SUPPLEMENTAL MATERIAL

Data S1.

Supplemental Methods

Search strategy.

<u>PubMed</u> (n=200 on March 8, 2021)

("Tetralogy of Fallot"[Mesh] OR fallot* tetralogy OR tetralogy of fallot) AND (restrictive OR end-diastolic forward flow OR end diastolic forward flow OR antegrade diastolic pulmonary flow OR antegrade diastolic flow) in all fields

Embase (n=210 on March 8, 2021)

('fallot tetralogy'/exp OR 'fallot* tetralogy' OR 'tetralogy of fallot') AND ('restrictive' OR 'enddiastolic forward flow' OR 'end diastolic forward flow' OR 'antegrade diastolic pulmonary flow' OR 'antegrade diastolic pulmonary artery flow' OR 'antegrade diastolic flow') in all fields

<u>Scopus</u> (n=142 on March 8, 2021)

(TITLE-ABS-KEY ("fallot's tetralogy" OR "fallot* tetralogy" OR "tetralogy of fallot") AND TITLE-ABS-KEY ("restrictive" OR "end-diastolic forward flow" OR "end diastolic forward flow" OR "antegrade diastolic pulmonary flow" OR "antegrade diastolic pulmonary artery flow" OR "antegrade diastolic flow"))

Supplemental Results

Subgroup analyses

Subgroup analysis revealed that significantly different results were observed by prospective and retrospective studies for the following variables: right ventricular mass indexed (RVMi), right ventricular end-diastolic pressure (RVEDP), left ventricular stroke volume indexed (LVSVi), and left ventricular ejection fraction (LVEF). Prospective studies reported a significantly greater RVMi in end-diastolic forward flow (EDFF) (mean difference [MD] 3.81 g/m², 95% 1.42-6.21, 6 studies), whereas a retrospective study³⁷ reported lower RVMi (MD -0.70 g/m², 95% CI -1.21;-0.18, 1 study) (p<0.001). Furthermore, retrospective studies reported higher RVEDP in patients with EDFF (MD 1.78, 95% CI 0.93-2.63, 3 studies), as well as lower LVSVi (MD -2.03, 95% CI -2.48;-1.57, 1 study³⁷) and higher LVEF (MD 0.95%, 95% 0.60-1.30, 6 studies). In contrast, prospective studies found no significant differences in either RVEDP (MD 0.00 mmHg, 95% CI -0.75-0.75, 1 study²⁵), LVSVi (MD -0.25 ml/m², 95% CI -1.13-0.63, 1 study²⁷), or LVEF (MD -1.08%, 95% CI -2.37-0.21, 3 studies) (test for subgroup differences: all p<0.001). Lastly, the association between transannular patch repair and EDFF found by prospective studies (odds ratio [OR] 2.46, 95% 1.47-4.13, 14 studies) was greater than that found by retrospective studies (OR 1.38, 95% CI 0.51-3.73, 7 studies) (test for subgroup differences: p=0.001). No other significant interaction effects were observed.

Meta-regression analyses

Meta-regression analysis revealed that in more recent samples (higher mean year of enrollment) reported a larger MD for right ventricular end-diastolic volume indexed (RVEDVi) (regression coefficient 1.762, 95% CI 0.395-3.129, p=0.018, 10 studies) and aortic cross-clamp time (regression coefficient 0.844, 95% CI 0.138-1.550, p=0.029, 6 studies) in EDFF compared to no EDFF. Furthermore, larger MD for RVEDVi were associated with larger MD for right

ventricular stroke volume indexed (RVSVi) (regression coefficient 0.465, 95% CI 0.144-0.786, p=0.016, 6 studies) and pulmonary regurgitation fraction (regression coefficient 0.214, 95% CI 0.003-0.424, p=0.048, 8 studies). Lastly, it was found that older age at evaluation was associated with smaller MD for RVSVi (regression coefficient -1.142, 95% CI -1.610;-0.674, p=0.003, 6 studies) and greater MD for N-terminal pro-brain natriuretic peptide (NT-proBNP) (regression coefficient 15.324, 95% CI 0.797-29.850, p=0.047, 3 studies). No other significant associations were found.

Figure S1. Forest plots. CI, confidence interval; EDFF, end-diastolic forward flow; MD, mean difference; SD, standard deviation.

A. Age at repair (years)

Study	Total	Mean	EDFF SD	Total	No Mean	EDFF SD		Mean	Differ	ence		MD	95	%-CI	Weight (fixed)	Weight (random)
Ahmad 2012	58	1.00	0.55	54	0.83	1.38			ŧ			0.17	[-0.23;	0.56]	1.3%	8.3%
Bonello 2013	38	7.50	1.50	110	4.62	1.08			-	-		2.88	[2.36;	3.39]	0.7%	7.5%
Choi 2008	15	1.12	0.30	28	2.63	1.35			+			-1.51	[-2.03;	-0.99]	0.7%	7.5%
Helbing 1996	13	1.42	0.67	6	1.58	0.83			+			-0.17	[-0.93;	0.59]	0.3%	6.0%
Kordybach-Prokopiuk 2018	16	12.60	10.50	67	11.70	12.60		-	-			0.90	[-5.06;	6.86]	0.0%	0.2%
Kutty 2018	122	0.90	0.29	277	1.32	0.58			. 1			-0.41	[-0.50;	-0.33]	27.1%	9.6%
Lee 2013	33	1.50	0.96	17	1.10	0.67			+			0.40	[-0.06;	0.86]	0.9%	7.9%
Mercer-Rosa 2018	77	0.35	0.07	11	0.35	0.10						0.00	[-0.06;	0.06]	53.1%	9.7%
Munkhammar 1998	13	0.77	0.18	34	0.64	0.26			e			0.13	[0.00;	0.26]	11.5%	9.5%
Norgard 1996	36	11.02	6.82	56	11.85	7.10		-	-+			-0.82	[-3.73;	2.08]	0.0%	1.0%
Norgard 1998 (early restriction)	16	11.07	6.75	18	1.20	0.33				- 2		9.88	[6.56; 1	13.19]	0.0%	0.8%
Norgard 1998 (late restriction)	10	10.93	6.75	22	3.16	1.57					+	7.77	[3.53; 1	12.00]	0.0%	0.5%
Samyn 2013	12	1.31	0.53	17	1.51	0.67			-			-0.20	[-0.63;	0.24]	1.0%	8.0%
Tominaga 2021	23	3.88	0.89	23	3.00	0.50			+			0.88	[0.46;	1.30]	1.1%	8.2%
van den Berg 2007	24	1.00	0.50	12	0.90	0.50			+			0.10	[-0.25;	0.45]	1.6%	8.6%
Xu 2014	30	1.48	1.70	50	0.78	0.60			+-			0.70	[0.07;	1.33]	0.5%	6.8%
Fixed-effects	536			802								-0.07	[-0.11;	0.02]	100.0%	
Random-effects									-			0.33	[-0.42;	1.08]		100.0%
Heterogeneity: $l^2 = 95\%$, $p < 0.00$	1							1	1							
Test for overall effect (fixed effect)	: z = -2	.90 (p =	= 0.004)			-10	-5	0	5	10					
Test for overall effect (random effe	ects): t	= 0.9	4(n = 0)	363)			10	0	-	~						

B. Time of follow-up since repair (years)

		E	DFF		No E	DFF									Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD		Mean	Diffe	rence	•	MD	95	5%-CI	(fixed)	(random)
Gatzoulis 1998	36	5.00	3.00	56	4.20	2.80				_		0.80	[-0.42;	2.02]	3.8%	13.6%
Helbing 1996	13	10.33	2.67	6	10.17	2.67		_	-			0.17	[-2.41;	2.75]	0.8%	6.8%
Kordybach-Prokopiuk 2018	16	20.90	6.10	67	21.80	7.10			• -	-		-0.90	[-4.34;	2.54]	0.5%	4.5%
Kutty 2018	122	17.36	2.38	277	18.82	2.22		-				-1.46	[-1.96;	-0.96]	22.8%	17.9%
Mori 2017	23	13.40	8.86	39	12.38	9.44			1			- 1.02	[-3.66;	5.70]	0.3%	2.8%
Norgard 1998 (early restriction)	16	1.88	0.45	18	1.80	0.47						0.07	[-0.23;	0.38]	59.2%	18.6%
Norgard 1998 (late restriction)	10	2.00	1.00	22	1.70	1.10			+			0.30	[-0.47;	1.07]	9.4%	16.4%
Samyn 2013	12	14.25	3.00	17	13.00	3.00			-#-	•	-	1.25	[-0.97;	3.47]	1.1%	8.2%
van den Berg 2007	24	16.00	2.00	12	13.25	2.50				-•		2.75	[1.12;	4.38]	2.1%	11.1%
Fixed-effects	272			514					-			-0.16	[-0.39;	0.08]	100.0%	
Random-effects							-	-	-	- 1 - C		0.32	[-0.65;	1.29]		100.0%
Heterogeneity: $I^2 = 83\%$, $p < 0.00$	1						1		1		1					
Test for overall effect (fixed effect): $z = -1$	1.30 (p =	= 0.19	4)			-4	-2	0	2	4					
Test for overall effect (random eff	ects): t	s = 0.75	(p =	0.472)												

C. Age at study (years)

			EDFF		No	EDFF				Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD	Mean Difference	MD	95%-CI	(fixed)	(random)
Aburawi 2014	9	11.00	2.60	11	10.00	0.90		1.00	[-0.78; 2.78]	2.5%	4.7%
Ahmad 2012	58	13.60	3.20	54	12.30	3.10		1.30	[0.13; 2.47]	5.9%	5.1%
Bonello 2013	38	36.77	3.14	110	30.02	3.25		6.75	[5.58; 7.92]	5.9%	5.1%
Chaturvedi 1999	4	1.88	1.60	7	1.31	0.45	-	0.57	[-1.03; 2.17]	3.1%	4.8%
Choi 2008	15	5.44	2.15	28	4.48	1.04	+	0.96	[-0.19; 2.11]	6.0%	5.1%
Cullen 1995	17	1.96	2.42	18	1.80	1.77	-	0.16	[-1.25; 1.57]	4.0%	5.0%
Gatzoulis 1995	17	28.30	6.60	12	27.60	5.50		0.70	[-3.72; 5.12]	0.4%	2.7%
Gatzoulis 1998	36	15.03	7.12	56	14.43	7.22		0.60	[-2.40; 3.60]	0.9%	3.7%
Helbing 1996	13	11.83	2.83	6	11.50	2.92		0.33	[-2.47; 3.13]	1.0%	3.9%
Kordybach-Prokopiuk 2018	16	30.30	9.90	67	31.80	12.00		-1.50	[-7.14; 4.14]	0.3%	2.1%
Kutty 2018	122	18.92	2.75	277	21.32	2.65		-2.40	[-2.98; -1.82]	23.9%	5.4%
Lee 2013	33	12.90	2.90	17	13.40	2.60		-0.50	[-2.08; 1.08]	3.2%	4.9%
Mercer-Rosa 2018	77	12.90	3.20	11	11.10	2.90		1.80	[-0.06; 3.66]	2.3%	4.7%
Mori 2017	23	15.83	9.64	39	15.63	11.73		0.20	[-5.19; 5.59]	0.3%	2.2%
Munkhammar 1998	13	5.90	3.60	34	3.40	2.70		2.50	[0.34; 4.66]	1.7%	4.4%
Rathore 2006	52	7.60	2.40	28	8.10	3.50		-0.50	[-1.95; 0.95]	3.8%	4.9%
Sachdev 2006	24	4.40	2.30	26	5.50	3.10		-1.10	[-2.61; 0.41]	3.5%	4.9%
Samyn 2013	12	16.25	4.00	17	15.00	2.67		1.25	[-1.34; 3.84]	1.2%	4.1%
Sandeep 2019	28	2.56	2.38	22	1.67	0.89	-	0.89	[-0.07; 1.85]	8.8%	5.2%
Sani 2020	18	25.40	9.10	12	28.20	9.80		-2.80	[-9.76; 4.16]	0.2%	1.6%
Shekerdemian 1999	8	3.25	3.92	15	2.05	1.62		1.20	[-1.64; 4.04]	1.0%	3.9%
Tominaga 2021	23	35.00	10.00	23	38.80	14.30		-3.80	[-10.93; 3.33]	0.2%	1.5%
van den Berg 2007	24	17.25	2.17	12	14.00	2.67		3.25	[1.51; 4.99]	2.6%	4.7%
Xu 2014	30	1.48	1.71	15	0.78	0.60		0.70	[0.02; 1.38]	17.2%	5.4%
Fixed-effects	710			917			8	0.33	[0.04; 0.61]	100.0%	
Random-effects								0.77	[-0.08; 1.62]		100.0%
Heterogeneity: $I^2 = 90\%$, $p < 0$	0.001						I I I I I				

Heterogeneity: $\Gamma = 90\%$, p < 0.001Test for overall effect (fixed effect): z = 2.26 (p = 0.024) Test for overall effect (random effects): $t_{23} = 1.87$ (p = 0.074)

-10 -5 0 5 10

Figure S2. Forest plots. BT, Blalock-Taussig; CI, confidence interval; EDFF, end-diastolic forward flow; MD, mean difference; OR, odds ratio; RVPA, right ventricle-pulmonary artery; SD, standard deviation.

A. Previous RVPA shunt



B. Previous BT shunt

		EDFF	Nol	EDFF				Weight	Weight
Study	Events	Total	Events	Total	Odds Ratio	OR	95%-CI	(fixed)	(random)
Cullen 1995	1	17	1	18		1.06	[0.06; 18.45]	2.6%	2.9%
Helbing 1996	4	13	1	6	<u> </u>	- 2.22	[0.19; 25.72]	2.7%	4.0%
Gatzoulis 1995	2	20	2	18		0.89	[0.11; 7.06]	5.3%	5.6%
Munkhammar 1998	4	13	9	23	_	0.69	[0.16; 2.93]	12.6%	11.5%
Norgard 1996	14	36	30	56		0.55	[0.24; 1.29]	40.3%	33.1%
Norgard 1998 (early restriction)	6	16	6	18		1.20	[0.29; 4.91]	9.9%	12.1%
Rathore 2006	2	52	1	28	 	1.08	[0.09; 12.46]	3.5%	4.0%
Samyn 2013	6	12	6	17		1.83	[0.41; 8.27]	7.0%	10.6%
Shekerdemian 1999	1	8	3	15		0.57	[0.05; 6.61]	5.1%	4.0%
Tominaga 2021	5	23	5	23		1.00	[0.25; 4.06]	11.0%	12.2%
Fixed-effects		210		222		0.87	[0.54; 1.40]	100.0%	
Random-effects					4	0.86	[0.62; 1.20]		100.0%
Heterogeneity: $I^2 = 0\%$, $p = 0.960$									
Test for overall effect (fixed effect)): z = -0.5	8 (p = (0.562)		0.1 0.5 1 2 10				
Test for overall effect (random effect	ects): t ₉ =	-0.99 (p = 0.347)					

C. Aortic cross-clamp time (min)

Study	Total	Mean	EDFF SD	Total	No Mean	EDFF SD	Mean Difference	MD	95%-CI	Weight (fixed)	Weight (random)
Cullen 1995	17	66.00	30.00	18	58.00	13.80		8.00	[-7.62; 23.62]	3.5%	10.0%
Helbing 1996	13	58.00	16.00	6	54.00	15.00		4.00	[-10.82; 18.82]	3.9%	10.6%
Norgard 1996	36	53.50	19.70	56	57.20	20.60		-3.70	[-12.10; 4.70]	12.0%	15.4%
Rathore 2006	52	70.50	12.10	28	66.20	7.70		4.30	[-0.05; 8.65]	44.7%	18.3%
Sachdev 2006	24	69.23	18.96	26	63.36	17.23		5.87	[-4.20; 15.94]	8.3%	14.1%
Sandeep 2019	28	102.89	17.14	22	76.40	13.74		- 26.49	[17.93; 35.05]	11.5%	15.3%
Xu 2014	30	51.00	19.00	50	42.00	9.00		9.00	[1.76; 16.24]	16.1%	16.3%
Fixed-effects	200			206			-	6.91	[4.00; 9.82]	100.0%	
Random-effects	79% 0	< 0.001						7.79	[-1.05; 16.62]		100.0%
Test for overall effe	ct (fixed	d effect)	7 = 46	6(p < 1)	0 001)		-30 -20 -10 0 10 20 30				
Test for overall effe	ct (rand	lom effe	cts); t.	= 2.16	(p = 0.0)	75)	00 20 10 0 10 20 00				

Figure S3. Forest plots. CI, confidence interval; CPB, cardiopulmonary bypass; EDFF, enddiastolic forward flow; MD, mean difference; OR, odds ratio; SD, standard deviation.

A. CPB time (min)

Study	Total	Mean	EDFF SD	Total	No Mean	EDFF SD	Mean Difference	MD	95%-CI	Weight (fixed)	Weight (random)
Chaturvedi 1999	4	77.20	18.40	7	110.00	39.70		-32.80	[-67.30; 1.70]	1.9%	8.9%
Cullen 1995	17	104.00	32.00	18	92.00	19.80		12.00	[-5.75; 29.75]	7.2%	13.8%
Norgard 1996	36	82.30	33.00	56	90.90	8.20		-8.60	[-19.59; 2.39]	18.8%	15.8%
Rathore 2006	52	105.60	17.20	28	112.40	23.20		-6.80	[-16.58; 2.98]	23.7%	16.1%
Sachdev 2006	24	124.38	34.24	26	112.89	27.31		11.49	[-5.77; 28.75]	7.6%	14.0%
Sandeep 2019	28	131.00	20.70	22	100.20	12.10		30.80	[21.62; 39.98]	26.9%	16.2%
Xu 2014	30	90.00	33.00	50	70.00	18.00		20.00	[7.18; 32.82]	13.8%	15.3%
Fixed-effects Random-effects	191			207				8.94 5.96	[4.17; 13.71] [-12.24; 24.17]	100.0%	
Heterogeneity: l^2 = Test for overall effective Test for overall effective	88%, p ect (fixe ect (rand	d effect): dom effe	z = 3.6 cts): t _e :	8 (p < 0 = 0.80 (0.001) (p = 0.45	4)	-60 -40 -20 0 20 40 60		-		

B. Transatrial repair

Study	Events	EDFF Total	No Events	EDFF Total	Odds Ratio	OR	95%-CI	Weight (fixed)	Weight (random)
Aburawi 2014	9	9	11	11				0.0%	0.0%
Choi 2008	0	15	7	28		0.09	[0.00; 1.74]	31.5%	10.6%
Cullen 1995	2	17	1	18		2.27	[0.19; 27.58]	5.2%	14.6%
Munkhammar 1998	3	13	16	34		0.34	[0.08; 1.45]	41.5%	42.0%
Gatzoulis 1995	3	20	4	18		0.62	[0.12; 3.23]	21.8%	32.7%
Fixed-effects		74		109	-	0.42	[0.18; 1.02]	100.0%	
Random-effects Heterogeneity: $I^2 = 2^{10}$ Test for overall effect	%, $p = 0.3$	383 ect): z =	= -1.93 (p	= 0.054	0.1 1 10 100	0.47	[0.10; 2.23]		100.0%

Test for overall effect (random effects): $t_3 = -1.53$ (p = 0.223)

C. Transannular patch repair

		EDFF	No	EDFF				Weight	Weight
Study	Events	Total	Events	Total	Odds Ratio	OR	95%-CI	(fixed)	(random)
Aburawi 2014	5	9	2	11	+∺ •	5.62	[0.75; 42.36]	0.7%	3.0%
Ahmad 2012	36	58	26	54	+ * -	1.76	[0.83; 3.74]	8.7%	7.7%
Bonello 2013	23	38	62	110		1.19	[0.56; 2.52]	10.7%	7.7%
Chaturvedi 1999	1	4	2	7		0.83	[0.05; 13.63]	0.9%	1.8%
Choi 2008	13	15	9	28	· · · · · · · · · · · · · · · · · · ·	13.72	[2.54; 74.13]	0.7%	3.8%
Cullen 1995	8	17	5	18		2.31	[0.57; 9.41]	2.2%	4.8%
Gatzoulis 1995	1	20	0	18		2.85	[0.11; 74.38]	0.4%	1.4%
Helbing 1996	9	13	1	6	•	11.25	[0.97; 130.22]	0.4%	2.3%
Kordybach-Prokopiuk 2018	6	16	27	67		0.89	[0.29; 2.73]	5.6%	5.9%
Kutty 2018	75	122	147	227		0.87	[0.55; 1.37]	33.8%	9.2%
Lee 2013	25	33	12	17		1.30	[0.35; 4.84]	3.3%	5.1%
Mercer-Rosa 2018	77	77	11	11				0.0%	0.0%
Norgard 1996	20	36	40	56		0.50	[0.21; 1.20]	11.9%	7.1%
Norgard 1998 (early restriction)	14	16	8	18	· · · · · · · · · · · · · · · · · · ·	8.75	[1.52; 50.31]	0.8%	3.7%
Rathore 2006	36	52	19	28	+ !}-	1.07	[0.40; 2.86]	6.5%	6.5%
Sachdev 2006	14	24	5	26		5.88	[1.65; 20.91]	1.7%	5.3%
Sandeep 2019	22	28	6	22		9.78	[2.66; 35.95]	1.2%	5.1%
Samyn 2013	4	12	4	17		1.62	[0.31; 8.39]	1.9%	4.0%
Shekerdemian 1999	4	8	4	15		2.75	[0.46; 16.59]	1.2%	3.5%
Tominaga 2021	8	23	9	23		0.83	[0.25; 2.75]	5.0%	5.6%
van den Berg 2007	17	24	6	12		2.43	[0.58; 10.18]	2.0%	4.7%
Xu 2014	30	30	42	50		- 12.20	[0.68; 219.48]	0.4%	1.7%
Fixed-effects		675		841	•	1.54	[1.22; 1.94]	100.0%	
Random-effects					÷	1.98	[1.26; 3.11]		100.0%
Heterogeneity: $I^2 = 56\%, p < 0.00$	1						-		

Test for overall effect (fixed effect): z = 3.67 (p < 0.001) Test for overall effect (random effects): $t_{20} = 3.17$ (p = 0.005)

0.01 0.1 1 10 100

Figure S4. Forest plots. CI, confidence interval; EDFF, end-diastolic forward flow; ICU, intensive care unit; MD, mean difference; OR, odds ratio; SD, standard deviation.

A. Outflow patch repair

Study	Events	EDFF Total	No E Events	DFF Total	Odds Ratio	OR	95%-CI	Weight (fixed)	Weight (random)
Choi 2008 Cullen 1995 Gatzoulis 1995 Norgard 1998 (early restriction)	2 2 3 2	15 17 20 16	12 3 4 9	28 18 18 18		0.21 0.67 0.62 0.14	[0.04; 1.09] [0.10; 4.58] [0.12; 3.23] [0.02; 0.82]	34.9% 12.4% 17.2% 35.6%	27.2% 20.4% 27.6% 24.8%
Fixed-effects Random-effects Heterogeneity: $I^2 = 0\%$, $p = 0.520$ Test for overall effect (fixed effect) Test for overall effect (random effect)): z = -2.7; ects): t ₃ =	68 2 (p = 0 -2.94 (0.006) (p = 0.061)	82	0.1 0.5 1 2 10	0.31 0.32	[0.13; 0.72] [0.09; 1.10]	100.0% 	 100.0%

B. ICU Length of stay (days)

Study	Total	E Mean	SD	Total	No E Mean	SD	Mean Difference	MD	95%-CI	Weight (fixed)	Weight (random)
Chaturvedi 1999 Sachdev 2006 Sandeep 2019 Xu 2014	4 24 28 30	10.70 5.10 8.92 7.00	3.10 3.70 1.24 3.00	7 26 22 50	3.00 2.80 4.15 3.00	0.63 2.00 1.18 2.00		7.70 2.30 4.77 4.00	[4.63; 10.77] [0.63; 3.97] [4.10; 5.44] [2.79; 5.21]	3.2% 10.7% 65.7% 20.4%	13.2% 24.1% 33.9% 28.8%
Fixed-effects Random-effects Heterogeneity: $I^2 =$ Test for overall effe Test for overall effe	86 75%, p ect (fixe	e = 0.00 d effect) dom effe	7): z = 1 ects):	105 15.94 (µ t ₃ = 4.6	o < 0.00 7 (p = 0)1) 0.019)	-10 -5 0 5 10	1.44 1.34	[3.89; 4.99] [1.38; 7.29]	100.0%	100.0%

Figure S5. Forest plots. CI, confidence interval; EDFF, end-diastolic forward flow; MD, mean difference; RVEDVi, right ventricular end-diastolic volume indexed; RVESVi, right ventricular end-systolic volume indexed; RVSVi, right ventricular stroke volume indexed; SD, standard deviation.

A. RVEDVi (mL/m²)

Study	Total	Mean	EDFF SD	Total	No Mean	EDFF SD	Mean Difference	MD	95%-CI	Weight (fixed)	Weight (random)
Aburawi 2014	9	158.00	40.00	11	99.00	22.00	:i	- 59.00	[29.81; 88.19]	0.3%	4.0%
Apitz 2010	8	128.00	13.10	17	134.00	6.70		-6.00	[-15.62; 3.62]	2.4%	8.8%
Bonello 2013	38	125.50	6.50	110	126.00	8.30		-0.50	[-3.08; 2.08]	33.9%	10.2%
Eroglu 1999	25	62.62	29.62	19	81.12	26.75		-18.50	[-35.22; -1.78]	0.8%	6.8%
Helbing 1996	13	129.00	40.00	6	106.00	19.00	++ ++++++	23.00	[-3.53; 49.53]	0.3%	4.5%
Kordybach-Prokopiuk 2018	16	158.80	45.10	67	143.20	40.10		15.60	[-8.49; 39.69]	0.4%	5.0%
Kutty 2018	122	142.30	10.90	277	131.20	7.60	H	11.10	[8.97; 13.23]	49.9%	10.2%
Lee 2013	33	167.50	41.00	17	166.20	59.10		1.30	[-30.08; 32.68]	0.2%	3.7%
Luijnenburg 2013	31	151.00	33.00	20	120.00	27.00		31.00	[14.42; 47.58]	0.8%	6.8%
Mercer-Rosa 2018	77	128.25	7.50	11	98.00	8.70	-	30.25	[24.84; 35.66]	7.7%	9.8%
Mori 2017	23	121.00	43.00	39	117.00	52.00		4.00	[-19.98; 27.98]	0.4%	5.0%
Munkhammar 2013	16	159.00	49.00	15	111.00	29.00		48.00	[19.86; 76.14]	0.3%	4.2%
Samyn 2013	12	126.00	14.00	17	109.80	19.50		16.20	[4.01; 28.39]	1.5%	8.1%
Sani 2020	18	191.50	61.30	12	154.40	37.60	+	37.10	[1.68; 72.52]	0.2%	3.1%
Tominaga 2021	23	165.17	31.30	23	156.00	44.00		9.17	[-12.89; 31.24]	0.5%	5.4%
van den Berg 2007	24	145.00	41.00	12	124.00	37.00		21.00	[-5.60; 47.60]	0.3%	4.5%
Fixed-effects	488			673			*	8.54	[7.03; 10.04]	100.0%	
Random-effects								14.71	[4.57; 24.84]		100.0%
Heterogeneity: $I^2 = 91\%$, $p < 0$	0.001										
Test for overall effect (fixed ef	fect): z	= 11.12	(p < 0.0)	01)			-50 0 50				

Test for overall effect (fixed effect): z = 11.12 (p < 0.001)Test for overall effect (random effects): $t_{15} = 3.09 (p = 0.007)$

B. RVESVi (mL/m²)

			EDFF		No	EDFF
Study	Total	Mean	SD	Total	Mean	SD
Aburawi 2014	9	82.00	31.00	11	44.00	12.00
Bonello 2013	38	53.55	8.83	110	58.25	5.17
Kordybach-Prokopiuk 2018	16	88.00	27.80	67	77.90	27.90
Kutty 2018	122	68.90	6.27	227	67.35	5.65
Lee 2013	33	86.30	24.90	17	94.60	55.80
Luijnenburg 2013	31	79.00	22.00	20	63.00	19.00
Mercer-Rosa 2018	77	50.50	4.67	11	38.50	3.00
Munkhammar 2013	16	83.00	34.00	15	52.00	18.00
Sani 2020	18	120.80	50.00	12	99.20	31.90
Tominaga 2021	23	101.83	22.47	23	86.00	28.00
van den Berg 2007	24	150.25	25.50	12	71.25	26.83
Fixed-effects	407			525		
Random-effects						
Heterogeneity: $I^2 = 95\%$, $p < 0$	0.001					
Test for overall effect (fixed eff	fect): z	= 7.76 (p	< 0.00	1)		
Test for overall effect (random	effects	s): $t_{10} = 2$	2.38 (p =	= 0.039)	

Mean Difference	MD	95%-CI	Weight (fixed)	Weight (random)
; ;	38.00	[16.54; 59.46]	0.2%	6.2%
	-4.70	[-7.67; -1.73]	12.1%	14.0%
	10.10	[-5.07; 25.27]	0.5%	8.7%
	1.55	[0.22; 2.88]	59.9%	14.3%
	-8.30	[-36.15; 19.55]	0.1%	4.5%
i	16.00	[4.63; 27.37]	0.8%	10.5%
	12.00	[9.94; 14.06]	25.2%	14.2%
i +	31.00	[12.01; 49.99]	0.3%	7.1%
	21.60	[-7.71; 50.91]	0.1%	4.2%
	15.83	[1.16; 30.50]	0.5%	8.9%
	79.00	[60.71; 97.29]	0.3%	7.4%
	4.08	[3.05; 5.11]	100.0%	
	16.15	[1.01; 31.28]		100.0%
-50 0 50				

C. RVSVi (mL/m²)

			EDFF		No	EDFF				Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD	Mean Difference	MD	95%-CI	(fixed)	(random)
Bonello 2013	38	60.75	3.83	110	65.75	3.17		-5.00	[-6.35; -3.65]	36.4%	19.2%
Kutty 2018	122	72.75	5.17	227	63.45	3.93	-	9.30	[8.25; 10.35]	60.5%	19.2%
Luijnenburg 2013	31	72.00	14.00	20	57.00	12.00		15.00	[7.79; 22.21]	1.3%	17.0%
Mercer-Rosa 2018	77	77.00	16.00	11	61.00	17.00		16.00	[5.34; 26.66]	0.6%	14.8%
Munkhammar 2013	16	76.00	19.00	15	59.00	13.00		17.00	[5.60; 28.40]	0.5%	14.3%
van den Berg 2007	24	69.00	14.00	12	60.00	14.00		9.00	[-0.70; 18.70]	0.7%	15.4%
Fixed-effects	308			395				4.25	[3.43; 5.06]	100.0%	
Random-effects								9.57	[0.67; 18.47]		100.0%
Heterogeneity: $I^2 = 98$	3%, p <	< 0.001									
Test for overall effect	(fived	effect)	7 = 10.1	19 (n <	0.001)		20 10 0 10 20				

Test for overall effect (random effects): $t_5 = 2.77 (p = 0.040)$

-20 -10 0 10 20

Figure S6. Forest plots. CI, confidence interval; EDFF, end-diastolic forward flow; MD, mean difference; RVEDP, right ventricular end-diastolic pressure; RVEF, right ventricular ejection fraction; RVESP, right ventricular end-systolic pressure; RVMi, right ventricular mass indexed; SD, standard deviation.

A. RVMi (g/m²)

Study	Total	Mean	EDFF SD	Total	No Mean	EDFF SD		Mear	Differ	ence		MD	95	%-CI	Weight (fixed)	Weight (random)
Bonello 2013	38	55.00	20.00	110	51.00	14.00		-	-+-			4.00	[-2.88; 1	0.881	0.3%	8.0%
Helbing 1996	13	26.00	6.00	5	25.00	7.00		-	i-		-	1.00	[-5.95;	7.95	0.3%	7.9%
Kordybach-Prokopiuk 2018	16	33.70	10.00	67	28.70	8.70			+	• •		5.00	[-0.32; 1	0.32	0.5%	10.8%
Kutty 2018	122	31.15	2.37	227	31.85	2.33						-0.70	[-1.22: -	0.18]	54.3%	22.5%
Luijnenburg 2013	31	25.67	1.32	20	22.80	0.81						2.87	[2.29;	3.45]	42.6%	22.5%
Samyn 2013	10	45.50	4.33	17	37.75	4.83					•	7.75	[4.22; 1	1.28]	1.2%	15.3%
van den Berg 2007	24	25.00	7.00	12	23.00	6.00				<u> </u>		2.00	[-2.40;	6.40]	0.8%	13.0%
Fixed-effects Random-effects	254			458					+			0.99	[0.61;	1.37] 5.611	100.0%	100.0%
Heterogeneity: $I^2 = 94\%$, $p < 1$	0.001							1								
Test for overall effect (fixed ef	fect): z	= 5.08	(p < 0.0)	01)			-10	-5	0	5	10					
Test for overall effect (random	effects	s): t _e = 2	2.57 (p	= 0.042	2)											

B. RVEF (%)

			EDFF		No	EDFF									Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD		Mean	Diffe	rence		MD	98	5%-CI	(fixed)	(random)
Bonello 2013	38	52.75	1.50	110	52.75	2.17			#	1		0.00	[-0.63;	0.63]	17.8%	11.7%
Helbing 1996	13	51.00	11.00	5	54.00	7.00				+		-3.00	[-11.57;	5.57]	0.1%	4.8%
Kordybach-Prokopiuk 2018	16	47.40	11.10	67	46.50	7.70		-	<u></u>	+		0.90	[-4.84;	6.64]	0.2%	7.1%
Kutty 2018	122	51.75	1.67	227	46.75	0.17				+		5.00	[4.70;	5.30]	79.1%	11.8%
Lee 2013	33	48.70	8.20	17	45.90	11.90		-	-	+	_	2.80	[-3.51;	9.11]	0.2%	6.6%
Mercer-Rosa 2018	77	60.00	8.00	11	61.00	5.00		_	-	- 1		-1.00	[-4.45;	2.45]	0.6%	9.5%
Mori 2017	23	49.20	6.60	39	50.30	8.40		_	-	- 1		-1.10	[-4.87;	2.67]	0.5%	9.2%
Munkhammar 2013	16	49.00	8.00	15	54.00	6.00	10 					-5.00	[-9.96;	-0.04]	0.3%	7.9%
Samyn 2013	12	59.00	4.33	17	59.50	6.00		-	-	-1		-0.50	[-4.26;	3.26]	0.5%	9.2%
Sani 2020	18	35.20	5.50	12	36.20	7.60		-		-		-1.00	[-5.99;	3.99]	0.3%	7.9%
Tominaga 2021	23	37.56	9.85	23	45.00	10.00			-	1		-7.44	[-13.18;	-1.70]	0.2%	7.1%
van den Berg 2007	24	49.00	6.00	12	49.00	9.00		_		+		0.00	[-5.63;	5.63]	0.2%	7.2%
Fixed-effects	415			555						÷.		3.91	[3.65;	4.18]	100.0%	-
Random-effects Heterogeneity: $I^2 = 96\%$, $p < 0$.001		(O	0043				_	+	1		-0.56	[-2.64;	1.53]		100.0%
Test for overall effect (fixed eff Test for overall effect (random	ect): z effects	= 29.02 s): t ₁₁ =	-0.59 (J	001) p = 0.5	70)		-10	-5	0	5	10					

C. RVEDP (mmHg)

		E	DFF		No E	DFF										Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD			lean	Diffe	rence	•	M	D	95%-CI	(fixed)	(random)
Apitz 2010	8	10.40	1.00	17	10.40	0.60				-	-11		0.0	0	[-0.75; 0.75]	45.5%	29.1%
Maskatia 2013	77	9.30	4.80	101	7.50	2.10					+	-	- 1.8	0	0.65; 2.95]	19.4%	24.6%
Mori 2017	23	10.00	2.00	39	8.00	2.00					4	-	- 2.0	0	0.97; 3.03]	24.1%	25.9%
Tominaga 2021	23	9.25	2.57	23	8.00	2.70				-		-	- 1.2	5 [[-0.27; 2.77]	11.0%	20.3%
Fixed-effects	131			180						2	4		0.9	7 [0.46; 1.47]	100.0%	
Random-effects	3									-		-	- 1.2	2 [-0.29; 2.72]		100.0%
Heterogeneity: $I^2 =$	= 76%, L	= 0.00	6						1			1					
Test for overall effe	ect (fixe	d effect): z = :	3.75 (p	< 0.001)	-3	-2	-1	0	1	2	3				

Test for overall effect (random effects): $t_3 = 2.56$ (p = 0.083)

D. RVESP (mmHg)

Study	Total	Mean	EDFF SD	Total	No Mean	EDFF SD		N	lean	Differen	ce		MD	9	5%-CI	Weight (fixed)	Weight (random)
Apitz 2010 Kordybach-Prokopiuk 2018	8	128.00	13.10 13.10	17 67	134.00	6.70			•				-6.00	[-15.62;	3.62]	6.9% 13.2%	14.3% 19.2%
Maskatia 2013 Mori 2017	77	45.00	13.00	101 39	39.00 42.00	14.00		-	-	_	-		6.00	[2.01;	9.99]	39.9% 30.9%	25.5%
Tominaga 2021	23	46.87	15.74	23	44.00	13.00			-	-			2.87	[-5.47;	11.21]	9.1%	16.5%
Fixed-effects Random-effects	147			247									1.46	[-1.06; [-5.56]	3.98]	100.0%	100.0%
Heterogeneity: $I^2 = 70\%$, $p = 0$ Test for overall effect (fixed eff Test for overall effect (random	0.010 fect): z effects	= 1.14 (p ;): t ₄ = 0.	o = 0.25 36 (p =	6) 0.738)		-	- <mark>1</mark> 5	-10	-5	0 5	10	15		•			

Figure S7. Forest plots. CI, confidence interval; EDFF, end-diastolic forward flow; LVEDVi, left ventricular end-diastolic volume indexed; LVEF, left ventricular ejection fraction; LVESVi, left ventricular end-systolic volume indexed; LVSVi, left ventricular stroke volume indexed; MD, mean difference; SD, standard deviation.

A. LVEDVi (mL/m²)

		EDFF	No	EDFF				Weight	Weight
Study	Total M	lean SD	Total Mear	n SD	Mean Difference	MD	95%-CI	(fixed)	(random)
Bonello 2013	38 7	4.00 5.70	110 73.75	5 3.17	: +	0.25	[-1.66; 2.16]	13.9%	34.9%
Helbing 1996	13 8	6.00 16.00	5 77.00) 14.00	÷	- 9.00	[-6.04; 24.04]	0.2%	7.4%
Kutty 2018	122 8	32.08 3.05	227 87.05	5 4.20	+	-4.97	[-5.74; -4.21]	85.2%	36.8%
Lee 2013	33 8	3.90 15.20	17 79.40	21.10		4.50	[-6.79; 15.79]	0.4%	11.4%
Mori 2017	23 9	4.00 26.00	39 88.00	23.00	<u> </u>	6.00	[-6.85; 18.85]	0.3%	9.5%
Fixed-effects Random-effects	229		398			-4.15	[-4.86; -3.44] [-6.33: 6.34]	100.0%	 100.0%
Heterogeneity: I ² = Test for overall effe Test for overall effe	88%, p < ect (fixed e ect (randor	< 0.001 effect): z = -1 m effects): t ₄	1.45 (p < 0.00 = 0.00 (p = 0	01) -).998)	20 -10 0 10 2	0	[-0.00, 0.04]	-	100.070

B. LVESVi (mL/m²)

Study	EDF Total Mean SI	F No ED D Total Mean	SD	Mean Difference	MD	95%-CI	Weight (fixed)	Weight (random)
Kutty 2018 Lee 2013	122 34.00 1.8 33 33.90 7.8	3 227 37.00 2 3 17 32.50 10	.47 .38	•	-3.00 - 1.40	[-3.46; -2.54] [-4.22; 7.02]	99.3% 0.7%	71.1% 28.9%
Fixed-effects Random-effects Heterogeneity: I^2 = Test for overall effect Test for overall effect	155 57%, <i>p</i> = 0.126 ect (fixed effect): <i>z</i> = ect (random effects)	244 -12.80 (p < 0.001) t t ₁ = -0.87 (p = 0.5	-(46)	-6 -4 -2 0 2 4 6	-2.97 -1.73	[-3.43; -2.52] [-27.07; 23.62]	100.0%	 100.0%

C. LVSVi (mL/m²)

		E	DFF		No E	DFF								Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD		Mear	n Diffe	rence		MD	95%-CI	(fixed)	(random)
Bonello 2013	38	46.50	2.33	110	46.75	2.50			-	_		-0.25	[-1.13; 0.63]	21.3%	47.7%
Kutty 2018	122	47.42	1.92	227	49.45	2.33	-					-2.03	[-2.48; -1.57]	78.7%	52.3%
Fixed-effects	160			337			-					-1.65	[-2.05; -1.24]	100.0%	
Random-effects												-1.18	[-12.44; 10.09]		100.0%
Heterogeneity: I ² =	92%, p	< 0.00	1												
Test for overall effe	ect (fixed	d effect)	: z = -	7.99 (p	< 0.00 33 (p =	1) 0 411	-2	-1	0	1	2				

D. LVEF (%)

			EDFF		No	EDFF				Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD	Mean Difference	MD	95%-CI	(fixed)	(random)
Ahmad 2012	58	57.30	7.20	54	57.20	7.50		0.10	[-2.63; 2.83]	1.3%	10.8%
Bonello 2013	38	63.50	2.00	110	64.50	1.70	-	-1.00	[-1.71; -0.29]	18.8%	23.1%
Choi 2008	15	66.80	4.30	28	67.72	3.38		-0.92	[-3.43; 1.59]	1.5%	11.8%
Helbing 1996	13	49.00	12.00	5	56.00	11.00		-7.00	[-18.64; 4.64]	0.1%	1.0%
Kutty 2018	122	58.25	1.67	227	57.25	1.50	•	1.00	[0.65; 1.35]	75.5%	24.6%
Lee 2013	33	59.50	6.52	17	59.60	8.17		-0.10	[-4.58; 4.38]	0.5%	5.5%
Mori 2017	23	59.10	6.60	39	57.40	7.10	- <u>+</u> +	1.70	[-1.80; 5.20]	0.8%	7.9%
Samyn 2013	12	61.25	3.83	17	63.25	3.83		-2.00	[-4.83; 0.83]	1.2%	10.3%
Tominaga 2021	23	49.70	9.30	23	49.00	7.00		0.70	[-4.06; 5.46]	0.4%	5.0%
Fixed-effects Random-effects	337			520			-	0.54 -0.20	[0.23; 0.85] [-1.26: 0.87]	100.0%	 100.0%
Heterogeneity: $I^2 =$	74%, p	< 0.00	1								
Test for overall effe	ct (five	d effect	z = 3	44 (n <	0.001		15 10 5 0 5 10 15				

Test for overall effect (fixed effect): z = 3.44 (p < 0.001)Test for overall effect (random effects): $t_8 = -0.42 (p = 0.682)$

-15 -10 -5 0 5 10 15

Figure S8. Forest plots. CI, confidence interval; EDFF, end-diastolic forward flow; MD, mean difference; RAAi, right atrial area indexed; RAVi, right atrial volume indexed; SD, standard deviation.

A. RAAi (cm²/m²)

Study	Total	E Mean	DFF SD	Total	No E Mean	DFF SD		Mean	Diffe	rence		MD	95%-CI	Weight (fixed)	Weight (random)
Ahmad 2012 Kutty 2018	58 122	10.60 13.50	3.40 0.70	54 227	8.90 12.95	1.90 0.77					•	- 1.70 0.55	[0.69; 2.71] [0.39; 0.71]	2.4% 97.6%	40.2% 59.8%
Fixed-effects Random-effects Heterogeneity: l^2 = Test for overall effect	180 79%, p ect (fixe	o = 0.02 d effect	8): z = 1	281 7.19 (p	< 0.001)	-2	-1	0	+ 	2	0.58 1.01	[0.42; 0.74] [-6.15; 8.18]	100.0%	 100.0%

B. RAVi (mL/m²)

Study	Total M	EDFF ean SE	: Total	No Mean	EDFF SD		Mean	Diffe	rence		MD	95%-	Weight CI (fixed)	Weight (random)
Kutty 2018 Luijnenburg 2013 Tominaga 2021	122 42 31 58 23 83	2.42 1.92 8.00 10.00 3.52 18.30	2 227 20 20 23	42.08 52.00 70.00	3.65 9.00 20.00			+	•		0.35 6.00 13.52	[-0.23; 0.9 [0.71; 11.2 [2.44; 24.6	3] 98.5% 9] 1.2% 0] 0.3%	45.8% 34.9% 19.3%
Fixed-effects Random-effects Heterogeneity: I^2 = Test for overall effect Test for overall effect	176 79%, <i>p</i> = ct (fixed ef ct (randon	0.008 ffect): z = 1 n effects): <i>i</i>	270 .53 (p = 2 = 1.40	: 0.125)) (p = 0.	297)	-20	-10	0	10	20	0.45 4.86	[-0.13; 1.0 [-10.11; 19.8	3] 100.0% 4]	 100.0%

Figure S9. Forest plots. CI, confidence interval; EDFF, end-diastolic forward flow; MD, mean difference; SD, standard deviation.

Study	Total	Mean	EDFF SD	Total	No Mean	EDFF SD	Mean Differenc	e	MD	95%-CI	Weight (fixed)	Weight (random)
Ahmad 2012	58	76.00	19.00	54	76.00	12.00	1 - <mark></mark> -	0	.00 [-5.84	4; 5.84]	26.1%	12.3%
Cardoso 2003	19	72.20	15.25	11	72.35	20.30	÷ •	-0	.15 [-13.97	; 13.67]	4.7%	9.1%
Cullen 1995	9	40.95	17.60	9	83.75	23.00	I	-42	.80 [-61.72	-23.88]	2.5%	7.1%
Gatzoulis 1995	20	45.65	13.10	17	57.65	53.60		-12	.00 [-38.12	; 14.12]	1.3%	5.0%
Helbing 1996	13	60.00	14.00	6	65.00	12.00		-5	.00 [-17.2	5; 7.25]	5.9%	9.7%
Munkhammar 1998	13	60.00	13.00	34	60.00	13.00		0	.00 [-8.3	1; 8.31]	12.9%	11.4%
Norgard 1998 (late restriction)	10	70.00	16.00	22	80.00	20.00		-10	.00 [-22.9]	7; 2.97]	5.3%	9.4%
Rathore 2006	52	70.50	7.50	28	88.00	14.00		-17	.50 [-23.07	; -11.93]	28.7%	12.3%
Sachdev 2006	24	70.98	19.90	26	96.90	23.40		-25	.92 [-37.93	; -13.91]	6.2%	9.8%
Samyn 2013	12	65.70	16.90	17	68.80	17.30		-3	.10 [-15.7	1; 9.51]	5.6%	9.6%
Vukomanovic 2006	18	207.81	51.45	42	243.38	61.95	•	-35	.57 [-65.83	3; -5.31]	1.0%	4.1%
Fixed-effects	248			266			•	-9	.19 [-12.17	; -6.20]	100.0%	
Random-effects								11	.59 [-20.85	; -2.32]		100.0%
Heterogeneity: $l^2 = 79\%$, $p < 0.0$	001							1 1				
Test for overall effect (fixed effect	ct): z = -	6.04 (p <	< 0.001))			60 -40 -20 0 20	40 60				
Test for overall effect (random e	ffects):	$t_{10} = -2.7$	'9 (p =	0.019)								

A. E wave velocity at the tricuspid valve (cm/sec)

B. E wave duration at the tricuspid valve (msec)



C. E wave deceleration at the tricuspid valve (msec)

Study	Total	Mean	EDFF SD	Total	No Mean	EDFF SD		Mean	Differe	nce		MD	ç	5%-CI	Weight (fixed)	Weight (random)
Cullen 1995	9	96.75	50.60	9	126.00	15.00		+	#			-29.25	[-63.73	5.23]	0.5%	10.0%
Gatzoulis 1995	20	123.15	31.55	17	145.25	35.65						-22.10	[-43.97;	-0.23]	1.2%	13.7%
Gatzoulis 1998	36	120.80	31.00	52	120.10	29.50			++-			0.70	[-12.22;	13.62]	3.3%	16.2%
Helbing 1996	13	164.00	47.00	6	141.00	62.00		-	<u>+</u> +++++++++++++++++++++++++++++++++++			23.00	[-32.80;	78.80]	0.2%	5.9%
Kutty 2018	122	180.30	11.80	277	185.75	12.50			-			-5.45	[-8.01;	-2.89]	84.4%	17.9%
Munkhammar 1998	13	140.20	36.20	34	129.80	30.00			+++-			10.40	[-11.71;	32.51]	1.1%	13.6%
Rathore 2006	52	99.40	18.00	28	139.65	16.20		-				-40.25	[-47.99;	-32.51]	9.2%	17.3%
Sachdev 2006	24	86.90	21.70	26	151.40	152.60		•				-64.50	[-123.80;	-5.20]	0.2%	5.4%
Fixed-effects	289			449					0			-8.62	[-10.97;	-6.27]	100.0%	
Random-effects									÷			-14.51	[-34.45;	5.43]		100.0%
Heterogeneity: $I^2 = 9^{\circ}$	1%, p <	0.001						1					11			
Test for overall effect	(fixed e	effect): z	= -7.19	(p < 0.	001)		-100	-50	0	50	100					
Test for overall effect	(rando	m effects	s): t ₇ = .	-1.72 (p	= 0.129)										

Figure S10. Forest plots. CI, confidence interval; EDFF, end-diastolic forward flow; MD, mean difference; SD, standard deviation.

A. A wave velocity at the tricuspid valve (cm/sec)

			EDFF		No	EDFF									Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD		Mean	Differ	ence		MD	95	%-CI	(fixed)	(random)
Ahmad 2012	58	50.00	15.00	54	50.00	12 00			-			0.00	[-5.01	5 0 11	17.7%	13.0%
Cardoso 2003	19	62.05	12.20	11	71.40	12.50	_		-11			-9.35	[-18.55:	-0.151	5.2%	9.9%
Cullen 1995	9	41.50	18.85	9	51.00	16.80				-		-9.50	[-26.00;	7.001	1.6%	5.7%
Gatzoulis 1995	20	28.70	21.34	17	27.46	7.62			-	_		1.24	[-8.79; 1	1.27]	4.4%	9.3%
Helbing 1996	13	50.00	8.00	6	50.00	10.00		-		-		0.00	[-9.11;	9.11]	5.4%	10.0%
Munkhammar 1998	13	48.00	11.00	34	49.00	15.00			-	-		-1.00	[-8.82;	6.82]	7.3%	10.9%
Norgard 1998 (late restriction)	10	50.00	20.00	22	60.00	16.00			÷.			-10.00	[-24.08;	4.08]	2.2%	6.8%
Rathore 2006	52	70.00	8.00	28	60.00	6.50						10.00	[6.76; 1	[3.24]	42.2%	14.0%
Sachdev 2006	24	71.76	7.90	26	75.67	14.80		-				-3.91	[-10.42;	2.60]	10.5%	11.9%
Samyn 2013	12	45.00	15.10	17	45.00	15.60		-				0.00	[-11.31; 1	1.31]	3.5%	8.5%
Fixed-effects	230			224					-			2.92	[0.82;	5.03]	100.0%	
Random-effects							_	-	-			-1.20	[-5.68;	3.27]		100.0%
Heterogeneity: $I^2 = 76\%$, $p < 0.0$	D1						1	1	1	1						
Test for overall effect (fixed effec	t): z = 2	2.72 (p	= 0.007)			-20	-10	0	10	20					
Test for overall effect (random ef	fects):	t 9 = -0.1	61 (p =	0.558)												

B. A wave duration at the tricuspid valve (msec)



C. E/A at the tricuspid valve

		E	DFF		No E	DFF				Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD	Mean Difference	MD	95%-CI	(fixed)	(random)
Ahmad 2012	58	1.52	127	45	1.52	1 00	\$_ _	0.00	[-0 44: 0 44]	3.0%	6.3%
Cardoso 2003	19	1.20	0.25	11	1.00	0.30		0.20	[-0.01; 0.41]	13.2%	13.0%
Gatzoulis 1998	36	1.70	0.49	56	1.84	0.56		-0.14	[-0.36: 0.08]	12.3%	12.7%
Helbing 1996	13	1.19	0.22	6	1.36	0.32		-0.17	[-0.45; 0.11]	7.3%	10.3%
Kutty 2018	122	1.85	0.13	277	1.85	1.13		0.00	[-0.14; 0.14]	31.9%	16.0%
Norgard 1998 (late restriction)	10	1.40	0.80	22	1.33	1.25	·	- 0.07	[-0.65; 0.79]	1.1%	2.9%
Sachdev 2006	24	0.98	0.17	26	1.33	0.49		-0.35	[-0.55; -0.15]	14.5%	13.4%
Samyn 2013	12	1.57	0.59	17	1.69	0.66		-0.12	[-0.58; 0.34]	2.8%	5.9%
Sani 2020	18	1.20	0.50	12	1.20	0.50	+	0.00	[-0.37; 0.37]	4.4%	7.9%
Vukomanovic 2006	18	1.49	0.38	42	1.88	0.58		-0.39	[-0.64; -0.14]	9.4%	11.5%
Fixed-effects	330			514			***	-0.09	[-0.17; -0.02]	100.0%	
Random-effects Heterogeneity: $l^2 = 60\%$, $p = 0.0$	08							-0.11	[-0.25; 0.03]		100.0%
Test for overall effect (fixed effec	t): z = -	2.40 (p	= 0.0	16)			-0.5 0 0.5				
Test for overall effect (random ef	fects):	t9 = -1.7	72 (p =	= 0.119)						

Figure S11. Forest plots. CI, confidence interval; EDFF, end-diastolic forward flow; MD, mean difference; SD, standard deviation.

A. E' at the tricuspid valve (cm/sec)

Study	Total	E Mean	SD	Total	No E Mean	SD SD		Mea	n Differer	nce	M	9	5%-CI	Weight (fixed)	Weight (random)
Ahmad 2012	58	11.00	2.00	54	11.00	3.00					0.0	0 [-0.95	; 0.95]	81.7%	58.4%
Samyn 2013	12	14.60	2.60	16	12.40	2.80				•	- 2.2	0 [0.19	; 4.21]	18.3%	41.6%
Fixed-effects	70			70					1		0.4	0 [-0.46	1.26]	100.0%	-
Random-effects	700/	0.05	~	-	_		-			-	0.9	1 [-12.86;	14.69]	-	100.0%
Heterogeneity: /- =	13%, p	0 = 0.05	3	02/2	- 0.250		÷.				4				
Test for overall effe	ect (ran	dom effe	ects):	$t_1 = 0.8$	= 0.358 34 (p = 1	0.554)	-4	-2	U	2	4				

B. A' at the tricuspid valve (cm/sec)

		E	DFF		No E	DFF								Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD		Mean	Diffe	rence		MD	95%-CI	(fixed)	(random)
Ahmad 2012	58	5.00	2.00	54	5.00	1.00		-				0.00	[-0.58; 0.58]	86.0%	86.0%
Samyn 2013	12	7.00	2.20	17	7.00	1.50 -			+			- 0.00	[-1.43; 1.43]	14.0%	14.0%
Fixed-effects	70			71					÷			0.00	[-0.54; 0.54]	100.0%	
Random-effects												0.00	[0.00; 0.00]		100.0%
Heterogeneity: $I^2 =$	0%, p	= 1.000						1		1					
Test for overall effe	ct (fixed	d effect)	: z = (0.00 (p	= 1.000))	-1	-0.5	0	0.5	1				
Test for overall effe	ct (rand	dom effe	ects):	$t_1 = NA$	A(p = N	A)									

C. E/E' at the tricuspid valve

		E	DFF		No E	DFF					Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD	Mean Differe	nce	MD	95%-CI	(fixed)	(random)
Ahmad 2012	58	7.00	2.50	54	7.80	3.20			-0.80	[-1.87; 0.27]	53.4%	53.4%
Samyn 2013	12	4.70	1.70	17	5.70	1.30			-1.00	[-2.14; 0.14]	46.6%	46.6%
Fixed-effects	70			71					-0.89	[-1.67; -0.11]	100.0%	
Random-effects									-0.89	[-2.16; 0.37]		100.0%
Heterogeneity: $I^2 =$	0%, p	= 0.802					1 1 1	1, 1				
Test for overall effe	ect (fixe	d effect): z = .	2.24 (= 0.02	5)	-2 -1 0	1 2	2			
Test for overall effe	ect (ran	dom eff	ects):	$t_1 = -8.$	95 (p =	0.071)						

Figure S12. Forest plots. CI, confidence interval; EDFF, end-diastolic forward flow; MD, mean difference; OR, odds ratio; PR, pulmonary regurgitation; SD, standard deviation.

A. Moderate to severe PR

Study	Events	EDFF Total E	No Events	EDFF Total	Odds Ratio	OR	95%-CI	Weight (fixed)	Weight (random)
Ahmad 2012 Mori 2017 Xu 2014	39 12 19	58 23 30	34 18 28	54 39 50		1.21 - 1.27 - 1.36	[0.55; 2.63] [0.45; 3.57] [0.54; 3.44]	45.0% 24.9% 30.1%	44.1% 25.0% 30.9%
Fixed-effects Random-effects Heterogeneity: J^2 = Test for overall eff Test for overall eff	s = 0%, p = 0 fect (fixed e fect (randor	111 0.982 effect): z m effects	= 0.90 (s): t ₂ = 6	143 p = 0.366 .75 (p = 0	0.5 1 2	1.27 1.27	[0.76; 2.13] [1.09; 1.48]	100.0% 	 100.0%

B. PR fraction (%)

Study	Total	Meen	EDFF	Total	No	EDFF	Maan Difference	MD	05% CI	Weight	Weight
Study	Total	wean	30	Total	mean	30	Mean Difference		95%-01	(lixed)	(random)
Apitz 2010	8	38.90	2.90	17	28.60	5.20	- - ;	10.30	[7.11; 13.49]	8.1%	19.6%
Kordybach-Prokopiuk 2018	16	29.90	14.00	67	23.50	17.50	+++	6.40	[-1.64; 14.44]	1.3%	7.3%
Kutty 2018	122	38.38	4.42	277	25.75	5.38		12.62	[11.62; 13.63]	81.1%	27.3%
Lee 2013	33	44.20	8.90	17	36.70	12.10		7.50	[1.00; 14.00]	1.9%	9.9%
Luijnenburg 2013	31	36.00	13.00	20	15.00	17.00		21.00	[12.26; 29.74]	1.1%	6.4%
Munkhammar 2013	16	45.00	9.00	15	23.00	19.00	€ + − −	22.00	[11.42; 32.58]	0.7%	4.7%
Samyn 2013	12	44.75	5.50	17	28.00	8.00		16.75	[11.84; 21.66]	3.4%	13.7%
van den Berg 2007	24	33.25	9.17	12	21.50	8.30		11.75	[5.79; 17.71]	2.3%	11.0%
Fixed_effects	262			112				12 54	[11 63· 13 //]	100.0%	
Random-effects	LUL							12.66	[8.91: 16.41]		100.0%
Heterogeneity: $l^2 = 56\%$, $p = 0$	025										
Test for overall effect (fixed eff	fect): z =	= 27.07	(p < 0)	001)			-30 -20 -10 0 10 20 30				
Test for overall effect (random	effects): t ₇ = 7	7.99 (p	< 0.001	I)		20 20 10 3 10 20 00				

C. PR duration (msec)

Study	Total	Mean	EDFF SD	Total	No Mean	EDFF SD	Mean Difference	MD	95%-CI	Weight (fixed)	Weight (random)
Gatzoulis 1995 Lee 2013 Mercer-Rosa 2018 Munkhammar 1998 Norgard 1998 (early restriction) Norgard 1998 (late restriction) Sachdev 2006	20 33 77 13 16 10 24	300.20 325.60 42.50 253.30 171.00 219.80 166.60	65.40 77.10 2.67 41.90 76.00 52.00 79.50	18 17 11 34 18 22 26	442.10 321.80 31.25 353.00 174.00 254.60 233.30	54.10 55.70 2.83 71.80 39.00 40.60 86.80		-141.90 3.80 11.25 -99.70 -3.00 -34.80 -66.70	[-179.93; -103.87] [-33.52; 41.12] [9.47; 13.03] [-132.88; -66.52] [-44.37; 38.37] [-71.22; 1.62] [-112.80; -20.60]	0.2% 0.2% 98.7% 0.3% 0.2% 0.2% 0.1%	14.1% 14.2% 15.6% 14.4% 13.9% 14.2% 13.5%
Fixed-effects Random-effects Heterogeneity: $l^2 = 95\%$, $p < 0.00$ Test for overall effect (fixed effect) Test for overall effect (random effe	193 1 1: z = 1 ects): t	1.49 (p < s = -2.11	0.001) (p = 0.0	146			-150 -50 0 50 100 150	10.34 -46.57	[8.58; 12.11] [-100.46; 7.32]	100.0% 	 100.0%

Figure S13. Forest plots. BNP, brain natriuretic peptide; CI, confidence interval; EDFF, enddiastolic forward flow; MD, mean difference; NT-proBNP, N-terminal pro hormone brain natriuretic peptide; OR, odds ratio; SD, standard deviation.

A. QRS duration (msec)

Study	Total	Mean	EDFF SD	Total	No Mean	EDFF SD	Mean Difference	MD	95%-CI	Weight (fixed)	Weight (random)
Aburawi 2014	9	123.00	29.00	11	114.00	25.00		9.00	[-15.03; 33.03]	0.3%	3.9%
Ahmad 2012	58	148.00	29.00	54	139.00	23.00	 • -	9.00	[-0.66; 18.66]	2.0%	6.5%
Apitz 2010	8	148.70	10.30	17	158.50	5.90		-9.80	[-17.47; -2.13]	3.2%	6.8%
Bonello 2013	38	146.00	27.00	110	147.00	23.00		-1.00	[-10.60; 8.60]	2.0%	6.5%
Cardoso 2003	19	130.00	20.00	11	100.00	40.00	l	30.00	[4.71; 55.29]	0.3%	3.7%
Eroglu 1999	25	140.00	18.00	19	156.00	24.00	_ _	-16.00	[-28.89; -3.11]	1.1%	5.9%
Gatzoulis 1998	36	123.30	16.60	56	125.40	18.50	- 	-2.10	[-9.37; 5.17]	3.5%	6.9%
Kordybach-Prokopiuk 2018	16	132.90	33.70	67	154.60	21.80		-21.70	[-39.02; -4.38]	0.6%	5.1%
Kutty 2018	122	138.50	7.70	227	143.50	5.70	•	-5.00	[-6.55; -3.45]	76.7%	7.4%
Lee 2013	33	137.60	19.30	17	136.90	28.10	— <u><u></u><u></u><u></u></u>	0.70	[-14.19; 15.59]	0.8%	5.5%
Mori 2017	23	137.00	32.00	39	129.00	41.00	- <u> </u>	8.00	[-10.35; 26.35]	0.6%	4.9%
Norgard 1998 (early restriction)	16	71.90	17.30	18	70.60	12.20		1.30	[-8.88; 11.48]	1.8%	6.4%
Norgard 1998 (late restriction)	10	116.20	15.20	22	117.40	12.90		-1.20	[-12.05; 9.65]	1.6%	6.3%
Samyn 2013	12	143.75	15.83	17	85.00	16.67		- 58.75	[46.79; 70.71]	1.3%	6.1%
Sani 2020	18	156.70	13.70	12	142.50	14.80	<u> </u> 	14.20	[3.70; 24.70]	1.7%	6.3%
Sani 2020	18	156.70	13.70	12	142.50	14.80	↓	14.20	[3.70; 24.70]	1.7%	6.3%
Tominaga 2021	23	152.38	21.83	23	145.00	29.00		7.38	[-7.45; 22.21]	0.8%	5.5%
-											
Fixed-effects	484			732			*	-2.90	[-4.26; -1.54]	100.0%	
Random-effects								4.98	[-4.30; 14.26]		100.0%
Heterogeneity: $I^2 = 90\%, p < 0.00$	1										
Test for overall effect (fixed effect)): z = -4	.18 (p <	0.001)				-60 -40 -20 0 20 40 60				

Test for overall effect (random effects): $t_{16} = 1.14$ (p = 0.272)

B. BNP (pg/mL)

	E	DFF	No EDFF				Weight	Weight
Study	Total Mean	SD Total M	lean SD	Mean Difference	MD	95%-CI	(fixed)	(random)
Apitz 2010 Mori 2017 Samyn 2013	8 37.60 6 23 29.10 26 12 42.50 20	6.50 17 28 6.20 39 22 0.67 17 17	8.60 5.20 2.00 30.00 7.50 6.33		9.00 7.10 - 25.00	[3.86; 14.14] [-7.16; 21.36] [12.92; 37.08]	76.3% 9.9% 13.8%	44.8% 25.5% 29.7%
Fixed-effects Random-effects Heterogeneity: I^2 = Test for overall effect Test for overall effect	43 67%, <i>p</i> = 0.049 ct (fixed effect): <i>z</i> ct (random effect)	73 = 4.81 (p < 0. s): t ₂ = 2.45 (p	.001) o = 0.134)	-30 -20 -10 0 10 20 30	11.02 - 13.26	[6.53; 15.51] [-10.05; 36.58]	100.0% 	 100.0%

C. NT-proBNP (pg/mL)

			EDFF		N	D EDFF				Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD	Mean Difference	MD	95%-CI	(fixed)	(random)
Kordybach-Prokopiuk 2018	16	433.00	686.90	67	219.60	292.40	- <u> </u>	- 213.40	[-130.38; 557.18]	1.8%	1.8%
Luijnenburg 2013	31	144.14	90.09	20	81.08	81.08		63.06	[15.43; 110.69]	93.0%	93.0%
Mori 2017	21	158.30	175.50	34	183.80	555.10		-25.50	[-226.62; 175.62]	5.2%	5.2%
Fixed-effects	68			121			÷	61.12	[15.19; 107.06]	100.0%	
Random-effects								61.12	[-25.40; 147.65]		100.0%
Heterogeneity: $I^2 = 0\%$, $p = 0$.											
Test for overall effect (fixed eff	= 2.61 (#	o = 0.009)		-400 -200 0 200 400						
Test for overall effect (random	effects	s): t ₂ = 3.	04(p = 0)	0.093)							

Figure S14. Forest plots. CI, confidence interval; EDFF, end-diastolic forward flow; MD, mean difference; OR, odds ratio; SD, standard deviation; VO2, oxygen consumption.

A. Peak VO2 (%)

Study	Total	Mean	EDFF SD	Total	No Mean	EDFF SD	Mean Difference	MD	95%-CI	Weight (fixed)	Weight (random)
Babu-Narayan 2012 Bonello 2013 Gatzoulis 1995 Lee 2013 Mercer-Rosa 2018 Samyn 2013 van den Berg 2007	27 38 17 33 63 12 24	85.00 76.05 100.90 70.30 80.00 79.00 89.00	20.00 4.17 13.80 11.50 17.00 11.30 11.00	37 110 12 17 23 17 12	70.00 75.50 82.50 54.70 73.00 68.50 97.00	15.00 4.30 10.10 12.90 18.00 7.67 17.00		15.00 0.55 18.40 15.60 7.00 10.50 -8.00	[6.04; 23.96] [-1.00; 2.10] [9.70; 27.10] [8.32; 22.88] [-1.47; 15.47] [3.14; 17.86] [-18.58; 2.58]	2.5% 82.9% 2.6% 3.8% 2.8% 3.7% 1.8%	13.5% 17.3% 13.7% 14.6% 13.8% 14.6% 12.4%
Fixed-effects Random-effects Heterogeneity: $I^2 = 88$ Test for overall effect Test for overall effect	214 %, <i>p</i> < (fixed e (randor	0.001 ffect): z = n effects	= 3.25 ()): t ₆ = 2	228 p = 0.0 .43 (p :	01) = 0.051))	-20 -10 0 10 20	2.34 8.43	[0.93; 3.75] [-0.05; 16.92]	100.0% 	 100.0%

B. Peak VO2 (mL/kg/min)

		E	DFF		No E	DFF				Weight	Weight	
Study	Total	Mean	SD	Total	Mean	SD	Mean Difference	MD	95%-CI	(fixed)	(random)	
Bonello 2013	38	25.30	1.50	110	26.50	1.70		-1.20	[-1.77; -0.63]	26.1%	20.1%	
Kutty 2018	122	27.73	1.58	277	24.35	1.87		3.38	[3.02; 3.73]	67.4%	20.2%	
Mercer-Rosa 2018	63	34.00	8.00	23	29.00	7.00) +	5.00	[1.52; 8.48]	0.7%	15.8%	
Rathore 2006	52	26.30	3.10	28	29.20	2.60)	-2.90	[-4.18; -1.62]	5.2%	19.5%	
van den Berg 2007	24	39.00	9.00	12	45.00	8.00)	-6.00	[-11.78; -0.22]	0.3%	11.4%	
Fixed-effects	317			462			4	1.85	[1.55; 2.14]	100.0%		
Random-effects								0.65	[-3.86; 5.15]		100.0%	
Heterogeneity: $l^2 = 98\%$, $p < 0.001$												
Test for overall effect (fixed effect): $z = 12.36 (p < 0.001)$ -10 -5 0 5 10												
Test for overall effect (random effects): $t_5 = 0.37$ ($p = 0.727$)												

Figure S15. Publication bias analysis by funnel plot graphic. (A) transannular patch repair. (Begg and Mazumdar's test: p=0.025, Egger's test: p=0.002). (B) right atrial volume indexed. (Begg and Mazumdar's test: p=0.117, Egger's test: p=0.014). (C) pulmonary regurgitation fraction. (Begg and Mazumdar's test: p=0.453, Egger's test: p=0.038). (D) A wave velocity at the tricuspid valve. (Begg and Mazumdar's test: p=0.655, Egger's test: p=0.005).

