

SUPPLEMENTAL MATERIAL

Data S1.

Supplemental Methods

Search strategy.

PubMed (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 pulmonary artery 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 'end-diastolic 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

Scopus (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% CI 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% CI 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% CI 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.

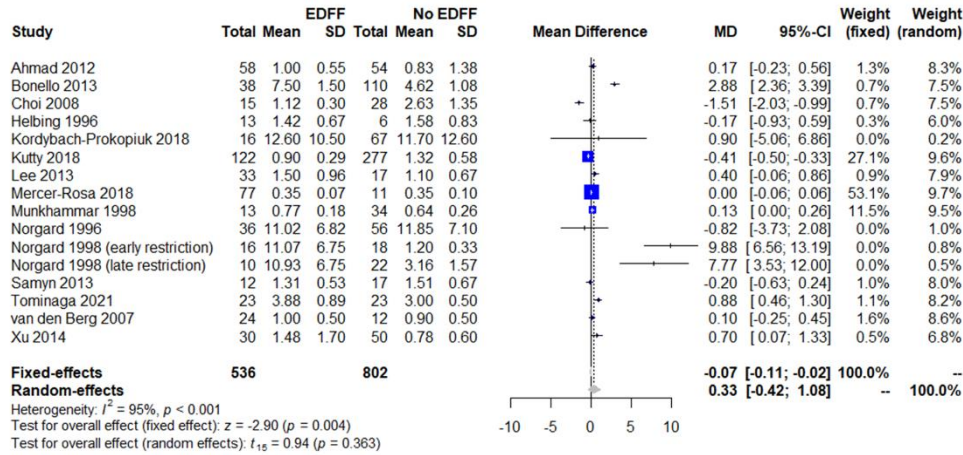
Meta-regression analyses

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

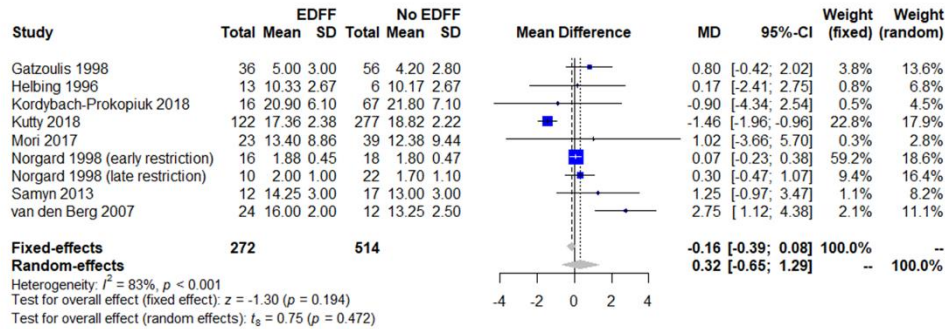
ventricular stroke volume indexed (RVSVi) (regression coefficient 0.465, 95% CI 0.144-0.786, $p=0.016$, 6 studies) and pulmonary regurgitation fraction (regression coefficient 0.214, 95% CI 0.003-0.424, $p=0.048$, 8 studies). Lastly, it was found that older age at evaluation was associated with smaller 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)



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



C. Age at study (years)

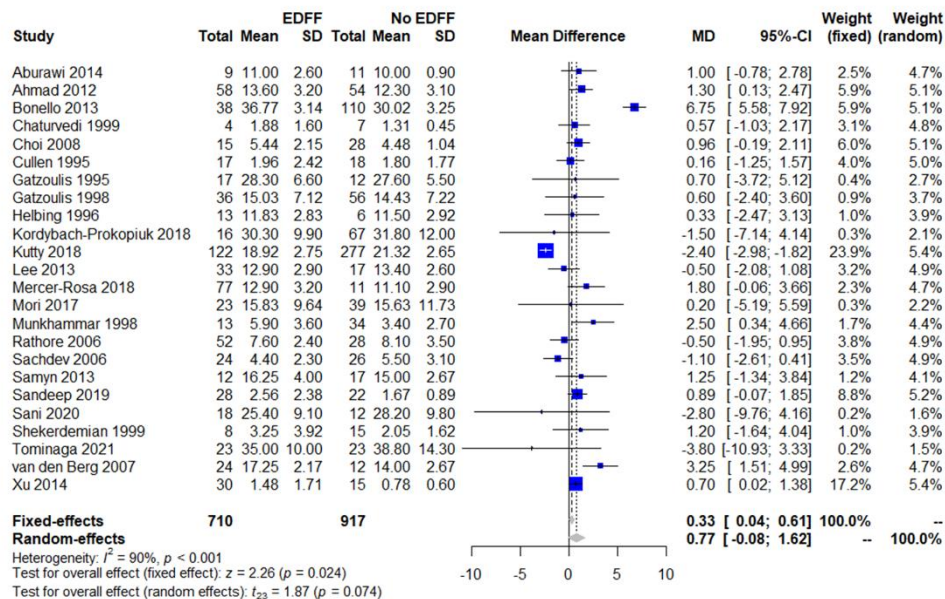
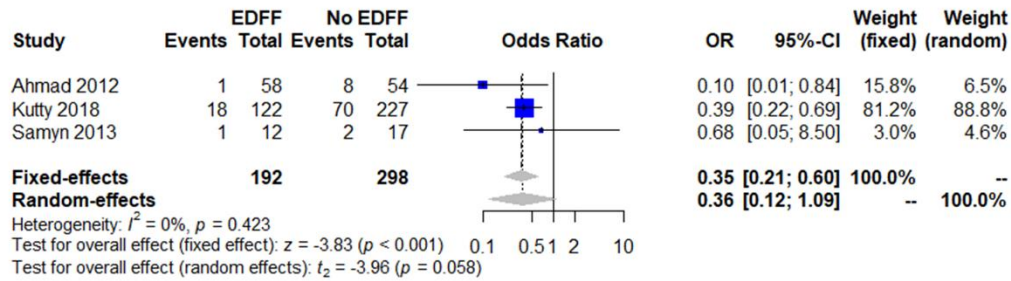
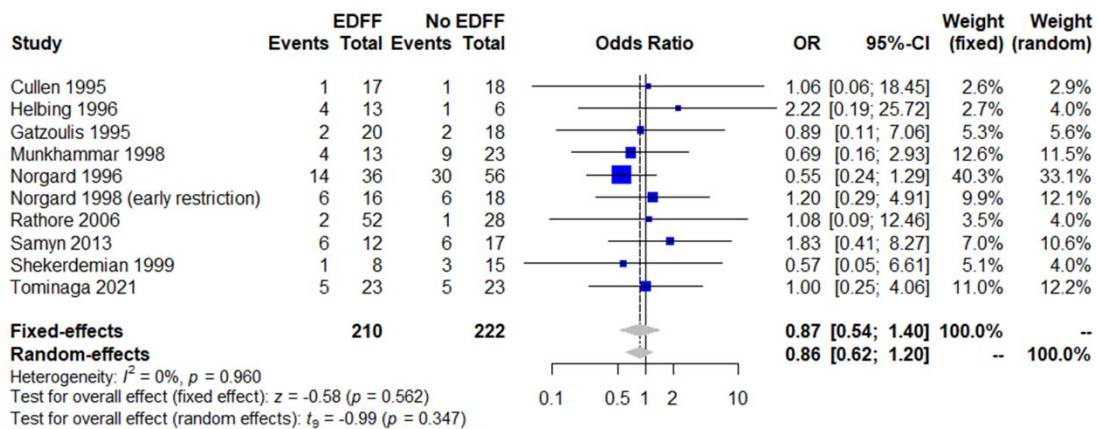


Figure S2. Forest plots. BT, Blalock-Taussig; CI, confidence interval; EDFF, end-diastolic forward flow; MD, mean difference; OR, odds ratio; RVPA, right ventricle-pulmonary artery; SD, standard deviation.

A. Previous RVPA shunt



B. Previous BT shunt



C. Aortic cross-clamp time (min)

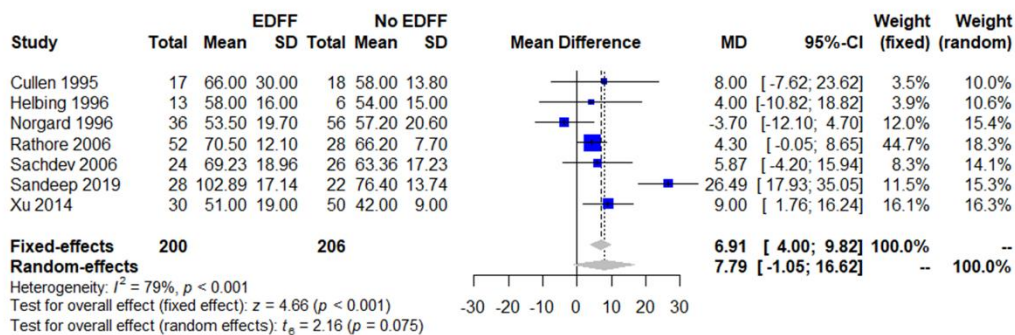
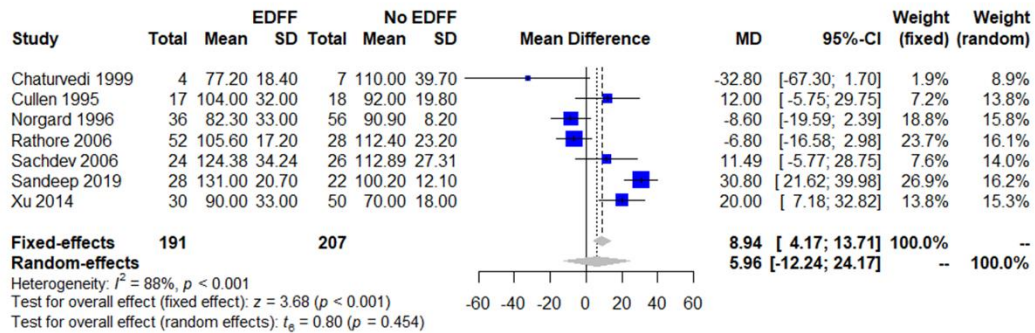
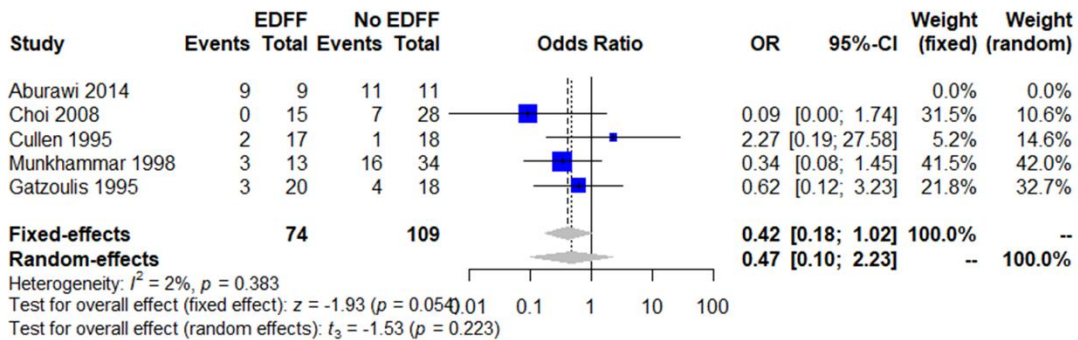


Figure S3. Forest plots. CI, confidence interval; CPB, cardiopulmonary bypass; EDFF, end-diastolic forward flow; MD, mean difference; OR, odds ratio; SD, standard deviation.

A. CPB time (min)



B. Transatrial repair



C. Transannular patch repair

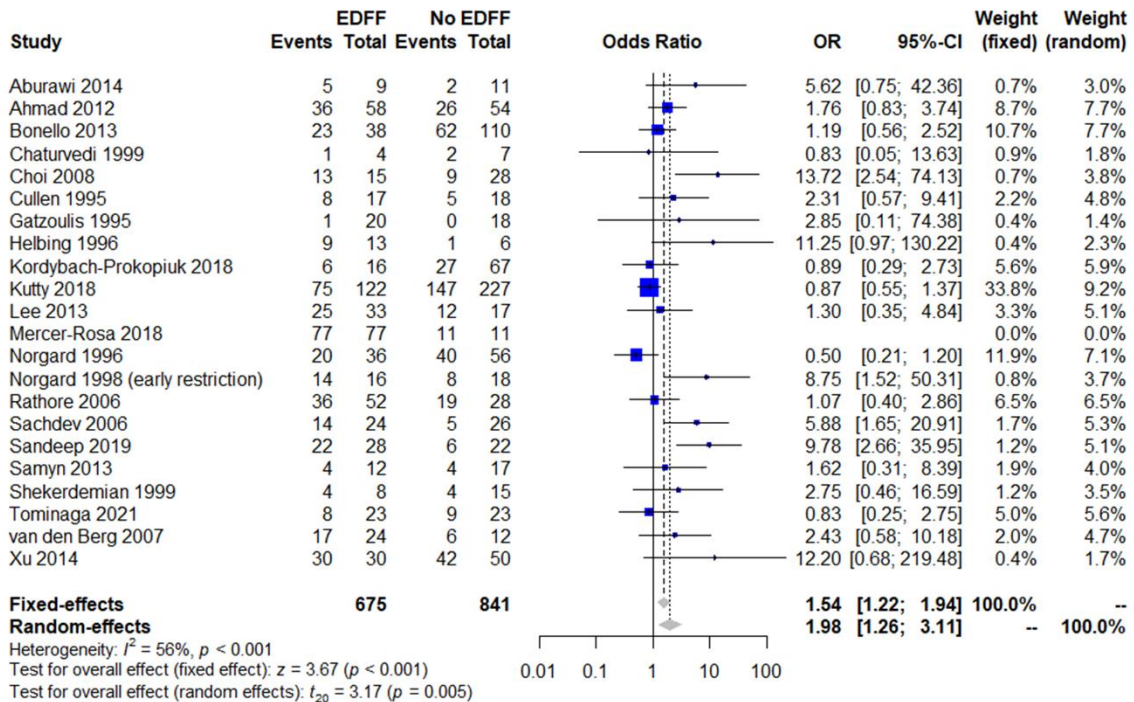
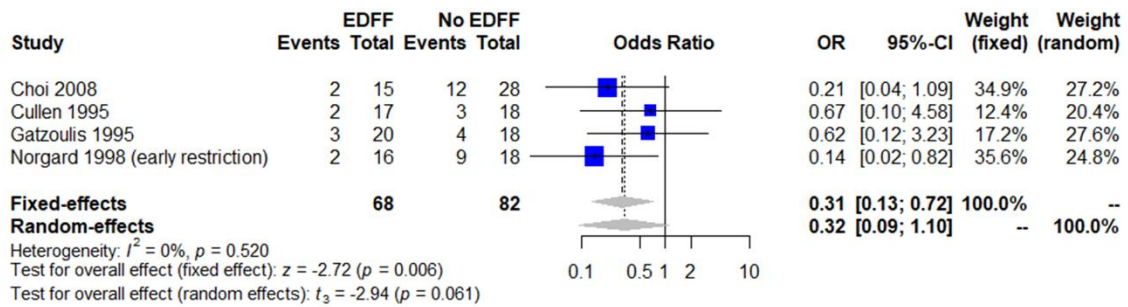


Figure S4. Forest plots. CI, confidence interval; EDFF, end-diastolic forward flow; ICU, intensive care unit; MD, mean difference; OR, odds ratio; SD, standard deviation.

A. Outflow patch repair



B. ICU Length of stay (days)

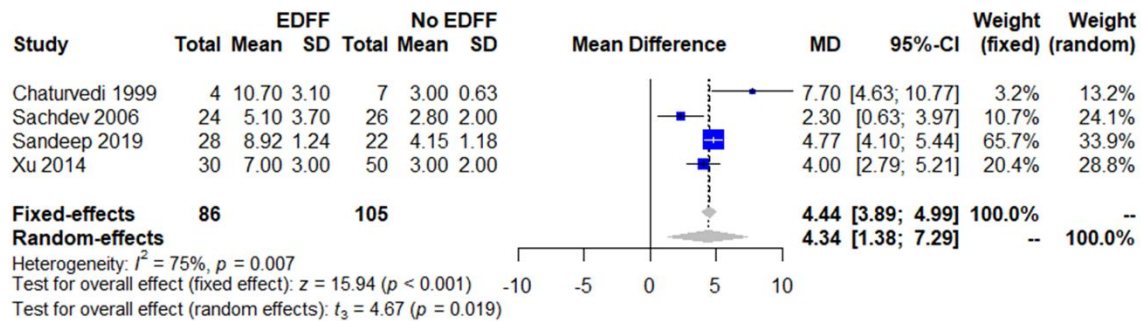
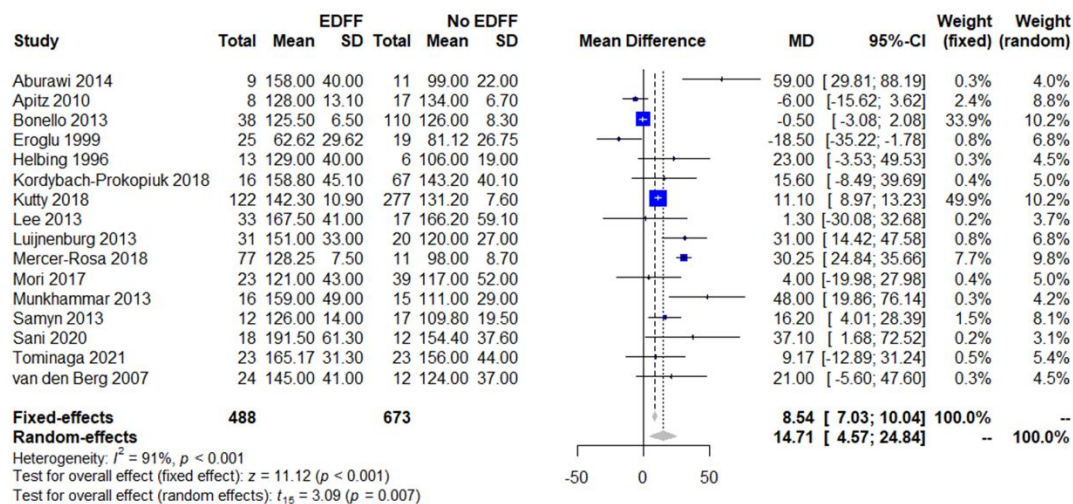
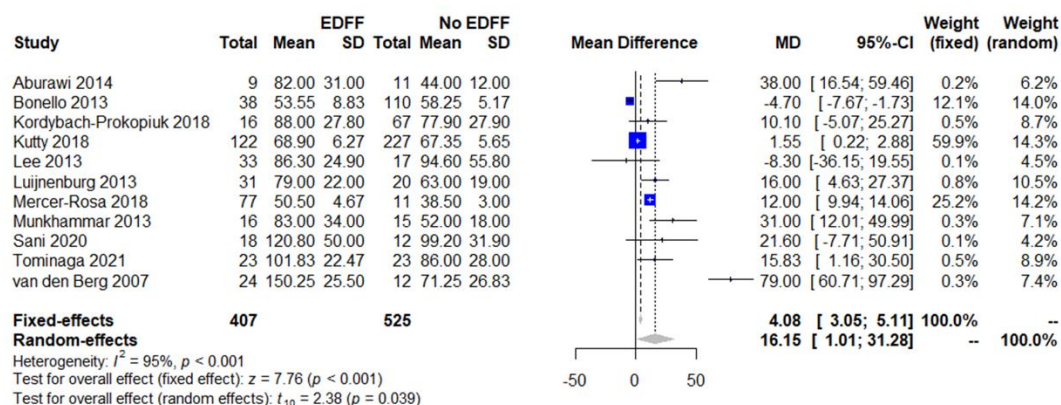


Figure S5. Forest plots. CI, confidence interval; EDFF, end-diastolic forward flow; MD, mean difference; RVEDVi, right ventricular end-diastolic volume indexed; RVESVi, right ventricular end-systolic volume indexed; RVSVi, right ventricular stroke volume indexed; SD, standard deviation.

A. RVEDVi (mL/m²)



B. RVESVi (mL/m²)



C. RVSVi (mL/m²)

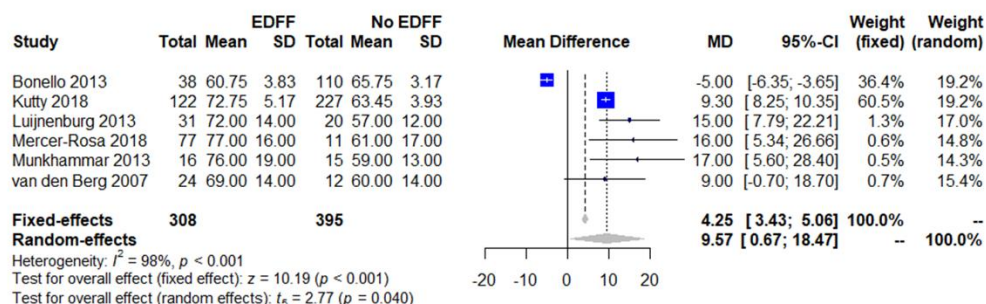
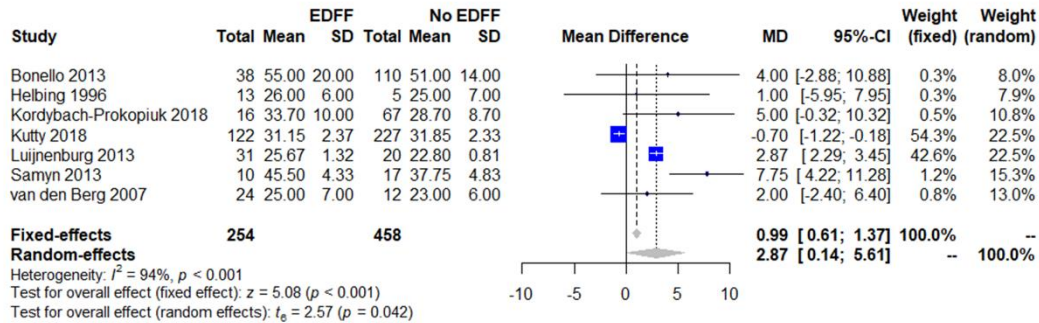
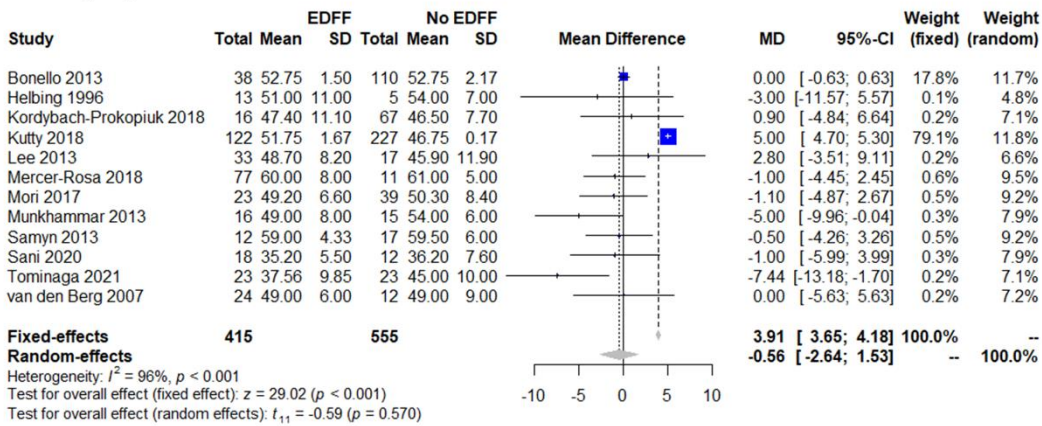


Figure S6. Forest plots. CI, confidence interval; EDFF, end-diastolic forward flow; MD, mean difference; RVEDP, right ventricular end-diastolic pressure; RVEF, right ventricular ejection fraction; RVESP, right ventricular end-systolic pressure; RVMi, right ventricular mass indexed; SD, standard deviation.

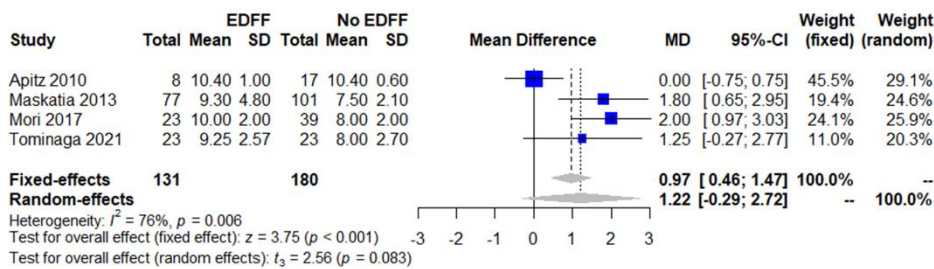
A. RVMi (g/m²)



B. RVEF (%)



C. RVEDP (mmHg)



D. RVESP (mmHg)

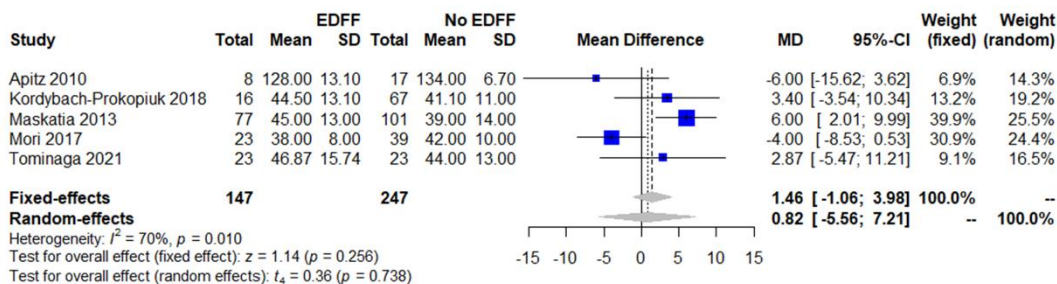
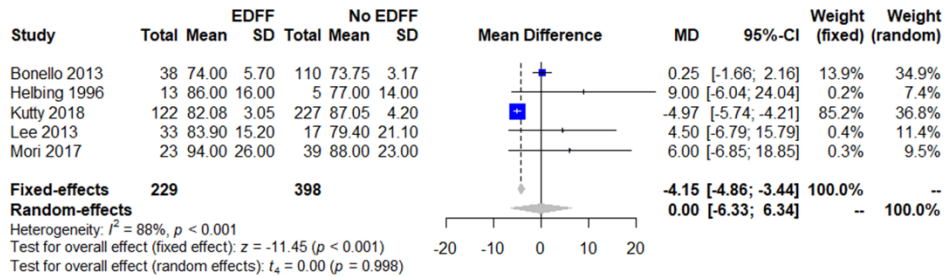
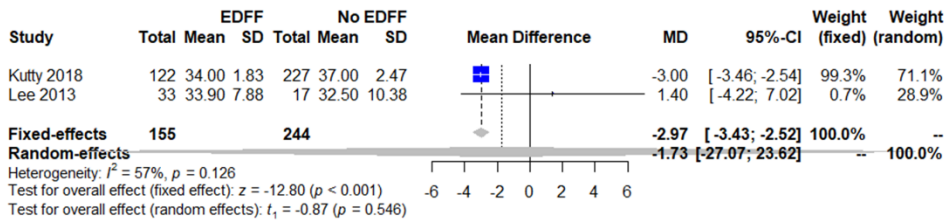


Figure S7. Forest plots. CI, confidence interval; EDFF, end-diastolic forward flow; LVEDVi, left ventricular end-diastolic volume indexed; LVEF, left ventricular ejection fraction; LVESVi, left ventricular end-systolic volume indexed; LVSVi, left ventricular stroke volume indexed; MD, mean difference;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

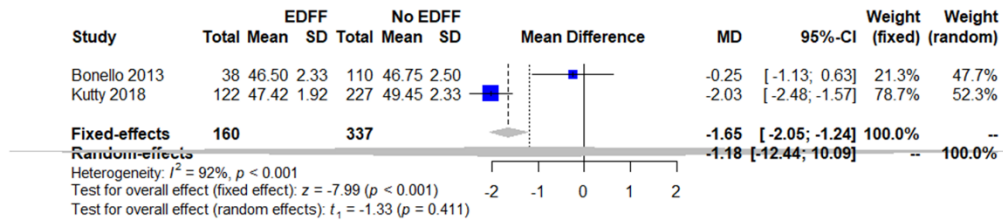
A. LVEDVi (mL/m²)



B. LVESVi (mL/m²)



C. LVSVi (mL/m²)



D. LVEF (%)

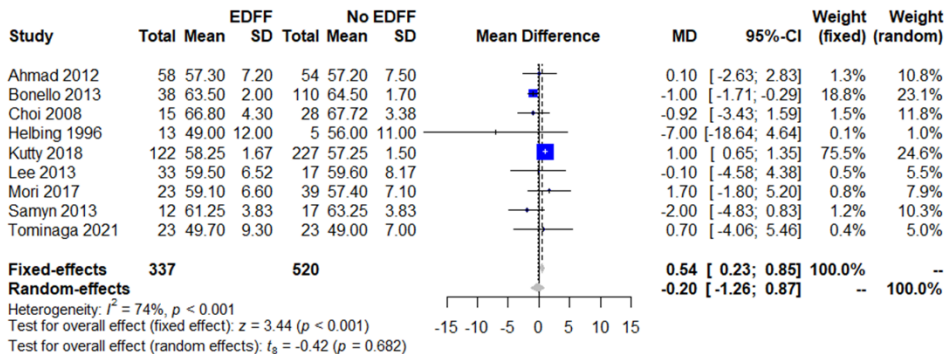
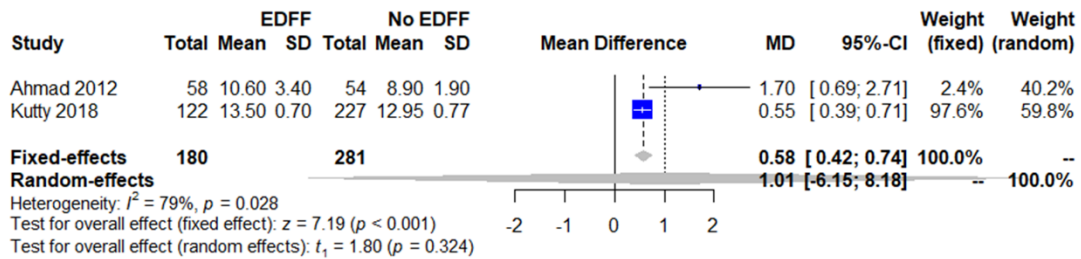


Figure S8. Forest plots. CI, confidence interval; EDFF, end-diastolic forward flow; MD, mean difference; RAAi, right atrial area indexed; RAVi, right atrial volume indexed; SD, standard deviation.

A. RAAi (cm²/m²)



B. RAVi (mL/m²)

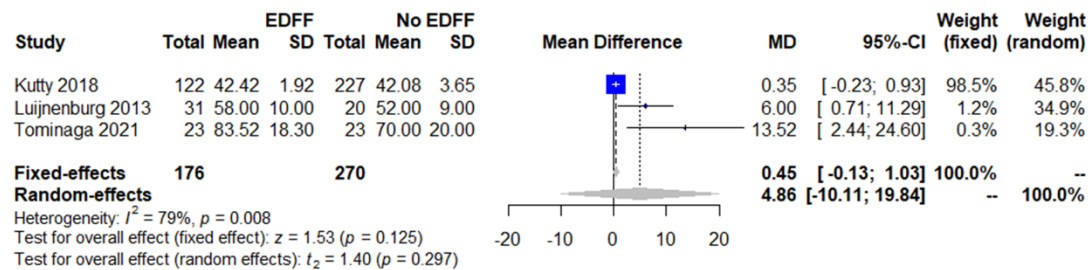
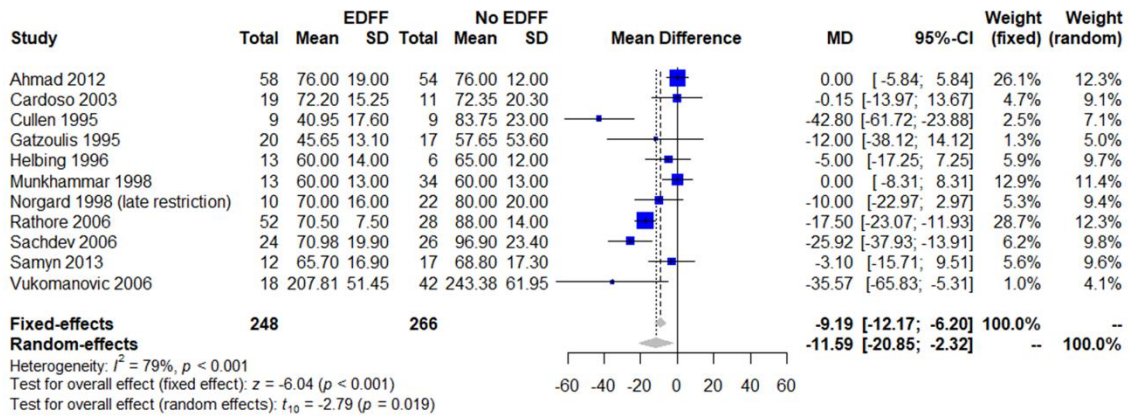
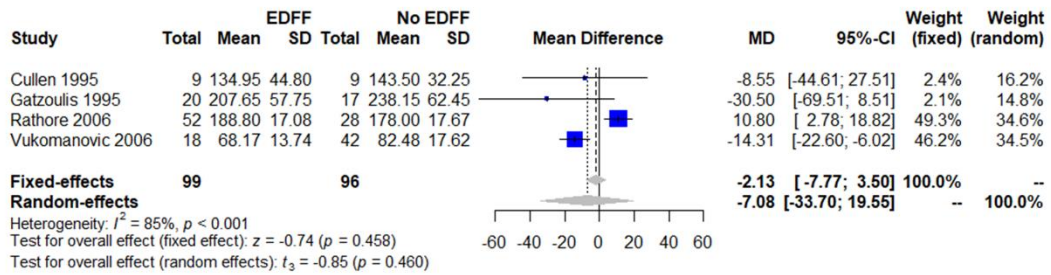


Figure S9. Forest plots. CI, confidence interval; EDFF, end-diastolic forward flow; MD, mean difference; SD, standard deviation.

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)

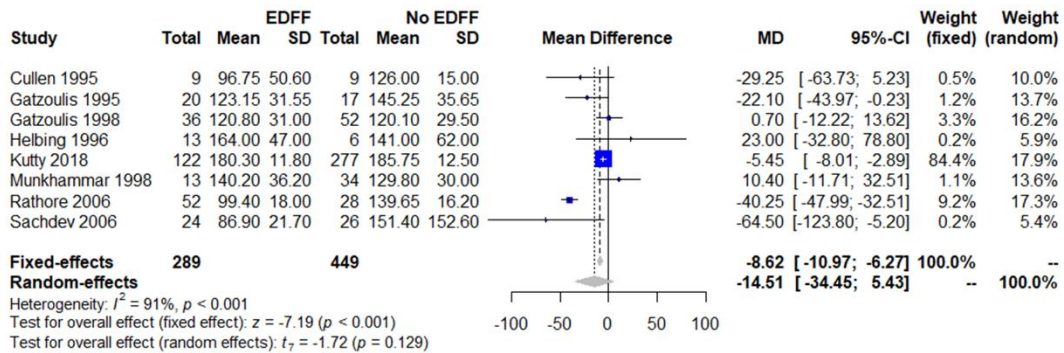
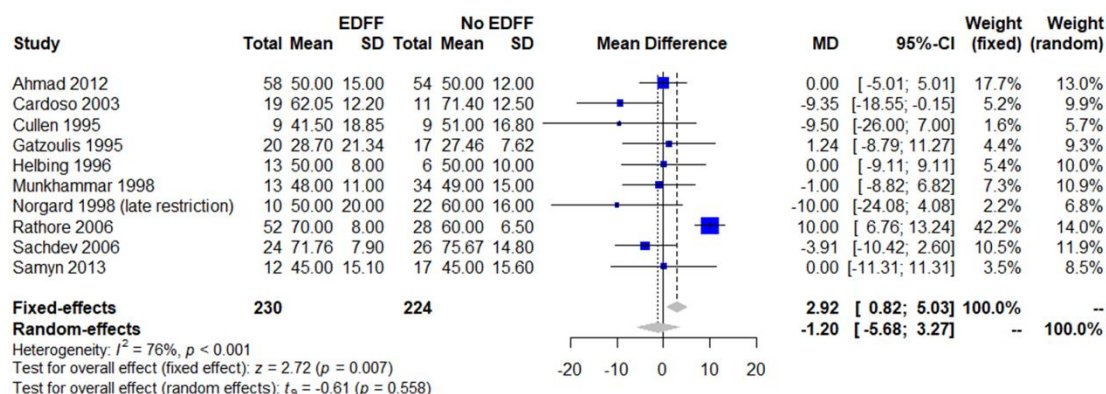
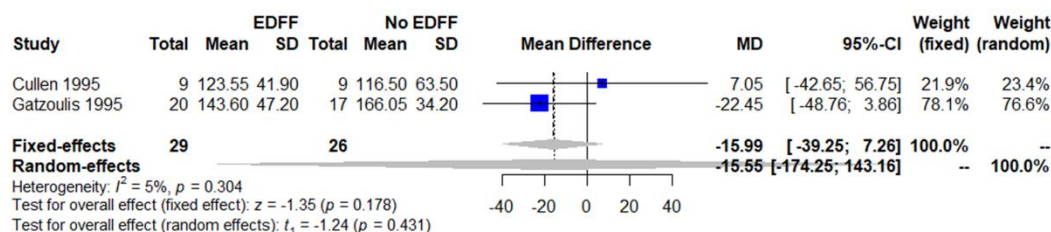


Figure S10. Forest plots. CI, confidence interval; EDFF, end-diastolic forward flow; MD, mean difference; SD, standard deviation.

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



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



C. E/A at the tricuspid valve

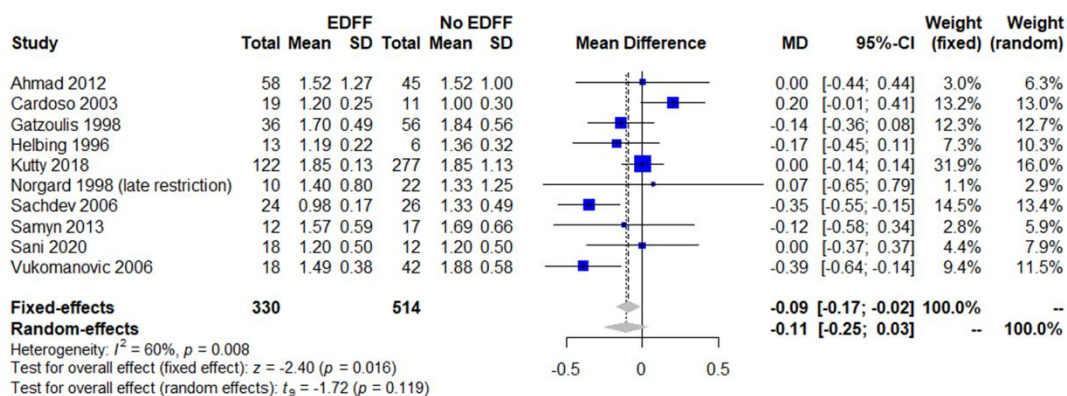
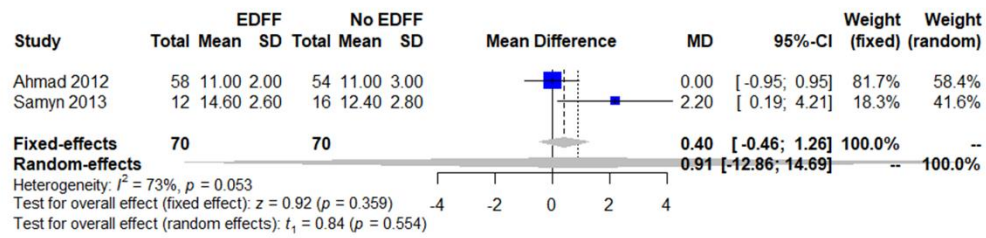
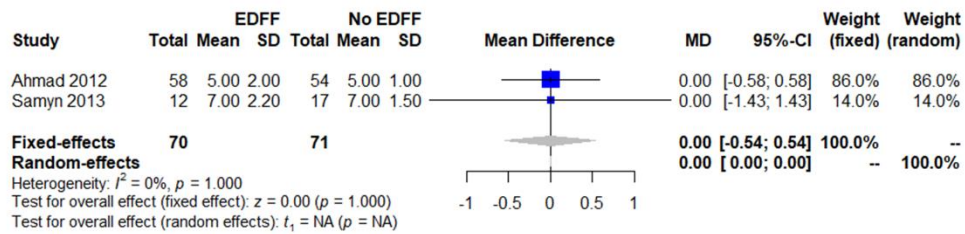


Figure S11. Forest plots. CI, confidence interval; EDFF, end-diastolic forward flow; MD, mean difference; SD, standard deviation.

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



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



C. E/E' at the tricuspid valve

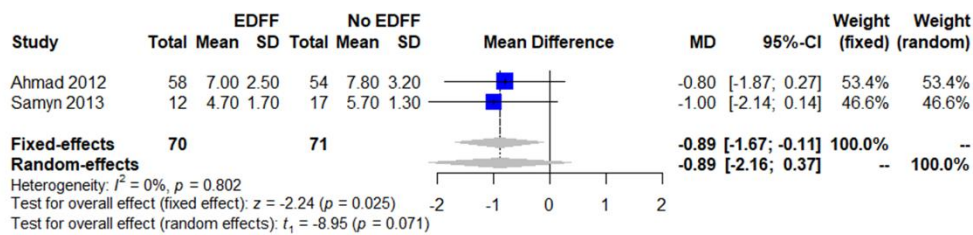
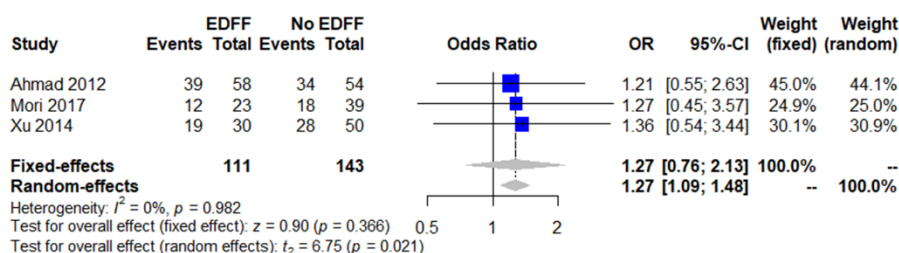
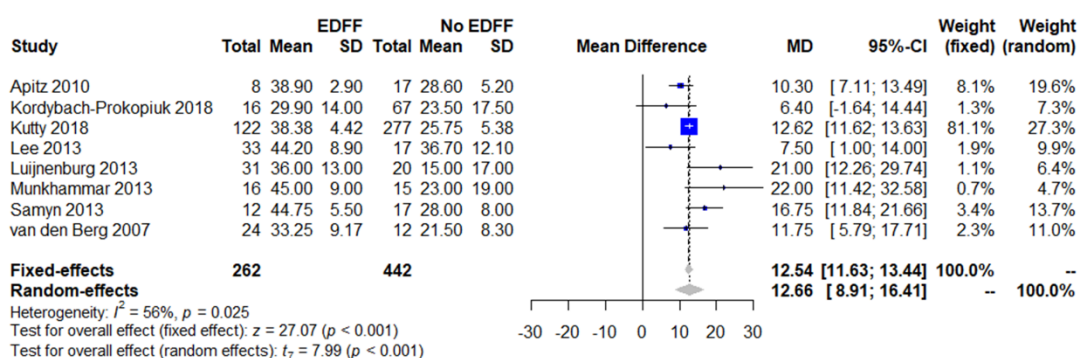


Figure S12. Forest plots. CI, confidence interval; EDFF, end-diastolic forward flow; MD, mean difference; OR, odds ratio; PR, pulmonary regurgitation; SD, standard deviation.

A. Moderate to severe PR



B. PR fraction (%)



C. PR duration (msec)

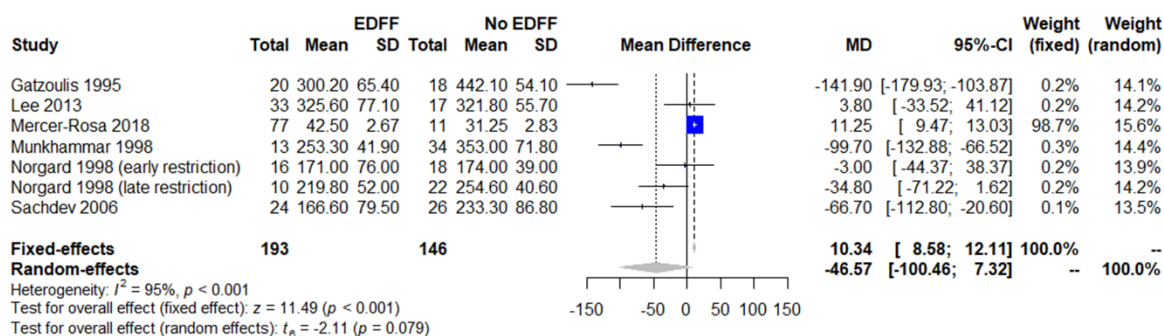
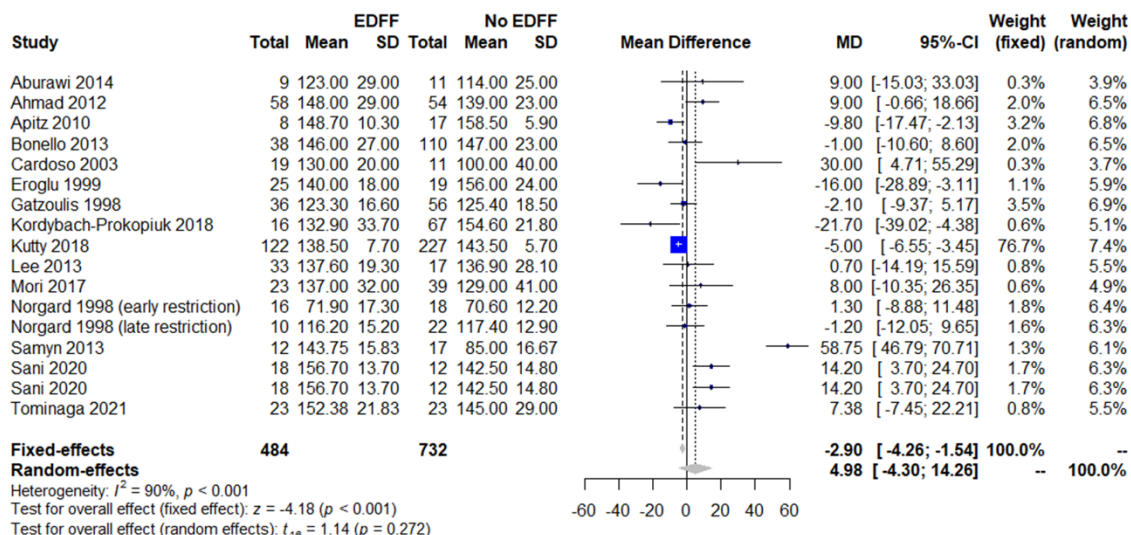
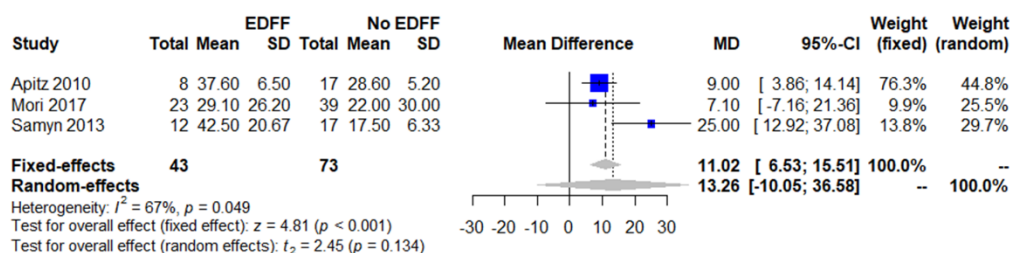


Figure S13. Forest plots. BNP, brain natriuretic peptide; CI, confidence interval; EDFF, end-diastolic forward flow; MD, mean difference; NT-proBNP, N-terminal pro hormone brain natriuretic peptide; OR, odds ratio; SD, standard deviation.

A. QRS duration (msec)



B. BNP (pg/mL)



C. NT-proBNP (pg/mL)

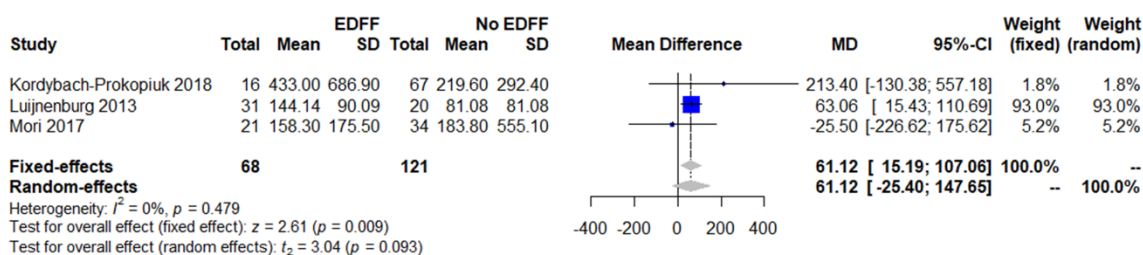
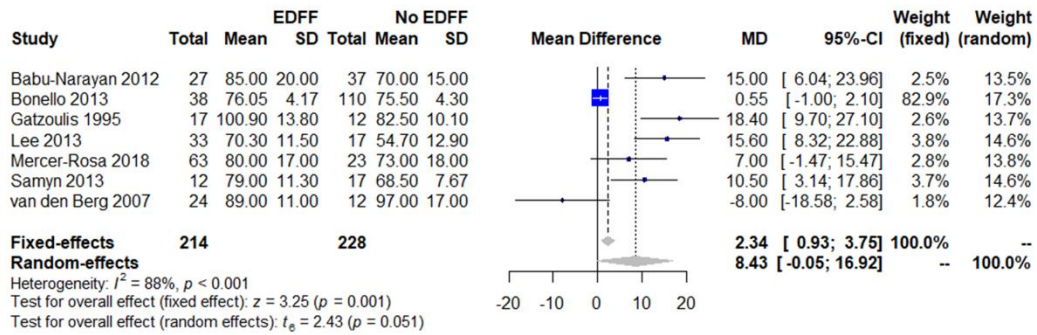


Figure S14. Forest plots. CI, confidence interval; EDFF, end-diastolic forward flow; MD, mean difference; OR, odds ratio; SD, standard deviation; VO₂, oxygen consumption.

A. Peak VO₂ (%)



B. Peak VO₂ (mL/kg/min)

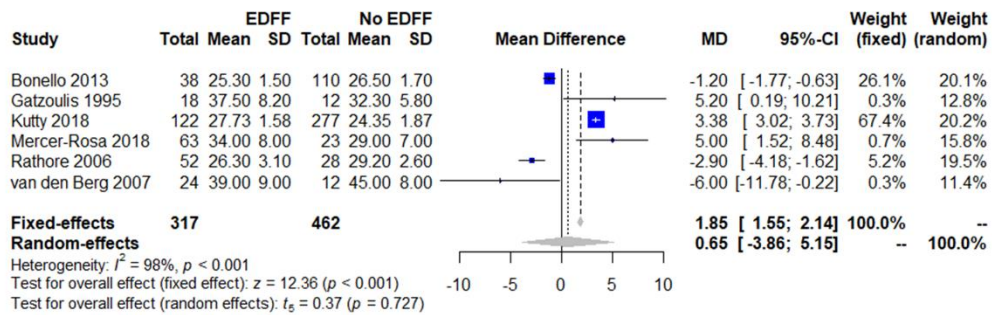


Figure S15. Publication bias analysis by funnel plot graphic. (A) transannular patch repair. (Begg and Mazumdar's test: $p=0.025$, Egger's test: $p=0.002$). **(B) right atrial volume indexed.** (Begg and Mazumdar's test: $p=0.117$, Egger's test: $p=0.014$). **(C) pulmonary regurgitation fraction.** (Begg 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: $p=0.005$).

