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# Does upgrade to tri-ventricular pacemaker improve long-term clinical response in non-responders to biventricular cardiac resynchronization therapy?

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# Does upgrade to tri-ventricular pacemaker improve long-term clinical response in non-responders to biventricular cardiac resynchronization therapy?

## Purpose

- Up to one third of patients with biventricular (BiV) cardiac resynchronization therapy (CRT) are non-responders.<sup>1</sup>
- Greater clinical response to CRT has been shown in patients given TriV CRT compared to BiV CRT as de novo device therapy.<sup>2</sup> This abstract investigates if upgrade to TriV CRT in non-responders to BiV CRT will improve long-term clinical outcome.

## Methods

- Prospective randomized controlled study of non-responders to optimized, biventricular CRT-pacemakers or CRT-defibrillators (at least 6 months of biventricular CRT) with New York Heart Association (NYHA) class III symptoms and left ventricular ejection fraction of  $\leq 35\%$ .
- The study conformed to the Declaration of Helsinki of the World Medical Association.
- Participants were randomized (2:1) to the upgrade to TriV CRT group or no upgrade group.
- Primary outcome was clinical response to CRT. Each patient was assessed for the worst outcome among the following categories of worsened clinical response: death from any cause, hospitalisation for heart failure, worsening of symptoms perceived by patients and worsening of NYHA class perceived by health professionals. Subjects were included only in one subcategory.
- Secondary outcomes were all-cause mortality and procedural complications. LV ejection fraction (LVEF) and LV end systolic volume (LVESV) were compared between the 2 groups on the last available echocardiogram during follow up.
- Cursor date was on 13<sup>th</sup> January 2015.

Variable	No upgrade (n=7)	Upgrade to TriV CRT (n=13)	P-value (2-tailed)
Age (years)	70.4±9.3	64.5±11.9	0.27
Gender (male) (%)	5 (71.4)	10 (76.9)	0.79
Time since BiV CRT (months)	21 (IQ 12-32)	18 (IQ 13-45.5)	0.70
Ischaemic heart failure (%)	4 (57.1)	8 (61.5)	0.85
NYHA: Class III (%)	7 (100)	13 (100)	1.0
Atrial arrhythmias (%)	3 (42.9)	1 (7.7)	0.06
Intrinsic PR or AR interval (ms)	250.0±26.9	180±60	0.09
BiV QRS duration (ms)	158.2±24.0	153.5±14.5	0.61
Intrinsic QRS duration (ms)	154.8±16.8	148.4±23.6	0.60
Minnesota Living with Heart Failure score	33.0±14.5	62±25.0	*0.01
Heart failure medication (%):			
-Beta-blocker	5 (71.4)	11 (84.6)	0.48
-ACEi or ARB	6 (85.7)	13 (100)	0.16
-Spironolactone	3 (42.9)	8 (61.5)	0.42
-Diuretics	6 (85.7)	13 (100)	0.16
Percentage BiV pacing (%)	99 (IQ94-99)	99.5 (IQ94.8-100)	0.34
Old LV lead in posterolateral or lateral CS branch (%)	3 (42.9)	7 (53.8)	0.60
LVEF (%)	26.8±5.6	27.1±6.2	0.95
LVESV (ml)	125.1±60.0	128.9±43.4	0.91

Table 1. Baseline characteristics of non-responders to biventricular CRT: upgrade to TriV CRT vs no upgrade group. Continuous data expressed as mean ± SD or median and interquartile range for non-parametric data. \*p<0.05.

## Results

- 20 patients were recruited between July 2009 and August 2010 (13 received upgrade to TriV CRT and 7 did not receive upgrade of their biventricular CRT).
- Baseline characteristics (Table 1) were similar between the two groups except for the Minnesota Living with Heart Failure score (TriV 62.0±25.0 vs Control 33.0±14.5, p=0.01).
- At 5 years, fewer patients in the upgrade to TriV group had worsened clinical response compared to the no upgrade group (38.5% vs 85.7%, p=0.04).
- At 5 years, the cumulative probability of survival was higher in the Upgrade to TriV group vs no upgrade group (Kaplan-Meier Method, Log-rank test, p=0.021).
- No difference was found in percentage improvement in LVEF or percentage reduction in LVESV between the 2 groups on echocardiography during follow up (no upgrade group: 19.0±21.2 months vs upgrade to TriV group: 25±17.9 months; p=0.55).
- 1 wound infection, 2 failures to upgrade and 1 lead displacement were observed in the upgrade to TriV group.

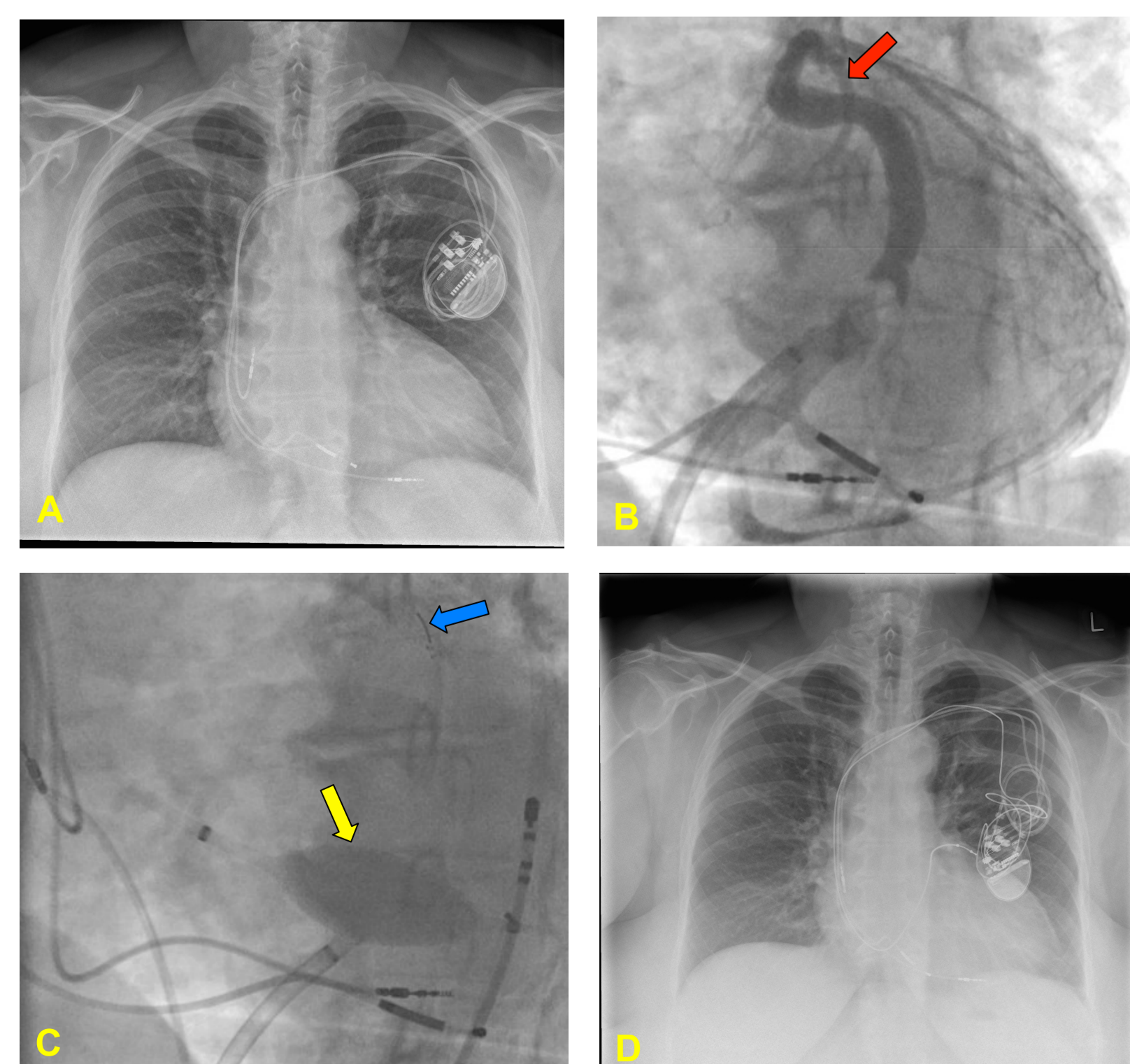


Fig. 1. Four patients in the upgrade to TriV CRT group underwent non-contact mapping of the left ventricle (LV) with the EnSite 3000 Array catheter to study the LV activation time from BiV and TriV pacing in different CS branches prior to the upgrade. Fig. 1A to 1D were obtained from the same patient. Fig. 1A: CXR prior to upgrade of BiV CRT. Fig. 1B: CS venogram showing the anteroseptal vein (yellow arrow). Fig. 1C: Fluoroscopy image showing the Ensite 3000 Array catheter for non-contact mapping of the LV (green arrow) and the pacing wire in a new site in the anteroseptal CS branch (blue arrow). Fig. 1D: CXR after upgrade of BiV to TriV CRT.

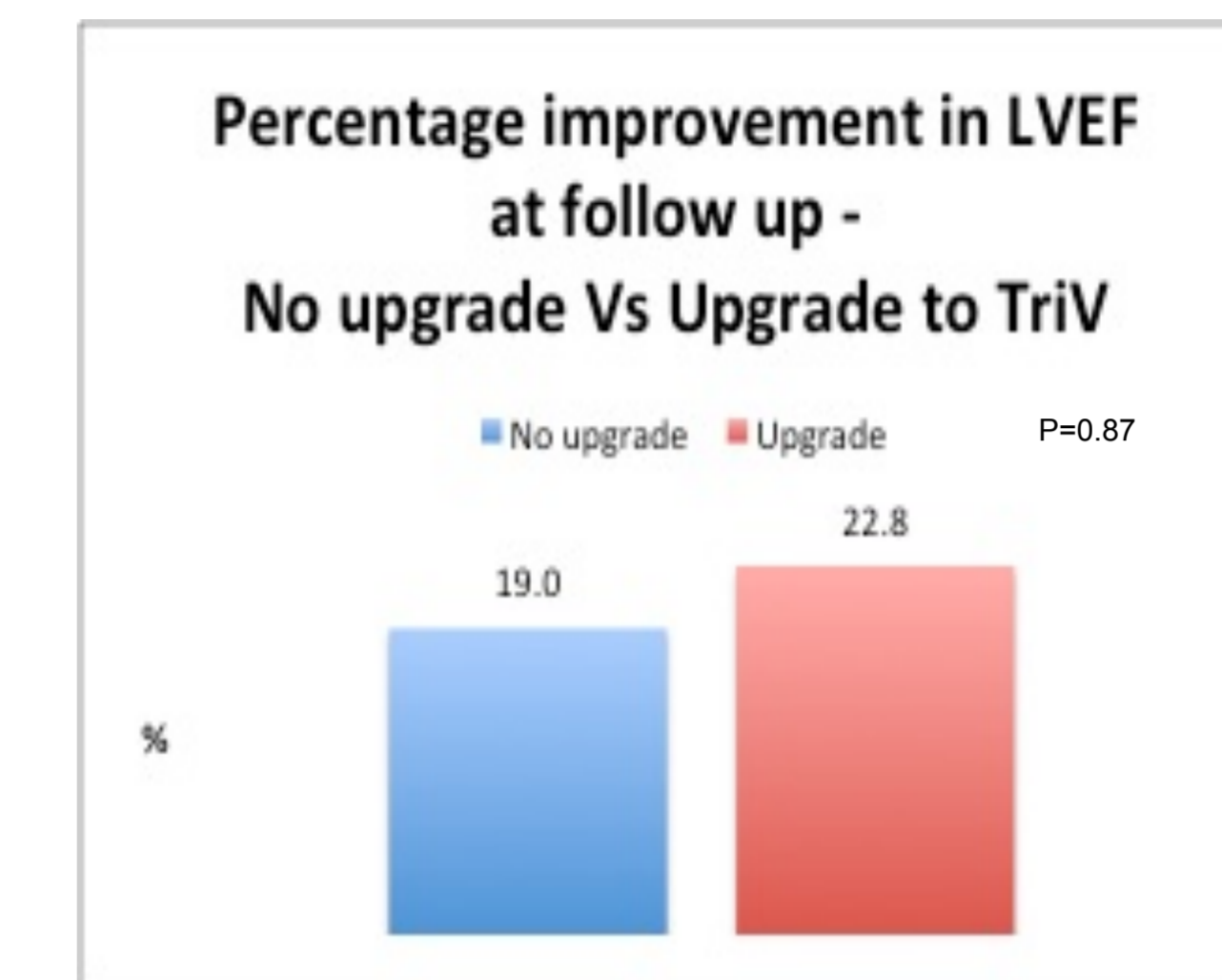


Fig. 2. Percentage improvement in LVEF on echocardiography at follow up in the no upgrade of BiV group Vs upgrade to TriV CRT group, P=0.87.

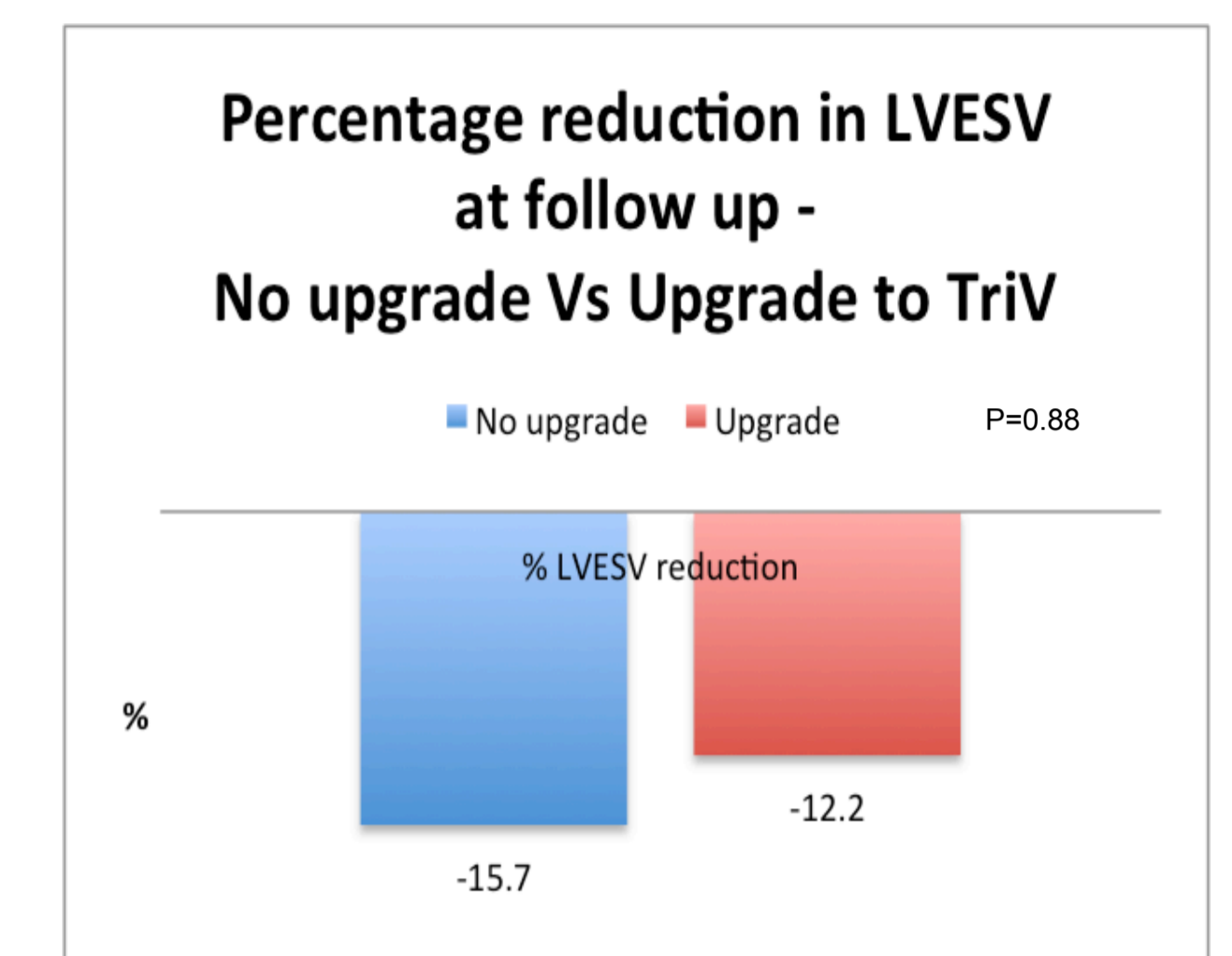


Fig. 3. Percentage reduction in LV end systolic volume (LVESV) on echocardiography at follow up in the no upgrade of BiV group Vs upgrade to TriV CRT group, P=0.88.

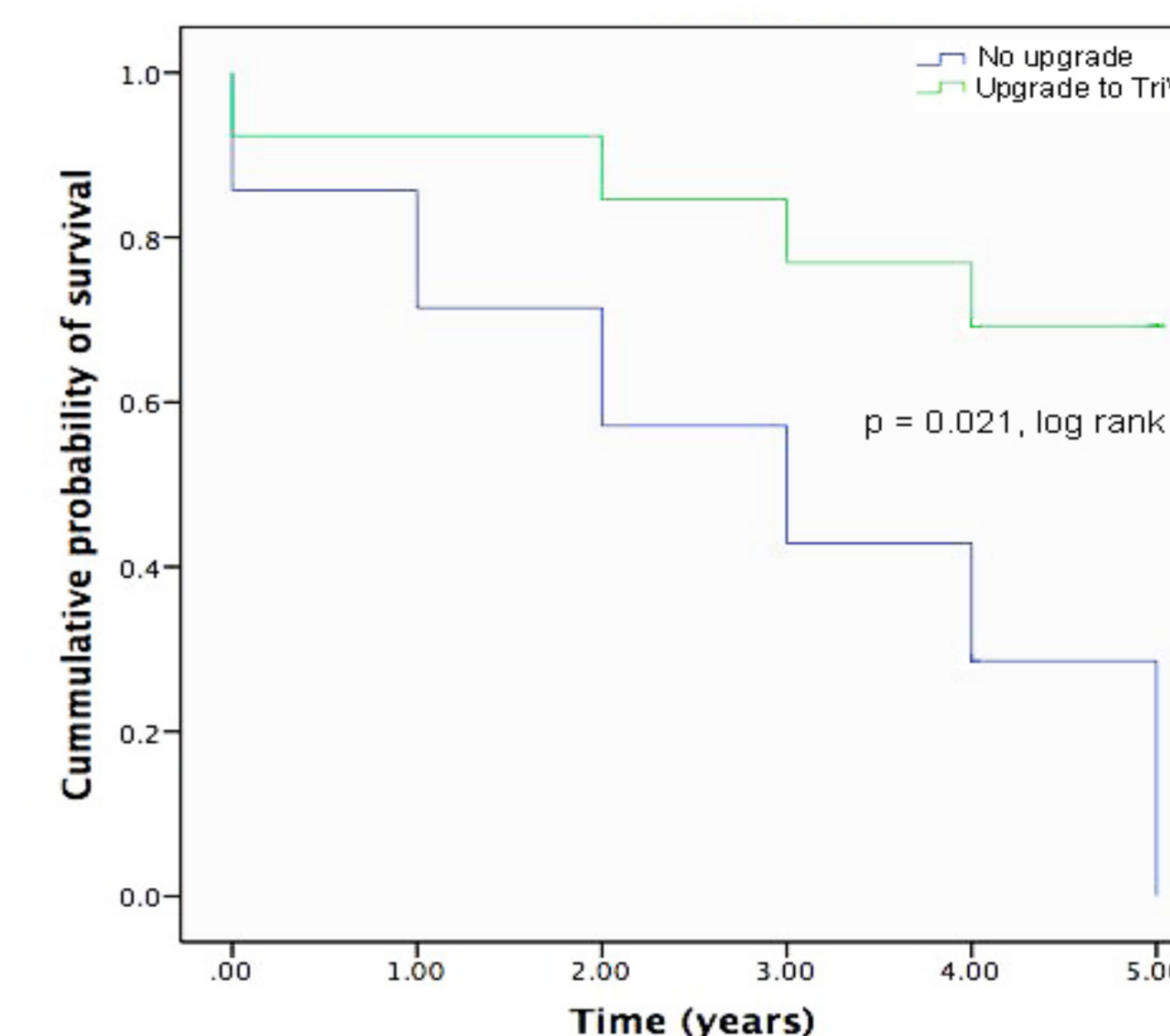


Fig. 4. Cumulative probability of survival at 5 years in non-responders to biventricular CRT: upgrade to tri-ventricular CRT (TRIVENT) group vs no upgrade (Control). Kaplan-Meier Method, Log-rank test, \*p<0.05.

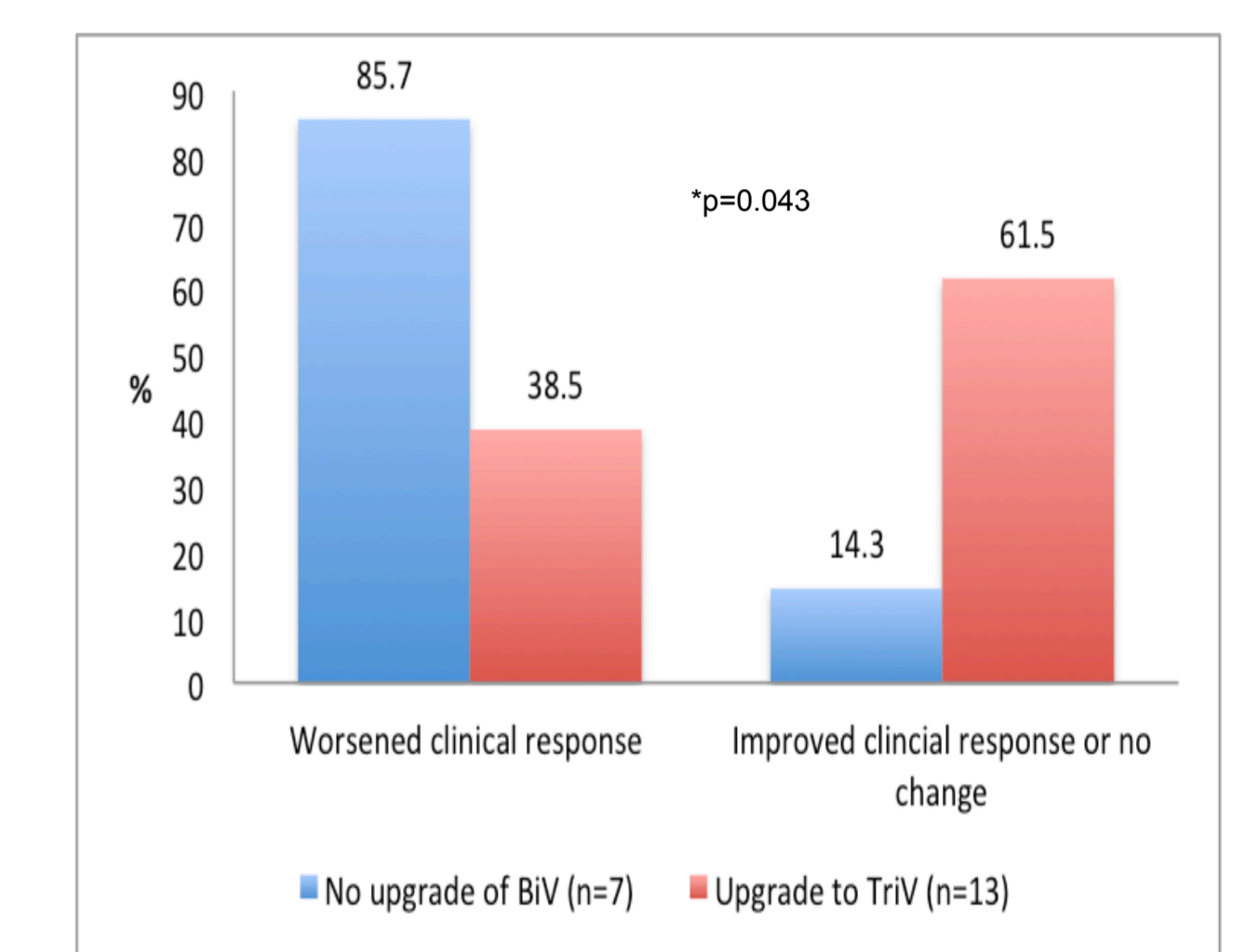


Fig. 5. Clinical response to CRT at 5 years in non-responders to CRT: upgrade to TriV CRT vs no upgrade. \*p<0.05 Chi-squared test.

## Conclusion

- Upgrade to tri-ventricular CRT in non-responders to biventricular CRT may potentially improve clinical response to CRT and long-term survival.
- The rate of procedural complications may reflect the risks associated with a complex upgrade procedure.
- Mechanism of survival benefit from upgrade to tri-ventricular CRT is not explained by LV ejection fraction or LV end systolic volume.
- These findings warrant further evaluation in a large randomized control trial.

## References

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