Table 1: Studies on the change in diastolic dysfunction in patients with AS after AVR

1st Author / Year	N	AVR	Diastolic dysfunction evaluation	Diastolic dysfunction variables	Grading	Change in diastolic dysfunction after AVR
Villari 1995[A]	12	SAVR	Cath	Peak filling rate early and late, and the myocardial stiffness constant (b)	No	**Baseline** / **Early (22m)** / **Late (81m)** PFR Early: 402±111 / 372±83 / 330 ±132 PFR Late: 370±107 / 332 ±121 / 276±123 b: 21±6 / 30±7 / 11 ±4
Villari 1996[B]	10	SAVR	Cath	Peak filling rate, myocardial stiffness constant (b)	No	**Baseline** / **Early (21m)** / **Late(89m)** PFR: 384 ±95 / 388±57 / 353 ±79 b: 19±5 / 28±7 / 10±3 * * P<0.001 early vs. late after AVR
Bech-Hanssen 1999[C]	239	SAVR	TTE	E/A, S/D, DT	None, mild to moderate, severe	**Baseline** / **2 years** **Mechanical Valves** E/A: 1.0 ± 0.74 / 1.02 ± 0.31 P=0.4 S/D: 1.41 ± 0.64 / 1.26 ± 0.33 P<0.01 DT: 239 ± 99.5 / 238 ± 72.5 P=0.21 **Biologic prosthetic valves** E/A: 1.0 ± 0.57 / 0.94 ± 0.3 P=0.4 S/D: 1.36 ± 0.58 / 1.29 ± 0.53 P=0.15 DT: 268 ± 120 / 241 ± 68 P=0.15
McKenney 1999[D]	14	SAVR	TTE	LVED area at similar pulmonary arterial wedge pressure, DT	No	**Baseline** / **Postprocedural** LVED area: 17.9 ±1.7 / 12.1 ±1.2 P< 0.0001 DT: 260 ±30 / 108 ±4 P<0.0001
Ikonomidis 2001[E]	41	SAVR	TTE	E/A, IVRT, DT	No	**Baseline** / **2w after SAVR** / **4y after SAVR** DT: 241 ±102 / 205 ±77 / 226 ±96 * IVRT: 93 ± 20 / 78 ±12 / 81 ±15 * E/A: 1.05 ±0.5 / 1.0 ±0.5 / 91 ±0.3 * P<0.05 baseline vs. 4y after SAVR
Lamb 2002[F]	12	SAVR	MRI	E/A peak	No	**Baseline** / **Postprocedural** E/A peak: 1.40 ±0.88 / 1.34 ±0.6 P=NS
Gjertsson 2005[G]	57	SAVR	TTE	DT	None, Grade I, Grade II, Grade III	**Baseline** / **2y** / **10y** DT: 272±107 / 248 ±73 (P<0.05) / 236 ±88 (P<0.05) 10y follow-up: 61% decrease in patients with moderate to severe diastolic dysfunction (P< 0.0001)
Ding 2007[H]	66	SAVR	TTE	E/A, IVRT	No	**Baseline** / **46 months** E/A: 2.6±0.2 / 1.9±0.1 P<0.05 IVRT: 57±4 / 69±3 P<0.01
Brown 2009[I]	115	SAVR	TTE	E/e', LA size, DT	None, delayed relaxation, increased LA pressure	Diastolic dysfunction persisted postoperatively in 84% of patients with baseline diastolic dysfunction, while 46% of them (persisted diastolic dysfunction) had P/PM
Guaraccino 2010[J]	30	SAVR & TAVR	TEE	Vp, e'	No	**Baseline** / **Postprocedural** **TAVR** Vp: 35 ± 6.4 / 43 ±7.5 *

						e' 4.0 ±0.5 5.0 ±0.7 * **SAVR** Vp 37 ±6.0 29 ±5.4 * e' 4.2 ±0.5 3.1 ±0.7 * * p <0.001 baseline vs. postprocedural
Seo 2012[K]	38	SAVR	TTE	e', E/A, E/e', DT	No	**Baseline** **25weeks** **50weeks** E/A 1.2±0.4 0.9±0.3 * 0.9±0.3 DT 237.8±54 177.8±30.6 * 162.7±35.6 E/e' 15.5±4.7 16.9±4.8 * 17.8±5 e' 6.3±1.8 7.8±2.0 * 9.2±3.3 * * P<0.05 baseline vs. 25w or 50w
Gotzmann 2010[L]	39	TAVR	TTE	e', E/e'	No	**Baseline** **30d** **6m** e' 5.19 ± 1.56 5.62 ± 1.54 (P=0.15) 5.8 ± 1.53 (P=0.004) E/e' 20 ± 6.7 18.1 ± 5.7 (P=0.153) 17.2 ± 5.4 (P=0.21)
Vizzardi 2010[M]	135	TAVR	TTE	E/A, E/e', DT	None, Grade I, Grade II, Grade III	**Baseline** **6 months** DT 210±48 230 ±71 P=0.08 e' 4.1 6 ±1.7 5.6±2.2 P<0.0001 E/e' 24 ±7 17±6 P<0.0001
Tzikas 2011[N]	63	TAVR	TTE	E/A, DT, e', E/e'	None, Grade I, Grade II, Grade III	**Baseline** **Discharge** **1y** Grade I 59% 51% 57% Grade II 23% 36% 33% Grade III 18% 13% 10% P=1.0
Gonzalvez 2011[O]	61	TAVR	TTE & TEE	E/A, IVRT, DT	None, Grade I, Grade II, Grade III	**Baseline** **Postprocedural** E/A 1.2 (0.9; 1.4) 1.5 (1.2; 1.8) P=0.002 DT 211.2 (191.7; 230.6) 252.7 (226.8; 278.7) P=0.001 IVRT 83.0 (73.8; 92.8) 97.1 (87.9; 106.4) P=0.003
Spethmann 2013[P]	46	TAVR	TTE	E/e'	None, Grade I, Grade II, Grade III	46.9% of the patients improved by at least one grade **Baseline** **8 days after TAVR** E/e' 18.7±8 17.6±7.3 P=NS
Spethmann 2014[Q]	54	TAVR	TTE	e', E/e', E/A, DT, IVRT	None, Grade I, Grade II, Grade III	**Baseline** **12months post TAVR** e' 5.5±1.6 6.2±1.9 E/E' 17.4±7.4 15.9±6 IVRT 108.9±37.5 120.4 ±33.6 DT 204.1±73.7 224.2 ±62.5 E/A 1.16 ±0.77 1.16± 0.83 P=0.17 for e', P = NS otherwise Diastolic dysfunction grade III 24% 10% grade II 34% 26% grade I 42% 52% None 0 12% P=NS
Aslan 2015[R]	55	TAVR	TTE	E/e'	No	**Pre-operation** **7-days after TAVR** E/e' 13.7±4.6 11.5 ± 4.1 P< 0.001
Muratori 2015[S]	358	TAVR	TTE	E/A ratio, DT, e', E/e'	None, Grade I, Grade II, Grade III	***LVEF<50%*** **Baseline** **12months** Diastolic dysfunction grade ≥II 100% 58.8% *

						LVEF ≥ 50% **Baseline** **12months** Diastolic dysfunction grade ≥II 100% 87.1% * * P < 0.001

AS=Aortic Stenosis, AVR=Aortic Valve Replacement, SAVR=Surgical Aortic Valve Replacement, TAVR=Transcatheter Aortic Valve Replacement, TEE=Transesophageal echocardiogram, TTE=Transthoracic echocardiogram, LA=Left Atrial, LVEF=Left Ventricular Ejection Fraction, LVED=Left Ventricular End Diastolic; DT= deceleration time, Vp=transmitral flow propagation velocity. E=peak early transmitral velocity, A= peak late transmitral velocity, e'= peak early mitral annular velocity Doppler, S= peak systolic pulmonary vein flow velocity, D= peak diastolic pulmonary vein velocity, CV=Cardiovascular, P/PM=Patient-Prosthesis Mismatch, HR= Hazard Ratio, OR=Odds Ratio

Table 2: Studies on the impact of diastolic dysfunction on clinical outcomes of patients with AS undergoing AVR

1st Author / Year	N	AVR	Diastolic dysfunction evaluation	Diastolic dysfunction variables	Diastolic dysfunction grading	Measured outcome	Results
Lund 1997[T]	91	SAVR	TTE	LV fast filling fraction, LV late filling fraction	No	Short and long-term mortality	LV fast filling fraction <45% had a regression coefficient = 0.98 (p=0.03) for crude mortality and 1.07 (p=0.03) for aortic stenosis specific deaths
Bernard 2001[U]	66	SAVR	TTE	E/A, DT, S/D	None, Grade I, Grade II, Grade III	Need for inotropic support 0-12 hours after surgery	Diastolic dysfunction OR: 6.17; 95% CI: (1.9–19.8), P= 0.002
Gjertsson 2005[V]	399	SAVR	TTE	E/A, S/D	None, Grade I, Grade II, Grade III	Long-term mortality	Grade II-III vs. Grade I-normal: HR 1.72; p=0.005 for mortality risk Patients with mild diastolic dysfunction did not have decreased survival compared to the general population
Denault 2006[W]	54	SAVR	TTE	e'	None, Grade I, Grade II, Grade III	Separation from cardiopulmonary bypass	65.5% of the patients with moderate to severe diastolic dysfunction had a difficulty in the separation from the cardiopulmonary bypass vs. 40.9% for patients with no or mild diastolic dysfunction, P = 0.017
Ding 2010[X]	112	SAVR	TTE	E/A	No	Short and long-term mortality	HR 1.85; 95% CI: (1.06–3.22),P= 0.03 for short term mortality HR 2.09; 95% CI: (1.24–3.12) p<0.01 for long-term mortality HR 3.35; 95% CI: (1.23–9.17); p<0.01 for long-term mortality (elderly only)
Linker 2010[Y]	108	SAVR	TEE	E/A, DT, S/D	None, Grade I, Grade II, Grade III	Weaning off ventilator	Diastolic dysfunction was a risk factor for post-CPB LV dysfunction. Multivariate logistic regression for Vp<40cm/s effect in weaning off ventilator: OR = 0.65; 95% CI: 0.52-0.81
Chang 2010[Z]	248	SAVR	TTE	E/e'	No	In-hospital and Long-term CV Events	E/e' >12 was associated with increased in- hospital (P=0.04) and long-term CV events (10.1% vs. 2.8%, P=0.03)
Rassi 2013[AA]	1267	SAVR	Exercise TTE	E/A, S/D, LA size	Normal, stage I, stage II	Long term Mortality or AVR (combined)	Baseline stage II diastolic dysfunction was an independent predictor of the composite endpoint of death and AVR, HR; 1.75; 95% CI: 1.13-2.71, P= 0.012. Mild diastolic dysfunction had not a significant association with the endpoint
Tann 2015[BB]	432	SAVR	TTE	E/e'	No	Combined Endpoint*, Long-term mortality	Combined Endpoint* adjusted OR:1.40; 95% CI: 1.03-1.78 Long-term mortality adjusted OR:1.51; 95% CI: 1.18-1.92

Muratori 2015[S]	358	TAVR	TTE	E/A, DT, e', E/e'	None, Grade I, Grade II, Grade III	1 year mortality	Similar mortality among patients with advanced vs. mild diastolic dysfunction Patients with baseline severe diastolic dysfunction who showed an improvement in their diastolic dysfunction after TAVR had better one year survival, compared to those who did not show an improvement
Kampaktsis 2016[CC]	195	TAVR	TTE	e', LAVI, E/A, DT	None, Grade I, Grade II, Grade III	Long-term mortality	Severe diastolic dysfunction was not independently associated with mortality Severe diastolic dysfunction with Post-TAVR AR was associated with increased mortality (HR: 3.89; 95% CI: 1.76–8.6; P=0.001)

*combined endpoint: in-hospital mortality or major morbidity defined as all-cause death, stroke, renal failure (Risk, Injury, Failure, Loss of kidney function or End-stage kidney disease [RIFLE] classification ≥3)

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