# Online Supplementary

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**Figure S1:** PRISMA flowchart outlining the literature search

**PRISMA Checklist**



|  |  |
| --- | --- |
| **PubMed 669** | **("mitral valve insufficiency"[MeSH Terms] OR ("mitral"[All Fields] AND "valve"[All Fields] AND "insufficiency"[All Fields]) OR "mitral valve insufficiency"[All Fields] OR ("mitral"[All Fields] AND "regurgitation"[All Fields]) OR "mitral regurgitation"[All Fields]) OR ("mitral valve insufficiency"[MeSH Terms] OR ("mitral"[All Fields] AND "valve"[All Fields] AND "insufficiency"[All Fields]) OR "mitral valve insufficiency"[All Fields] OR ("mitral"[All Fields] AND "valve"[All Fields] AND "regurgitation"[All Fields]) OR "mitral valve regurgitation"[All Fields]) OR ("Musculoskelet Regen"[Journal] OR "Ment Retard"[Journal] OR "mr"[All Fields]) AND ("transcatheter aortic valve replacement"[MeSH Terms] OR ("transcatheter"[All Fields] AND "aortic"[All Fields] AND "valve"[All Fields] AND "replacement"[All Fields]) OR "transcatheter aortic valve replacement"[All Fields]) OR (("embryo implantation"[MeSH Terms] OR ("embryo"[All Fields] AND "implantation"[All Fields]) OR "embryo implantation"[All Fields] OR "implantation"[All Fields]) AND tavr[All Fields]) AND outcomes[All Fields]** |
| **Cochranelibrary.com 1836 results** | **mitral regurgitation OR MR AND transcatheter aortic valve replacement OR TAVR OR transcatheter aortic valve implantation** |

**Table S1:** Detailed search strategy – mitral regurgitation studies

**Table S2:** Detailed search strategy – mitral stenosis studies.

|  |  |
| --- | --- |
| **PubMed 2504 results** | **("mitral valve stenosis"[MeSH Terms] OR ("mitral"[All Fields] AND "valve"[All Fields] AND "stenosis"[All Fields]) OR "mitral valve stenosis"[All Fields] OR ("mitral"[All Fields] AND "stenosis"[All Fields]) OR "mitral stenosis"[All Fields]) OR ("mitral valve stenosis"[MeSH Terms] OR ("mitral"[All Fields] AND "valve"[All Fields] AND "stenosis"[All Fields]) OR "mitral valve stenosis"[All Fields]) OR ("Ms"[Journal] OR "Med Sci (Paris)"[Journal] OR "ms"[All Fields]) AND ("transcatheter aortic valve replacement"[MeSH Terms] OR ("transcatheter"[All Fields] AND "aortic"[All Fields] AND "valve"[All Fields] AND "replacement"[All Fields]) OR "transcatheter aortic valve replacement"[All Fields] OR ("transcatheter"[All Fields] AND "aortic"[All Fields] AND "valve"[All Fields] AND "implantation"[All Fields]) OR "transcatheter aortic valve implantation"[All Fields]) OR ("transcatheter aortic valve replacement"[MeSH Terms] OR ("transcatheter"[All Fields] AND "aortic"[All Fields] AND "valve"[All Fields] AND "replacement"[All Fields]) OR "transcatheter aortic valve replacement"[All Fields]) OR TAVR[All Fields] AND outcomes[All Fields]** |
| **Cochranelibrary.com 1342 results** | **mitral stenosis OR MS AND transcatheter aortic valve replacement OR TAVR OR transcatheter aortic valve implantation** |

**Table S3:** Detailed search strategy – tricuspid regurgitation studies.

|  |  |
| --- | --- |
| **PubMed 2501 results** | **("tricuspid valve insufficiency"[MeSH Terms] OR ("tricuspid"[All Fields] AND "valve"[All Fields] AND "insufficiency"[All Fields]) OR "tricuspid valve insufficiency"[All Fields] OR ("tricuspid"[All Fields] AND "regurgitation"[All Fields]) OR "tricuspid regurgitation"[All Fields]) OR ("tricuspid valve insufficiency"[MeSH Terms] OR ("tricuspid"[All Fields] AND "valve"[All Fields] AND "insufficiency"[All Fields]) OR "tricuspid valve insufficiency"[All Fields] OR ("tricuspid"[All Fields] AND "valve"[All Fields] AND "regurgitation"[All Fields]) OR "tricuspid valve regurgitation"[All Fields]) OR ("Anat Rec A Discov Mol Cell Evol Biol"[Journal] OR "Adm Radiol"[Journal] OR "Adm Radiol J"[Journal] OR "Action Res (Lond)"[Journal] OR "ar"[All Fields]) AND ("transcatheter aortic valve replacement"[MeSH Terms] OR ("transcatheter"[All Fields] AND "aortic"[All Fields] AND "valve"[All Fields] AND "replacement"[All Fields]) OR "transcatheter aortic valve replacement"[All Fields] OR ("transcatheter"[All Fields] AND "aortic"[All Fields] AND "valve"[All Fields] AND "implantation"[All Fields]) OR "transcatheter aortic valve implantation"[All Fields]) OR ("transcatheter aortic valve replacement"[MeSH Terms] OR ("transcatheter"[All Fields] AND "aortic"[All Fields] AND "valve"[All Fields] AND "replacement"[All Fields]) OR "transcatheter aortic valve replacement"[All Fields]) OR tavr[All Fields] AND outcomes[All Fields]** |
| **Cochranelibrary.com 1274 results** | **tricuspid regurgitation OR TR AND transcatheter aortic valve replacement OR TAVR OR transcatheter aortic valve implantation** |

**Table S4:** Study characteristics of included studies on mitral regurgitation

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study, year** | **Mean****Follow-up** | **N****total** | **Male****(%)** | **Mean Age****(years )** | **Valve****Used** | **Covariates adjusted for** | **Outcomes** | **Technique to classify valvular heart disease** | **Criteria used to classify valvular heart disease** |
| Toggweiler, 2012[1] | 2 year | 451 | 212(47) | 81.5 | BEV | The HR were adjusted for STS score, mean gradient, PA, site, access route, NYHA class, AFib, CVA, kidney function, P-htn, COPD, and gender. | Mortality | [Transthoracic echocardiography](https://www.sciencedirect.com/topics/medicine-and-dentistry/transthoracic-echocardiography)   | MR severity was graded as none or trivial, mild, moderate, or severe according to the ACC/AHA/ESC recommendations, incorporating structural, Doppler, and quantitative parameters ([16](https://www.sciencedirect.com/science/article/pii/S0735109712009230%22%20%5Cl%20%22bib16)) |
| Barbanti, 2013 (PARTNER A)[2] | 2 years | 331 | 192(58) | 83.64 | BEV | The HR were adjusted for Age, female sex, malignant tumor, previous balloon aortic valvuloplasty, previous PVD, previous MI, baseline LVEF, and baseline LVESD | Mortality | Transthoracic 2-dimensional echocardiography  | MR severity was graded as none, trace, mild, moderate, or severe according to the ASE recommendations, incorporating structural, Doppler, and quantitative parameters. |
| Bedogni, 2013[3] | 1 year | 1,007 | 452(44.9) | 81.2±5.6 | BEV | The HR adjusted for SPH, log EuroScore, STS score, previous MI, COPD, previous stroke, AFib, creatinine clearance <30 mL/min, and MR severity improvement ≥1 grade). | Mortality | Transthoracic echocardiography  | MR severity was graded as no/mild (0/1), moderate (2), or severe (3).  |
| Khawaja, 2014[4] | 2 year | 316 | 181(57.3) | 82.06 | BEV | The HR were adjusted for Logistic EuroScore, STS, NYHA, LVEF, Aortic regurgitation ≥grade 3, TR ≥grade 3 | Mortality | Transthoracic and/or transesophageal echocardiography  |  |
| Sullivan, 2015[5] | 1 year | 113 | 67(59.3) | 82.09 | BEV/SEV | The HR were adjusted for PVD and logistic Euroscore. | Mortality | Transthoracic echocardiography  | MR severity was graded as trivial, mild, moderate and severe according to the ACC/AHA/ESC recommendations. Structural parameters utilized for severity assessment included left atrium size, left ventricle size, mitral valve leaflets and subvalvular apparatus. Meanwhile, Doppler parameters used in assessing the severity of MR included ratio of jet area to left atrium area using color flow and jet profile using continuous wave Doppler. In cases when greater than mild MR was present, quantitative methods such as effective regurgitant orifice area (EROA) and regurgitant volume were utilized to assess MR severity. |
| Feldt, 2019[6] | 30 days | 1,712 | 856(50) | 81.45 | BEV/SEV | The HR were adjusted for age, sex, BMI, recent MI, DM, COPD, claudication, AFib, NYHA class, aortic valve area, LVEF, and HTN. | Mortality | Transthoracic echocardiography | MR severity graded as none/trivial, mild, moderate, or severe as per the ESC/ACC/AHA guideline recommendations.  |
| Miura, 2020 [7] | 776.0 days | 1587 | 473 (29.8) | 85.05 | BEV/SEV | The HR were adjusted for independent variables including age (per 1-year increase), male gender, DM, chronic heart failure, chronic kidney disease, coronary artery disease, LVEF < 60%, STS score ≥ 8.0%, and a transapical approach. | Mortality | Transthoracic echocardiography  | MR severity was graded as none or trivial, mild, moderate, or severe according to the regurgitant volume, regurgitant fraction and effective regurgitant orifice area in line with the recommendations of the ASE. |

BEV, balloon-expandable valve; SEV, self-expandable valve; NYHA, New York Heart Association; STS PROM, Society of Thoracic Surgeons predicted risk of mortality; LVEF, left ventricular ejection fraction; DM, diabetes mellitus; CAD, coronary artery disease; MI, myocardial infarction; COPD, chronic obstructive pulmonary disease; CABG, coronary artery bypass graft; PCI, percutaneous intervention; MR, mitral regurgitation. PA, porcelain aorta; AFib, atrial fibrillation; CVA, cerebrovascular accident; P-htn, pulmonary hypertension; PVD, peripheral vascular disease; LVESD, Left ventricular end-systolic diameter; SPH, severe pulmonary hypertension; ACC, American College of Cardiology; AHA, American Heart Association; ESC, European Society of Cardiology; ASE, American Society of Echocardiography.

**Table S5:** Patients’ baseline and procedural characteristics of included studies on mitral regurgitation.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study, year** | **NYHA III/IV (%)** | **EuroSCORE** | **STS PROM** | **DM (%)** | **Hypertension (%)** | **Atrial Fibrillation (%)** | **CAD %****(Prior MI)\*** | **COPD (%)** | **Pulmonary Hypertension (%)** | **Peripheral Vascular Disease (%)** | **Previous CABG****(Prior****PCI)\* (%)** | **LVEF %** | **Mean Aortic Gradient mmHg** | **Aortic Valve Area cm2** | **Mod- Severe MR (%)** |
| Toggweiler, 2012 | 402(89.13) | - | 7.83 | 127(28.16) | 349 (77.38) | 160 (35.5) | 331(73.39) | 125(27.72) | 75 (16.63) | - | - | 58.45 | 43.2 | 0.63 | 132(29.3) |
| Barbanti, | 176 | - | 11.86 | 127 | 294 (88.8) | - | 89 | 144 | - | 146 (44.1) | 146 | - | - | - | 65 |
| 2013 | (53.17) |  |  | (38.36) |  |  | (26.88)\* | (43.5) |  |  | (44.1) |  |  |  | (19.6) |
| (PARTNERA) |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Bedogni, 2013 | 701(63.3) | 23.1±14.1 | 8.0±2.4 | 280(27.8) | - | 171(16.98) | 218 (21.6)\* | 231(22.9) | 172 (17) | - | 308(30.6) | 51.5±11.9 | 44.6±13.4 | - | 337(33.5) |
| Khawaja, 2014 | 218(69.0) | 21.9 | 6.08 | - | - | - | - | - | 66 (20.9) | 40 (12.7) | - | 49.2 | 72.0 | 0.88 | 60 (19) |
| Sullivan, 2015 | 88(77.9) | 34.3 | 7.95 | 39(34.5) | 91 (80.5) | 26 (23) | 84(74.3) | 18(15.9) | - | 31 (27.4) | 30(26.5) | 34.26 | 28.46 | 0.73 | 61 (54) |
| Feldt, 2019 | 1586(92.6) | - | - | 380(22.2) | 1,222 (71.4) | 617 (36) | 98(5.72) | 346(20.2) | 89 (5.2) | - | 493 (28.8)\* | 1009(58.9)>50%LVEF | - | 0.64 | 308 |
|  Miuru, 2020 | 792 (49.9) | 13.2 | 6.8 | 420 (26.5) | 1,255 (79.1) | 323 (20.35) | 113 (7.1)\* | 293 (18.5) | - | 245 (15.4) | 115 (7.2) | 63.9 | 47.8  | 0.62  | 144 (9.1) |

BEV, balloon-expandable valve; SEV, self-expandable valve; NYHA, New York Heart Association; STS PROM, Society of ThoracicSurgeons predicted risk of mortality; LVEF, left ventricular ejection fraction; DM, diabetes mellitus; CAD, coronary artery disease; MI,myocardial infarction; COPD, chronic obstructive pulmonary disease; CABG, coronary artery bypass graft; PCI, percutaneous intervention; MR, mitral regurgitation. PA, porcelain aorta; AFib, atrial fibrillation; CVA, cerebrovascular accident; P-htn, pulmonary hypertension; PVD, peripheral vascular disease; LVESD, Left ventricular end-systolic diameter; SPH, severe pulmonary hypertension

**Table S6:** Study characteristics of included studies on mitral stenosis.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study, year** | **Mean Follow-****up** | **N total** | **Male (%)** | **Mean Age (years )** | **Valve Used** | **Covariates adjusted for** | **Outcome** | **Technique to classify valvular heart disease** | **Criteria used to classify valvular heart disease** |
| Abramowitz, 2017[8] | 1 year | 761 | 459(60.3) | 82.09 | BEV/SEV | The HR was adjusted to patient age, BMI, gender, DM, CAD, chronic lung disease, previous stroke/TIA, PAD, frailty, prior cardiac surgery, CRF, alternative access, STS score, LVEF, mean aortic valve gradient, CT meanannulus diameter, and LVOT calcification. | Mortality (Severe vs. None) | Electrocardiographically-gated multi-slice computed tomography angiography was performed. Additionally, MAC was quantitatively examined by means of the 3mensio Valves software. | The grading of severity of MAC was determined via the circumferential involvement of the mitral ring: mild as < 1/3; moderate as between 1/3 and 1/2; and severe as > 1/2 of the annulus involved. |
| Joseph, 2018[9] | 1 year | 44,755 | 23,385(52.3) | 81.6±8.5 | BEV/SEV | The HR was adjusted for age, sex, current/recent smoking status, DM, NYHA IV, COPD, eGFR, current dialysis, prior PCI, prior CABG, prior nonaortic and aortic valve procedure, acuity, aortic insufficiency (moderate/severe vs. other), mitral insufficiency (moderate/severe vs. other), access site (femoral vs. other), prior MI, prior stroke or TIA, prior PAD, carotid stenosis, prior Afib/flutter, home oxygen, hostile chest, and PA | Mortality (Severe vs. None) | Echocardiographic data were used only when cardiac catheterization data was also available alongside. | The grading of severity of MS was determined as per the 2014 AHA/ACC practice guidelines using MVA: no MS as > 4 cm2; nonsevere MS as between 1.51 cm2 and 4 cm2; and severe MS as ≤ 1.5 cm2 MVA. |
| Asami, 2018[10] | 1 year | 971 | 492 (50.67) | 82.2 ± 6.1 | BEV/SEV/MEV | The HR was adjusted for age, DM, NYHA III or IV, CAD, PAD, Afib, LVEF, and STS score. | Mortality (All vs. None) | All subjects underwent transthoracic and/or transesophageal echocardiography. MVA was assessed using pressure half-time in patients without signs of MS on visual inspection, while planimetry was preferred over pressure half- time for calculating MVA in patients with signs of MS on visual assessment of the mitral apparatus and/or increased transmitral gradients.  | The severity of MS was graded in line with the guideline recommendations of the ASE/EAE by using mean gradient (mild < 5 mmHg, moderate 5-10 mmHg, and severe > 10 mmHg) and MVA (normal >2.5 cm2 , mild 1.5–2.5 cm2 , moderate 1.0–1.5 cm2, and severe < 1.0 cm2) |
| Fischer, 2019[11] | 3±2 years | 2,133 | 1,126 (53.3) | 80 ± 9 | BEV/SEV | The HR was adjusted for age, gender, LVEF %, CAD, LVEF <50%, mean transmitral and transortic gradient (mmHg), and sPAP > 60 mm Hg | Mortality(All vs. None) | Transthoracic echocardiography  | Moderate to severe MS was defined as a mean transmitral gradient ≥ 5 mm Hg accompanied by an absence of severe MR (effective regurgitant orifice area ≥ 40 mm Hg and regurgitant volume ≥ 60 mL/beat at PISA). Thereby, the inclusion of functional elevated mitral gradients was avoided.  |
| Al-khadra, 2019[12] | In hospital | 62,120 | 32,675 (52.6) | 81 | BEV/SEV | The OR was adjusted for age, race, gender, urgency of TAVI (elective vs emergent), AFib, smoking, carotid artery disease, CAD, previous stroke, dyslipidemia, TAVI access, and hospital stay. | Mortality (All vs. None) | ICD-9-CM codes 394.0 and 396.0. |  |
|  |  |  |   |  |  |  |  |  |  |
| Sannino, 2019[13] | 40.8 months | 901 | 476/901 (52.8) | 81.3 | BEV/SEV |  A risk-adjusted Cox Proportional Hazards time-to-mortality model was used by including the US-TAVI score (modeled using a 3-knot restricted cubic spline function) as an adjustment covariate along with mean mitral gradient group. | Mortality (Severe vs. None) | Transthoracic echocardiography  | The grading of severity of MS was determined using MMG: MMG <5 mm Hg; MMG ≥5, and <10 mm Hg; MMG ≥10 mm Hg.  |
| Kato, 2019[14] | 30 days | 546 | 230 (41.67) | 76.7 | SEV | The HR were adjusted for age, NYHA III or IV, AFib, creatinine, DM, HTN, CVD, chronic lung disease, TAVR, and baseline LVEF | Mortality (All vs. None) | Transthoracic Echocardiography | The grading of severity of MS was assessed using MVA: significant MS as a MVA ≤2.0cm2 and mild mitral stenosis as a MVA >2.0 cm2 |

BEV, balloon-expandable valve; SEV, self-expandable valve; NYHA, New York Heart Association; STS PROM, Society of Thoracic Surgeons predicted risk of mortality; LVEF, left ventricular ejection fraction; DM, diabetes mellitus; CAD, coronary artery disease; MI, myocardial infarction; COPD, chronic obstructive pulmonary disease; CABG, coronary artery bypass graft; PCI, percutaneous intervention; PPI, permanent pacemaker implantation; AKI, acute kidney injury; NOAF, new onset atrial fibrillation. ; eGFR, estimated glomerular filtration rate; sPAP, systolic pulmonary artery pressure; PA, porcelain aorta; PAD, peripheral artery disease; ICD-9-CM, [International Classification of Disease](https://www.sciencedirect.com/topics/medicine-and-dentistry/international-classification-of-diseases), Ninth Edition, Clinical Modification; MAC, mitral annulus calcification; MMG, mean mitral gradient; MVA, mitral valve area; ASE, American Society of Echocardiography; EAE, European Association of Echocardiography; AHA, American Heart Association; ACC, American College of Cardiology.

**Table S7:** Patients’ baseline and procedural characteristics of included studies on mitral stenosis.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study, year** | **EuroScore** | **STS PROM** | **NYHA III/IV (%)** | **LVEF****%** | **DM (%)** | **Hypertension (%)** | **Dyslipidemia (%)** | **Atrial Fibrillation (%)** | **CAD %****(Prior MI)\*** | **COPD****/(Lung disease)\* (%)** | **Renal Failure (%)** | **Pulmonary Hypertension (%)** | **Peripheral Vascular Disease (%)** | **Previous CABG****(Prior****PCI)\* (%)** | **Mean Aortic Gradient mmHg** | **Aortic Valve Area cm2** |
| Abramowitz, 2017 | - | 6.7 | - | 56.86 | 244(32.06) | 693 (91.06) | - | 256(33.64) | 488(64.12) | 285 (37.45)\* | 137(18) | - | 272 (35.7) | 203 (26.7) | 45.48 | 0.64 |
| Joseph, | - | - | 9,097 | 53.5 | 16,742 | 40,035 | - | 18,357 | 11,345 | 6,128 | - | - | 13,883 | 13,220 | - | - |
| 2018 |  |  | (20.5) | ± | (37.4) | (89.5) |  | (41.1) | (25.4)\* | (13.8) \* |  |  | (31.0) | (29.6) |  |  |
|  |  |  | (IV) | 13.9 |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  | (withflutter) |  |  |  |  |  |  |  |  |
| Asami, | 20.5 ± | 6.0 ± | 648 | 54.1 | 246 | 817 (84.1) | 612 (63.0) | 319 (32.9) | 149 | 124 | 696 | 510 (76.7) | 149 (15.3) | 149 (15.3) | 42.3 ± | 0.71 |
| 2018 | 13.3 | 4.1 | (66.8) | ± | (25.3) |  |  |  | (15.3)\* | (12.8) | (71.7) |  |  |  | 18.0 | ± |
|  |  |  |  | 14.9 |  |  |  |  |  |  |  |  |  |  |  | 0.24 |
| Fischer, | - | 6.4 ± | 1,591 | 53.1 | 645 | - | - | - | 1081 | 443 | 1139 | - | 535 (25.3) | - | 45.0 ± | - |
| 2019 |  | 5.2 | (75.3) | ± | (69.5) |  |  |  | (51.2) | (21.0) | (54.2) |  |  |  | 17.0 |  |
|  |  |  |  | 12.8 |  |  |  |  |  |  |  |  |  |  |  |  |
| Al-khadra, | - | - | - | - | 21928 | 49,954 | 40,540 | 27,434 | 42,703 | 20,532 | 22,200 | - | 18,176 | - | - | - |
| 2019 |  |  |  |  | (35.3) | (80.4) | (65.26) | (44.2) | (68.7) | (33.05)\* | (35.7) |  | (29.3) |  |  |  |
| Sannino, | - | 7.77 | - | 54.61 | 359 | 777/901 | 673/901 | 280/901 | 646/901 | 249/901 | 30/901 | - | 287/901 | 436/901 | 44.7 | 0.68 |
| 2019 |  |  |  |  | (39.8) | (86.24) | (74.7) | (31.1) | (71.7) | (27.6) | (3.33) |  | (31.9) | (48.4) |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  | PCI+CABG |  |  |
| Kato, 2019 | - | - | 354 | 63± | 174 | 465 (82.24) | 472 (85.5) | 98 (17.8) | 90 | 182 (33) | - | - | - | 85 (15.4) | 53.3 | 0.8 |
|  |  |  | (64.1) | 9 | (31.5) |  |  |  | (16.3) |  |  |  |  |  |  |  |

BEV, balloon-expandable valve; SEV, self-expandable valve; NYHA, New York Heart Association; STS PROM, Society of Thoracic Surgeons predicted risk of mortality; LVEF, left ventricular ejection fraction; DM, diabetes mellitus; CAD, coronary artery disease; MI,

myocardial infarction; COPD, chronic obstructive pulmonary disease; CABG, coronary artery bypass graft; PCI, percutaneous intervention; PPI, permanent pacemaker implantation; AKI, acute kidney injury; NOAF, new onset atrial fibrillation. ; eGFR, estimated glomerular filtration rate; sPAP, systolic pulmonary artery pressure; PA, porcelain aorta; PAD, peripheral artery disease.

**Table S8:** Study characteristics of included studies on Tricuspid Regurgitation.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study, year** | **Mean****Follow- up** | **N****total** | **Male (%)** | **Mean Age (years )** | **Valve Used** | **Covariates adjusted for** | **Outcomes** | **Technique to classify valvular heart disease** | **Criteria used to classify valvular heart disease** |
| Barbanti, 2015[15] | 2 year | 518 | 285(55.1) | 81.5 ± 8.4 | SEV/BEV | The HR were adjusted for age, prior pacemaker, permanent AFib, mean transaortic gradient 40 mm Hg, renal insufficiency, baseline moderate/severe MR, NYHA class III/IV, LVEF 40%, sPAP>60 mmHg | Mortality | Transthoracic 2D echocardiograms  | The severity of TR was graded as none, trace, mild, moderate, or severe in accordance with the ASE recommendations, incorporating structural, Doppler, and quantitative parameters. |
| Lindman, 2015[16] | 1 year | 507 | 254/507 (50.1) | 84.6 ± 8.5 | BEV | The HR was adjusted for age, sex, BMI, STS score, prior MI, prior CABG, frailty, permanent pacemaker, atrial arrhythmia, aortic valve mean gradient, LVEF, and MR. | Mortality | Echocardiograms.  |  The level of TR severity was determined in line with the recommendations of the ASE. Therefore, tricuspid valve morphology, right atrial and right ventricular size, inferior vena cava size, jet area, vena contracta width, proximal isovelocity surface area radius, jet density and contour, and hepatic vein flow were assessed.  |
| Schymik , 2015[17] | 1 year | 2688 | 1138(42.3) | 81.4 ± 6.6 | BEV | The HR was adjusted for age, CAD, liver disease, renal insufficiency/failure, PA, AFib, cancer, COPD, NYHA III/IV, Logistic EuroScore, mean gradient, and BMI | Mortality | Echocardiography |  |
| Ito, 2016[18] | 412 days | 268 | 149/268 (55.6) | 80.5±7.9 | BEV | The HR were adjusted for age, sex, STS score and LVEF | Mortality | Transthoracic echocardiography  | TR severity was graded as mild, moderate, or severe and quantitated, according to the current ASE guidelines. Meanwhile, significant valvular regurgitation was defined as moderate or more.  |
| Schwartz, 2016[19] | 5 years | 519 | 223 (43) | 85.6± 6 | - | The HR were adjusted for age, gender, pacemaker, AFib, EuroScore, stroke volume index, deceleration time, sPAP, TR grade, and MR grade. | Mortality | Echocardiography  | TR severity was determined as per the recommendations of the ASE, thus including assessment of vena contracta width (79% of patients), proximal isovelocity surface area radius (9%), tricuspid valve morphology, right atrial and right ventricular size, inferior vena cava size, jet area, jet density and contour, and hepatic vein flow (in all patients). |

BEV, balloon-expandable valve; SEV, self-expandable valve; NYHA, New York Heart Association; STS PROM, Society of Thoracic Surgeons predicted risk of mortality; LVEF, left ventricular ejection fraction; DM, diabetes mellitus; CAD, coronary artery disease; MI,myocardial infarction; COPD, chronic obstructive pulmonary disease; CABG, coronary artery bypass graft; PCI, percutaneous intervention; TR, tricuspid regurgitation. sPAP, systolic pulmonary artery pressure; BMI, body mass index; PA, porcelain aorta; ASE, American Society of Echocardiography.

**Table S9:** Patients’ baseline and procedural characteristics of included studies on Tricuspid Regurgitation.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study, year** | **STS PROM** | **NYHA III/IV (%)** | **EuroScore** | **DM (%)** | **Hypertension (%)** | **Atrial Fibrillation (%)** | **CAD****(Prior MI)\* (%)** | **COPD/****(Chronic lung disease)\* (%)** | **Pulmonary Hypertension (%)** | **Peripheral Vascular Disease (%)** | **Previous CABG****(Prior PCI)\*****(%)** | **LVEF %** | **Mean Aortic Gradient mmHg** | **Aortic Valve Area cm2** | **Mod- Severe TR****(%)** |
| Barbanti, 2015 | 8.36±5.2 | 449 (86.7) | - | 156(30.1) | 402 (77.6) | 198 (38.2) | 173 (33.4)\* | 146(28.2) | 78 (15.1) | 142(27.49) | 166(32.0) | 53.96±13.9 | 42.26±16.3 | 0.76±0.4 | 79(15.25) |
| Lindman, 2015 | 10.52±5.5 | - | - | 177/507 (35) | 458/507 (90.3) | 187/507 (36.9) | 335/507 (66) | 139/507 (27.5) | - | 148/507 (29.14) | 132/507 (26.07) | 52.0 ±12.6 | 45.5 | 0.34 | 135/507 (26.6) |
| Schmiyk, 2015 | 7.9 ± 6.6 | 2,057/2,676 (76.9) | 20.4 ± 12.4 | 791(29.4) | 2,175 (80.9) | 685/2,676 (25.6) | 1,188(44.2) | 546/2,687 (20.3) | 685 (25.5) | 569/2,687 (21.2) | 431/2,688 (16.0) | 54.4 ±12.5 | 47.6 16.2 | 0.7± 0.2 | 343(14.1) |
| Ito, 2016 | 9.8 ± 5.1 | 242/268 (90.3) | - | 108/268 (40.3) | 236/268 (88.1) | 64/268 (23.9) | 164/268 (61.2) | 174/268 (64.9)\* | - | 164/268 (61.2) | 115/268 (42.9) | 54.6±12.9 | 50.4±13.4 | 0.79±0.16 | 52(19.4) |
| Schwartz, 2016 | - | 483 (93) | 20.5±14 | 182(35) | 452 (87) | 50 (9.6) | 311(60) | 88 (17) | - | - | - | 56.3±9.0 | 46.9±15 | 0.71±0.18 | 59(11.36) |

BEV, balloon-expandable valve; SEV, self-expandable valve; NYHA, New York Heart Association; STS PROM, Society of Thoracic Surgeons predicted risk of mortality; LVEF, left ventricular ejection fraction; DM, diabetes mellitus; CAD, coronary artery disease; MI,myocardial infarction; COPD, chronic obstructive pulmonary disease; CABG, coronary artery bypass graft; PCI, percutaneous intervention; TR, tricuspid regurgitation. sPAP, systolic pulmonary artery pressure; BMI, body mass index; PA, porcelain aorta.

 **Table S10:** Baseline characteristics of all four valvular etiologies

|  |  |  |  |
| --- | --- | --- | --- |
| **Characteristics** | **Patients in MR studies** | **Patients in MS studies** | **Patients in TR studies** |
| Total Patients | 5517  | 112187 | 4500 |
| Age (years) | 82.62 | 81.22 | 82.20 |
| Male Gender | 2433 (44.10%) | 58,915 (52.51%) | 2094 (46.535) |
| STS score | 7.65 | 7.16 | 8.42 |
| EuroScore | 18.20 | 20.5 | 20.42 |
| LVEF (%) | 57.83 | 53.67 | 54.31 |
| Diabetes Mellitus | 1373/5201 (26.40%) | 40,338 (35.96%) | 1414 (31.42%) |
| Hypertension | 3181/3412 (93.23%) | 92,741/110,060 (84.26%) | 3723 (82.73%) |
| Peripheral vasculardisease | 462/2347 (19.68%) | 33,302/111,670 (29.82%) | 1023 (22.73%) |
| Prior CABG | 1092/4750 (22.99%) | 14,093/47,967 (29.38%) | 844/3981 (21.20%) |
| Prior CAD | 933/5201 (17.94%)  | 55,872 (49.80%) | 2171 (48.24%) |
| Atrial fibrillation/flutter | 1297/4870 (26.63%) | 46,744/110,060 (42.47%) | 1184 (26.31%) |
| Baseline NYHA classIII/IV | 3963/5517 (71.83%) | 11,690/48,405 (24.15%) | 3231/3933 (80.91%) |

**Abbreviations**: MR: mitral regurgitation; MS: mitral stenosis; TR: tricuspid regurgitation; STS PROM: Society of Thoracic Surgeons predicted risk of mortality; LVEF: left ventricular ejection fraction; CABG: coronary artery bypass graft; CAD: coronary artery disease; NYHA: New York Heart Association

**Table S11:** Risk of bias in mitral regurgitation studies.

|  |
| --- |
| Newcastle-Ottawa scale for Non-RCTs |
|  | **Selection** | **Comparability** | **Outcome** |  |
| Author, Year | **Representativeness of the exposed cohort** | **Selection of non- exposed****cohort** | **Ascertainment of exposure** | **Demonstration that outcome was not PRESENT at start of study** | **Comparability of groups on the basis of analysis** | **Assessment of outcomes** | **Was follow up long enough for outcomes to occur?** | **Adequacy of follow up of cohorts** | **Total score** |
|  | *MR in AS population* | *TAVR/TAVI* | *Record* | *Prospective or retrospective record* | *Controlled* | *Records / Investigations* | *In hospital and longer* | *>90%* |  |
| Toggweiler, 2012 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 9 |
| Barbanti, 2013 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 9 |
| Bedogni, 2013 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 9 |
| Khawaja, 2014 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 9 |
| Sullivan, 2015 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 9 |
| Feldt, 2019 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 9 |
| Miura, 2020 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 9 |

**Table S12:** Risk of bias in mitral stenosis studies.

|  |
| --- |
| **Newcastle-Ottawa scale for Non-RCTs** |
|  | **Selection** | **Comparability** | **Outcome** |  |
| **Author, Year** | **Representativeness of the exposed cohort** | **Selection of non-exposed cohort** | **Ascertainment of exposure** | **Demonstration that outcome was not PRESENT at start of****study** | **Comparability of groups on the basis of analysis** | **Assessment of outcome** | **Was follow up long enough for outcomes to****occur?** | **Adequacy of follow up of cohorts** | **Total score** |
|  | *MS in AS population* | *TAVR/TAVI* | *Record* | *Prospective or retrospective record* | *Controlled* | *Records / Investigations* | *In hospital and longer* | *>90%* |  |
| **Abramowitz, 2017** | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 9 |
| **Joseph, 2018** | 1 | 1 | 1 | 1 | 2 | 0 | 1 | 1 | 9 |
| **Asami, 2018** | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 9 |
| **Fischer, 2019** | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 9 |
| **Al-khadra, 2019** | 1 | 1 | 1 | 1 | 2 | 0 | 1 | 1 | 9 |
| **Sannino, 2019** | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 9 |
| **Kato, 2019** | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 9 |

**Table S13:** Risk of bias in tricuspid regurgitation studies.

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| --- |
| **Newcastle-Ottawa scale for Non-RCTs** |
|  | **Selection** | **Comparability** | **Outcome** |  |
| **Author, year** | **Representativeness of the exposed cohort** | **Selection of non- exposed****cohort** | **Ascertainment of exposure** | **Demonstration that outcome was not PRESENT at start of study** | **Comparability of groups on the basis of analysis** | **Assessment of outcome** | **Was follow up long enough for outcomes to occur?** | **Adequacy of follow up of cohorts** | **Total score** |
|  | *TR in AS population* | *TAVR* | *Record* | *Prospective or retrospective record* | *Controlled* | *Records / Investigations* | *In hospital and longer* | *>90%* |  |
| **Barbanti,****2015** | 1 | 1 | 0 | 1 | 2 | 0 | 1 | 1 | 8 |
| **Lindman,****2015** | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 9 |
| **Schmiyk,****2015** | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 9 |
| **Ito, 2016** | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 9 |
| **Schwartz,****2016** | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 9 |

# References

1. Toggweiler S, Boone RH, Rodés-Cabau J, Humphries KH, Lee M, Nombela-Franco L, Bagur R, Willson AB, Binder RK, Gurvitch R, Grewal J, Moss R, Munt B, Thompson CR, Freeman M, Ye J, Cheung A, Dumont E, Wood DA, Webb JG. Transcatheter aortic valve replacement: outcomes of patients with moderate or severe mitral regurgitation. *J Am Coll Cardiol.* 59(23), 2068-74 (2012).
2. Barbanti M, Webb JG, Hahn RT, Feldman T, Boone RH, Smith CR, Kodali S, Zajarias A, Thompson CR, Green P, Babaliaros V, Makkar RR, Szeto WY, Douglas PS, McAndrew T, Hueter I, Miller DC, Leon MB; Placement of Aortic Transcatheter Valve Trial Investigators. Impact of preoperative moderate/severe mitral regurgitation on 2-year outcome after transcatheter and surgical aortic valve replacement: insight from the Placement of Aortic Transcatheter Valve (PARTNER) Trial Cohort A. *Circulation.* 128(25), 2776-84 (2013).
3. Bedogni F, Latib A, De Marco F, Agnifili M, Oreglia J, Pizzocri S, Latini RA, Lanotte S, Petronio AS, De Carlo M, Ettori F, Fiorina C, Poli A, Cirri S, De Servi S, Ramondo A, Tarantini G, Marzocchi A, Fiorilli R, Klugmann S, Ussia GP, Tamburino C, Maisano F, Brambilla N, Colombo A, Testa L. Interplay between mitral regurgitation and transcatheter aortic valve replacement with the CoreValve Revalving System: a multicenter registry. *Circulation.* 128(19), 2145-53 (2013).
4. Khawaja MZ, Wang D, Pocock S, Redwood SR, Thomas MR. The percutaneous coronary intervention prior to transcatheter aortic valve implantation (ACTIVATION) trial: study protocol for a randomized controlled trial. *Trials.* 15, 300 (2014).
5. O'Sullivan CJ, Stortecky S, Bütikofer A, Heg D, Zanchin T, Huber C, Pilgrim T, Praz F, Buellesfeld L, Khattab AA, Blöchlinger S, Carrel T, Meier B, Zbinden S, Wenaweser P, Windecker S. Impact of mitral regurgitation on clinical outcomes of patients with low-ejection fraction, low-gradient severe aortic stenosis undergoing transcatheter aortic valve implantation. *Circ Cardiovasc Interv.* 8(2):e001895 (2015).
6. Feldt K, De Palma R, Bjursten H, Petursson P, Nielsen NE, Kellerth T, Jönsson A, Nilsson J, Rück A, Settergren M. Change in mitral regurgitation severity impacts survival after transcatheter aortic valve replacement. *Int J Cardiol.* 294, 32-36 (2019).
7. Miura M, Yamaji K, Shirai S, Hayashi M, Kawaguchi T, Arai Y, Sakaguchi G, Ando K, Naganuma T, Mizutani K, Araki M, Tada N, Yamanaka F, Tabata M, Ueno H, Takagi K, Higashimori A, Watanabe Y, Yamamoto M, Hayashida K; of the OCEAN-TAVI Investigators. Clinical Impact of Preprocedural Moderate or Severe Mitral Regurgitation on Outcomes After Transcatheter Aortic Valve Replacement. *Can J Cardiol.* 36(7), 1112-1120 (2020).
8. Abramowitz Y, Kazuno Y, Chakravarty T, Kawamori H, Maeno Y, Anderson D, Allison Z, Mangat G, Cheng W, Gopal A, Jilaihawi H, Mack MJ, Makkar RR. Concomitant mitral annular calcification and severe aortic stenosis: prevalence, characteristics and outcome following transcatheter aortic valve replacement. *Eur Heart J.* 38(16), 1194-1203 (2017).
9. Joseph L, Bashir M, Xiang Q, Yerokun BA, Matsouaka RA, Vemulapalli S, Kapadia S, Cigarroa JE, Zahr F. Prevalence and Outcomes of Mitral Stenosis in Patients Undergoing Transcatheter Aortic Valve Replacement: Findings From the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapies Registry. *JACC Cardiovasc Interv.* 11(7), 693-702 (2018).
10. Asami M, Windecker S, Praz F, Lanz J, Hunziker L, Rothenbühler M, Räber L, Roost E, Stortecky S, Pilgrim T. Transcatheter aortic valve replacement in patients with concomitant mitral stenosis. *Eur Heart J.* 40(17), 1342-1351 (2019).
11. Fischer Q, Himbert D, Bernier M, Urena M, Nunes Ferreira-Neto A, Paradis JM, Mohammadi S, Iung B, Rodés-Cabau J. Impact of moderate to severe mitral stenosis in patients undergoing transcatheter aortic valve replacement. *Int J Cardiol.* 286, 36-42 (2019).
12. Al-Khadra Y, Alraies MC, Darmoch F, Pacha HM, Soud M, Kajy M, Kaki A, AlJaroudi WA, Kwok CS, Mamas M, Kapadia S. In-Hospital Outcomes of Transcatheter Aortic Valve Implantation in Patients With Mitral Valve Stenosis. *Am J Cardiol.* 123(9), 1510-1516 (2019).
13. Sannino A, Potluri S, Pollock B, Filardo G, Gopal A, Stoler RC, Szerlip M, Chowdhury A, Mack MJ, Grayburn PA. Impact of Mitral Stenosis on Survival in Patients Undergoing Isolated Transcatheter Aortic Valve Implantation. *Am J Cardiol.* 123(8), 1314-1320 (2019).
14. Kato N, Padang R, Pislaru C, Miranda WR, Hoshina M, Shibayama K, Watanabe H, Scott CG, Greason KL, Pislaru SV, Nkomo VT, Pellikka PA. Hemodynamics and Prognostic Impact of Concomitant Mitral Stenosis in Patients Undergoing Surgical or Transcatheter Aortic Valve Replacement for Aortic Stenosis. *Circulation.* 140(15), 1251-1260 (2019).
15. Barbanti M, Binder RK, Dvir D, Tan J, Freeman M, Thompson CR, Cheung A, Wood DA, Leipsic J, Webb JG. Prevalence and impact of preoperative moderate/severe tricuspid regurgitation on patients undergoing transcatheter aortic valve replacement. *Catheter Cardiovasc Interv.* 85(4), 677-84 (2015).
16. Lindman BR, Maniar HS, Jaber WA, Lerakis S, Mack MJ, Suri RM, Thourani VH, Babaliaros V, Kereiakes DJ, Whisenant B, Miller DC, Tuzcu EM, Svensson LG, Xu K, Doshi D, Leon MB, Zajarias A. Effect of tricuspid regurgitation and the right heart on survival after transcatheter aortic valve replacement: insights from the Placement of Aortic Transcatheter Valves II inoperable cohort. *Circ Cardiovasc Interv.* 8(4), 10.1161/CIRCINTERVENTIONS.114.002073 e002073 (2015).
17. Schymik G, Lefèvre T, Bartorelli AL, Rubino P, Treede H, Walther T, Baumgartner H, Windecker S, Wendler O, Urban P, Mandinov L, Thomas M, Vahanian A. European experience with the second-generation Edwards SAPIEN XT transcatheter heart valve in patients with severe aortic stenosis: 1-year outcomes from the SOURCE XT Registry. *JACC Cardiovasc Interv.* 8(5), 657-69 (2015).
18. Ito S, Pislaru SV, Soo WM, Huang R, Greason KL, Mathew V, Sandhu GS, Eleid MF, Suri RM, Oh JK, Nkomo VT. Impact of right ventricular size and function on survival following transcatheter aortic valve replacement. *Int J Cardiol.* 221, 269-74 (2016).
19. Schwartz LA, Rozenbaum Z, Ghantous E, Kramarz J, Biner S, Ghermezi M, Shimiaie J, Finkelstein A, Banai S, Aviram G, Ingbir M, Keren G, Topilsky Y. Impact of Right Ventricular Dysfunction and Tricuspid Regurgitation on Outcomes in Patients Undergoing Transcatheter Aortic Valve Replacement. *J Am Soc Echocardiogr.* 30(1), 36-46 (2017).