	1 (0.25%)	1 (0.18%)	NA	NA	NA
(d) ST. Post repair of aortic aneurysm	0 (0.0%)	0 (0.0%)	NA	NA	NA
(d) ST. Post thoracic endovascular aortic repair	0 (0.0%)	0 (0.0%)	NA	NA	NA
(d) Aortic regurgitation	7 (1.77%)	14 (2.58%)	0.45	[0.19, 1.07]	0.06
(p) Aortic valve replacement	6 (1.52%)	17 (3.13%)	1.44	[0.56, 3.68]	0.45
(d) Aortic stenosis	13 (3.28%)	25 (4.6%)	0.76	[0.39, 1.48]	0.42
(d) Mitral valve prolapse	1 (0.25%)	0 (0.0%)	NA	NA	NA
(p) Annuloplasty of mitral valve with ring or band	0 (0.0%)	1 (0.18%)	NA	NA	NA
(p) Percutaneous mitral valve repair with implant	1 (0.25%)	0 (0.0%)	NA	NA	NA
(p) Mitral valve replacement	5 (1.26%)	3 (0.55%)	3.55	[0.43, 28.94]	0.21
(d) Mitral regurgitation	19 (4.8%)	39 (7.18%)	0.7	[0.4, 1.19]	0.19
(d) Mitral stenosis	0 (0.0%)	4 (0.74%)	1.51	[0.16, 14.57]	0.72
(d) Diseases of the tricuspid valve	0 (0.0%)	0 (0.0%)	NA	NA	NA
(d) Replaced tricuspid valve	0 (0.0%)	0 (0.0%)	NA	NA	NA
(d) ST. Post tricuspid valve repair	0 (0.0%)	0 (0.0%)	NA	NA	NA
(p) Annuloplasty of tricuspid valve with ring or band	0 (0.0%)	1 (0.18%)	NA	NA	NA
(p) Tricuspid valve replacement	2 (0.51%)	1 (0.18%)	1	[0.09, 11.12]	1
(d) Tricuspid regurgitation	5 (1.26%)	6 (1.1%)	2.28	[0.49, 10.61]	0.28
(d) Tricuspid stenosis	0 (0.0%)	0 (0.0%)	NA	NA	NA
(d) Pulmonary regurgitation	2 (0.51%)	0 (0.0%)	NA	NA	NA
(d) Pulmonary stenosis	0 (0.0%)	0 (0.0%)	NA	NA	NA
(d) Mechanical complication due to heart valve prosthesis	0 (0.0%)	0 (0.0%)	NA	NA	NA
(d) Rheumatic heart failure (congestive)	0 (0.0%)	1 (0.18%)	NA	NA	NA

Data are presented as N (%). SDDs, subretinal drusenoid deposits; OR, odds ratio; CI, confidence interval; NA, not applicable; d, diagnosis; p, procedure, ST, status.

Table 2: Summary of the prevalence of valve-related diagnoses and procedures in the AMD cohort, with corresponding ORs for patients with SDDs vs. patients without SDDs.

Conclusion:

- Patients with AMD have a higher prevalence of VHD and are more likely to undergo a heart valve–related procedure compared to patients without AMD, with no difference between patients with SDDs and patients without SDDs in the AMD cohort.