# **Improved Left Atrial Function in CRT Responders: A Systematic Review and Meta-Analysis**

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## Supplementary data

**Table S1: Supplement 1.** Summary of quality assessment analysis (Quality Assessment of Diagnostic Accuracy Studies-QUADAS 2).

Domain	Questions	Judgments
Risk of bias		
1) Patient selection	Was a consecutive or random sample of patients enrolled?	Yes, No, Unclear
	Was a case-control design avoided?	Yes, No, Unclear
	Did the study avoid inappropriate exclusions?	Yes, No, Unclear
	Could the selection of patients have introduced bias?	Low, High, Unclear
Applicability	Is there concern that the included patients do not match	Low, High, Unclear
1) Patient selection	the review questions?	
Risk of bias	Were the index test results interpreted without knowledge	
2) Index test	of the results of the reference standard?	Yes, No, Unclear
	If a threshold was used, was it pre-specified?	Yes, No, Unclear
	Could the conduct or interpretation of the index test have	
	introduced bias?	Low, High, Unclear
Applicability	Is there concern that the index test, its conduct, or	
2) Index test	interpretation differ from the review question?	Low, High, Unclear
Risk of bias	Is the reference standard likely to correctly classify the	
3) Reference standard	target condition?	Yes, No, Unclear
	Were the reference standard results interpreted?	Yes, No, Unclear
	without knowledge of the results of the index test?	Yes, No, Unclear
	Could the reference standard, its conduct, or its interpretation	
	have introduced bias?	Low, High, Unclear
Applicability	Is there concern that the target condition as defined by the	
3) Reference standard	reference standard does not match the review question?	Low, High, Unclear
Risk of bias	Was there an appropriate interval between index test(s)	
4) Flow and timing	and reference standard?	Yes, No, Unclear
	Did all patients receive a reference standard?	Yes, No, Unclear
	Did patients receive the same reference standard?	Yes, No, Unclear
	Were all patients included in the analysis?	Yes, No, Unclear
	Could the patient flow have introduced bias?	Low, High, Unclear

Patients: Patients undergo CRT; Criteria for CRT.
Index test: Relationship between CRT responders and LA function
Comparator test (if applicable): Correlations of LA function parameters
Target condition: Correlations of LA function on related mean change of LVESV and/or LVEF;
Reference standard: Guidelines of heart failure and indications of Cardiac resynchronization therapy in heart failure.



Figure 1. Supplement 2. Flow chart of study section.

Study	Software	Platform	Probe	FR	Gating	Observer	Tissue	LA function measurements	
(Year)			(MHz)				Tracking	PALS	LA total EF
Yo 2007	GE	EchoPac	NR	NR	R-R	Two	End-	Peak LA wall strain	LAVmax-LAVmin
	Vivid 7					blinded	myocardial	during LV systole	/LAVmax
Marsan	iE33	QLAB	NR	20-35	-	Single	-	-	LAVmax-LAVmin
2008	Philips					blinded			/LAVmax
Donal	GE	EchoPac	NR	NR	R-R	Two	Endo-	Peak LA wall strain	LAVmax-LAVmin
2009	Vivid 7					blinded	epicardial	during LV systole	/LAVmax
Fenon	GE	EchoPac	2.5	60-80	R-R	Two	Endocardial	Peak LA wall strain	-
2015	Vivid 9					blinded		during LV systole	-
Valenzia	GE	EchoPac	3.5	NR	R-R	Single	Endocardial	Peak LA wall strain	-
2016	Vivid 7					blinded		during LV systole	-
Badran	GE	EchoPac	2.5	NR	R-R	Single	Endocardial	Peak LA wall strain	LAVmax-LAVmin
2017	Healthcare					blinded		during LV systole	/LAVmax
Hansen	GE	EchoPac	3–5	NR	-	Single	-	-	LAVmax-LAVmin
2017	Vivid 9					blinded			/LAVmax

 Table S2: Supplement 3. Echocardiographic characteristics of LA functional measurements.

#### a) Baseline of LVEDV in CRT responders vs. CRT non respondrers



	CRT responders			CRT non	-respon	ders	Mean Difference			Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	l.	IV, Ra	ndom,	95% CI	
Badran 2017	25	7.4	24	24	6.4	13	27.9%	1.00 [-3.57, 5.57]				-	
Donal 2009	26.6	6.7	23	22.4	6.6	23	31.0%	4.20 [0.36, 8.04]					
Feneon 2015	28	3.1	54	30	2.4	25	41.1%	-2.00 [-3.25, -0.75]			-		
Total (95% CI)			101			61	100.0%	0.76 [-3.34, 4.86]			+	-	
Heterogeneity: Tau <sup>2</sup> = 10.23; Chi <sup>2</sup> = 10.03, df = 2 (P = 0.007); l <sup>2</sup> = 80%									-20	-10		10	20
Test for overall effect: Z = 0.36 (P = 0.72)										LVEF Io	werLV	EF higher	20

**Figure S2: Supplement 4.** Comparison of baseline LVEDV, LVESV, LVEDd and EF in group of patients with CRT responds vs. CRT non responders.

#### a) Baseline of QRS duration in CRT responders vs. CRT non responders

	CRT re	spond	ders	CRT non	-respon	ders		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% Cl
Donal 2009	164	27	23	165	21	23	36.0%	-1.00 [-14.98, 12.98]	
Feneon 2015	158	30	54	163	27	25	39.9%	-5.00 [-18.27, 8.27]	
Valzania 2016	159	24	18	160	23	12	24.1%	-1.00 [-18.10, 16.10]	
Total (95% CI)			95			60	100.0%	-2.60 [-10.98, 5.79]	
Heterogeneity: Chi <sup>2</sup> = 0	0.21, df =	2 (P =	0.90); l <sup>2</sup>	* = 0%					
Test for overall effect:	Z = 0.61 (	P = 0.5	54)						QRS no duration prolonged QRS duration prolonged

## a) Baseline of LAD in CRT responders vs. CRT non responders

	CRT responders CRT non-responders				ders		Mean Difference		Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	Year	IV, Random, 95% CI
Yu 2007	52.2	8.8	62	55	9.9	45	34.1%	-2.80 [-6.43, 0.83]	2007	
Donal 2009	53	8	23	50	8	23	30.4%	3.00 [-1.62, 7.62]	2009	
Badran 2017	44	1.8	24	50	5.8	13	35.5%	-6.00 [-9.23, -2.77]	2017	
Total (95% CI)			109			81	100.0%	-2.17 [-7.01, 2.67]		
Heterogeneity: Tau <sup>2</sup> = 14.47; Chi <sup>2</sup> = 9.78, df = 2 (P = 0.008); l <sup>2</sup> = 80%										
Test for overall effect:	Z = 0.88 (	P = 0.3	38)							LAD decrearsed LAD increarsed

**Figure S3: Supplement 5.** Comparison of baseline QRS duration and LA dimension in group of patients with CRT responders vs. CRT non responders.

### Correlation between LA strain and LAEF



Figure S4: Supplement 6. Weighted summary correlation between LA strain and LAEF.



Figure S5: Supplement 7. Relationship between LA strain change and a) male gender; b) age.

Author		Ris	k of bias	Applicability concerns			
(year)	Patients	Index	Reference	Flow and	Patients	Index	Reference
reference	selection	test	standard	timing	selection	test	standard
Yo 2007	Low	Low	Low	Low	Low	Low	Low
Marsan 2008	Low	Low	Low	Low	Low	Low	Low
Donal 2009	Low	Unclear	Low	Low	Low	Unclear	Unclear
Feneon 2015	Low	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Valenzia 2016	Low	Low	Low	Low	Low	Low	Low
Badran 2017	Low	Low	Low	Low	Low	Low	Low
Hansen 2017	Unclear	Low	High	High	Unclear	Low	High

Table S3: Supplement 8. Summary of QUADAS-2 Assessment of Selected Studies.

QUADAS-2: Quality Assessment of Diagnostic Accuracy Studies-2.



Figure 6. Supplement 9. Summary of QUADAS-2 Assessment of Selected Studies.