

# Real-world effectiveness of automated dynamic optimization and left ventricular-only pacing algorithm of cardiac resynchronization therapy

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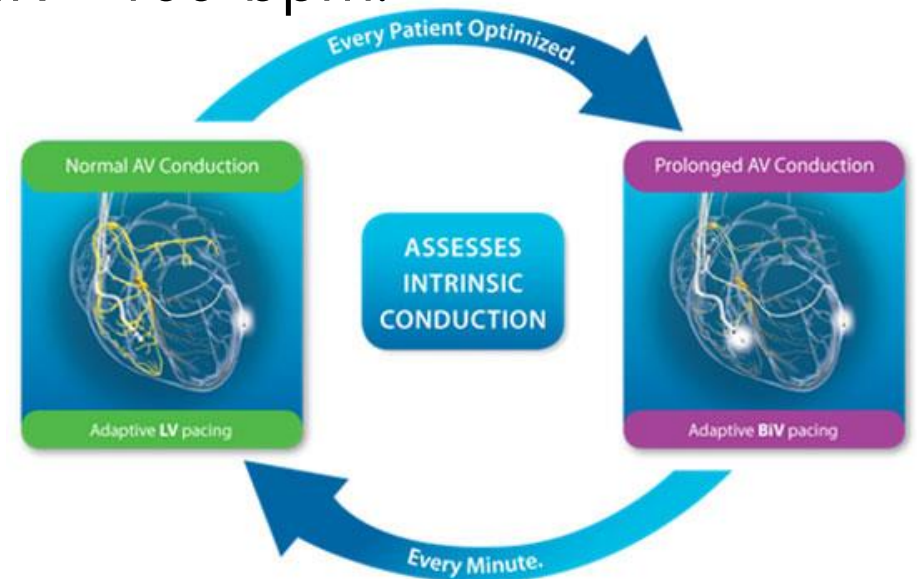
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# Background

- **Cardiac resynchronization therapy (CRT)** is a cornerstone of treatment for patients with HF and LV conduction delay, mostly typical LBBB.
- Clinical response to CRT have remained unchanged, and real world data demonstrate **non-response rates of between 30-50%**.
- Several factors associated with non-response included suboptimal AV timing, arrhythmia limiting the % Biventricular (BiV) pacing, epicardial LV lead location, suboptimal medical therapy, and persistent mechanical dyssynchrony.

# Adaptive CRT

- **Adaptive CRT(aCRT)** is an automated dynamic optimization algorithm to preserve intrinsic AV conduction via the RBB.
  - **EGM-based AV and VV interval adjustment.**
  - Paces LV only if at >70% the intrinsic AV interval during normal AV conduction (AV interval  $\geq 220$  ms) with HR <100 bpm.
  - Paces BiV if AV interval <220 ms.
  - Adjusts AV and VV interval every minute



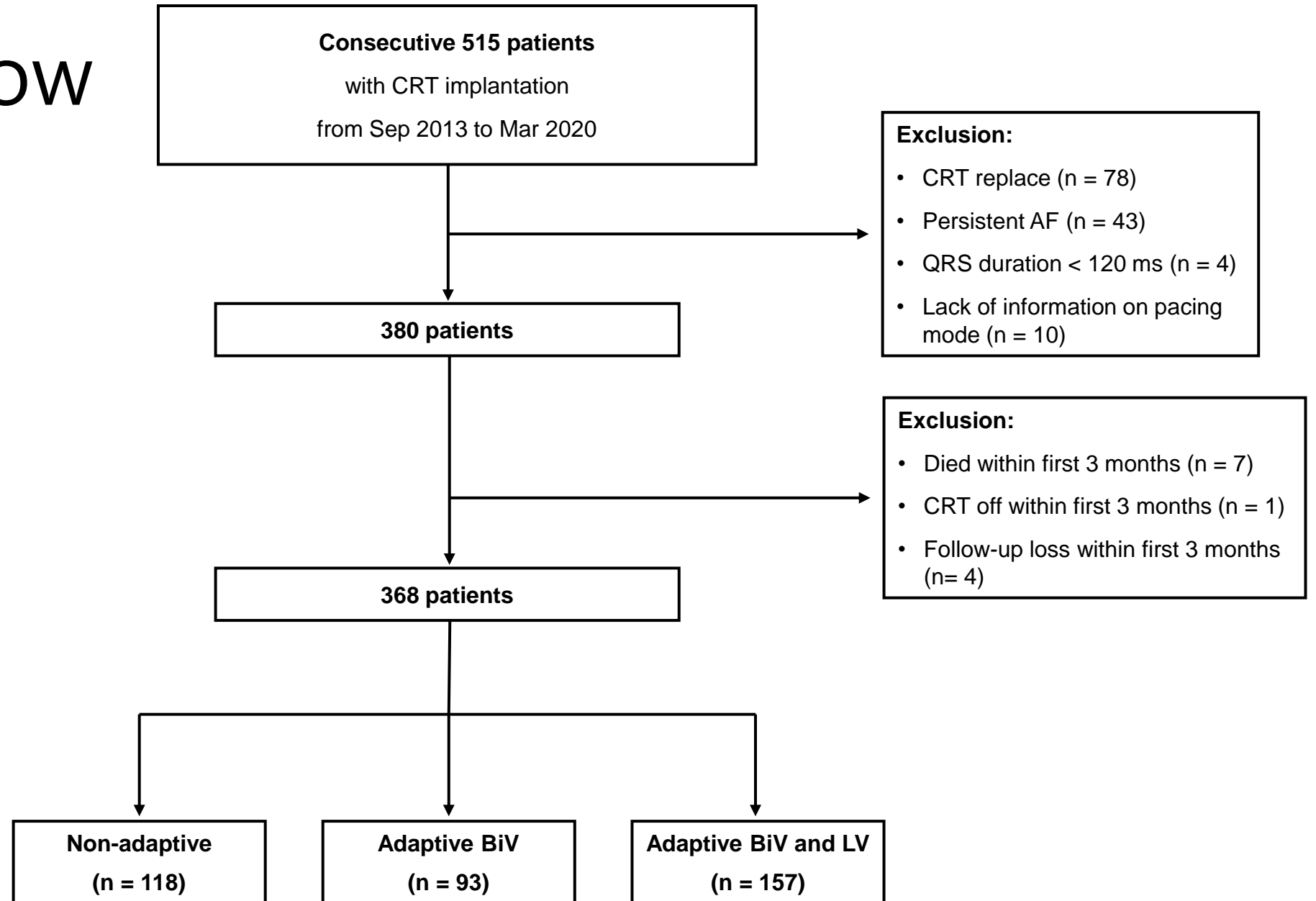
# Aim of the study

- The study hypothesis that **adaptive CRT reduces the incidence of the composite endpoint of all-cause mortality, HF decompensation, and defibrillator therapy, compared with conventional CRT**, among patients with a CRT-indicated, especially, LBBB and normal AV conduction.

# Study design

- Retrospective, multi-centered study
- At 25 centers in Korea
- Enrollment period: September 2013 to march 2020
- Inclusion criteria
  - Patients  $\geq$  19 years old
  - CRT-indicated patients with symptomatic HF, NYHA Fc II-IV
  - CRT implantation with adaptive CRT algorithm
- Exclusion criteria
  - CRT generator replacement
  - QRS duration  $<$ 120 ms
  - Persistent atrial fibrillation

# Study flow



# Baseline characteristics (1)

| Variables                      | Nonadaptive CRT<br>(n = 118) | Adaptive CRT          |                                  | P value |
|--------------------------------|------------------------------|-----------------------|----------------------------------|---------|
|                                |                              | Adaptive BiV (n = 93) | Adaptive BiV and LV<br>(n = 157) |         |
| <b>Age</b>                     | 65.1 ± 12.0                  | 67.3 ± 12.9           | 66.8 ± 11.7                      | 0.37    |
| <b>Male</b>                    | 79 (64.2)                    | 50 (58.8)             | 97 (60.6)                        | 0.71    |
| <b>BMI</b>                     | 23.9 ± 3.5                   | 24.0 ± 4.0            | 23.7 ± 3.8                       | 0.80    |
| <b>NYHA class II</b>           | 25 (20.3)                    | 19 (22.6)             | 37 (23.6)                        | 0.81    |
| <b>NYHA class III or IV</b>    | 98 (79.7)                    | 64 (76.2)             | 119 (77.2)                       | 0.72    |
| <b>Ischemic CMP</b>            | 16 (13.0)                    | 22 (25.9)             | 28 (17.5)                        | 0.06    |
| <b>Hypertension</b>            | 67 (54.5)                    | 56 (65.9)             | 87 (54.4)                        | 0.17    |
| <b>Diabetes</b>                | 46 (37.4)                    | 40 (47.1)             | 76 (47.5)                        | 0.19    |
| <b>Chronic kidney disease</b>  | 27 (22.0)                    | 18 (21.2)             | 40 (25.0)                        | 0.74    |
| <b>Cerebrovascular disease</b> | 10 (8.1)                     | 11 (12.9)             | 15 (9.4)                         | 0.50    |

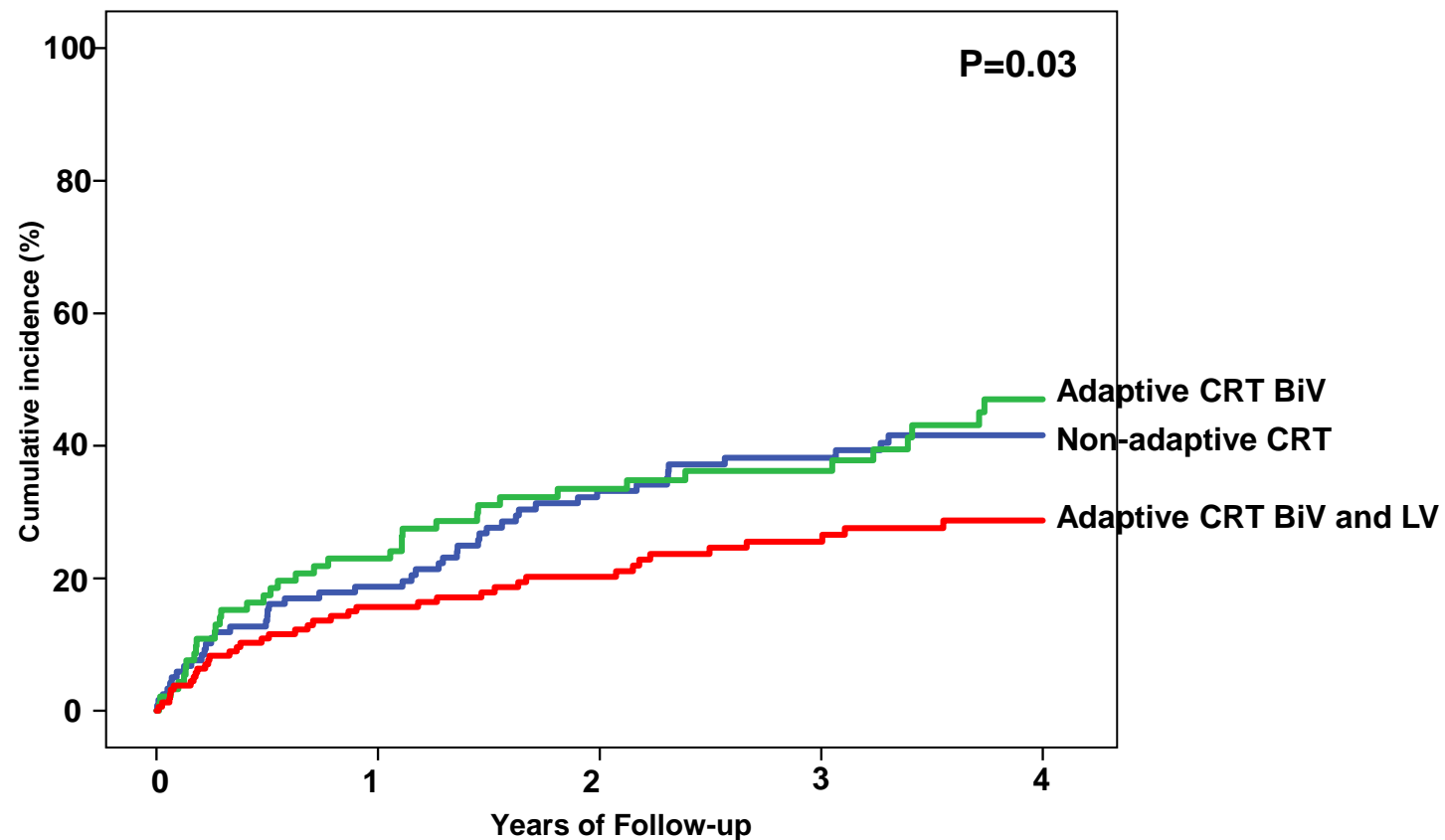
# Baseline characteristics (2)

| Variables                | Nonadaptive CRT<br>(n = 118) | Adaptive CRT          |                                  | P value |
|--------------------------|------------------------------|-----------------------|----------------------------------|---------|
|                          |                              | Adaptive BiV (n = 93) | Adaptive BiV and LV<br>(n = 157) |         |
| Paroxysmal AF            | 23 (18.7)                    | 15 (17.6)             | 21 (13.1)                        | 0.40    |
| PR interval, ms          | 194.2 ± 43.8                 | 200.4 ± 50.9          | 189.4 ± 32.8                     | 0.17    |
| QRS duration, ms         | 170.4 ± 23.0                 | 169.2 ± 25.7          | 163.9 ± 19.2                     | 0.04    |
| LBBB                     | 101 (82.1)                   | 64 (75.3)             | 143 (89.4)                       | 0.02    |
| LVEF, %                  | 24.8 ± 6.7                   | 25.1 ± 5.8            | 24.3 ± 6.0                       | 0.66    |
| LVEDD, mm                | 66.8 ± 8.9                   | 65.9 ± 8.6            | 66.6 ± 8.9                       | 0.65    |
| LVESD, mm                | 56.6 ± 10.2                  | 55.8 ± 9.3            | 58.4 ± 10.0                      | 0.10    |
| Beta blocker             | 101 (82.1)                   | 61 (71.8)             | 123 (76.9)                       | 0.21    |
| ACE inhibitor or ARB     | 102 (82.9)                   | 77 (90.6)             | 142 (88.8)                       | 0.20    |
| Aldosterone antagonist   | 87 (70.7)                    | 54 (63.5)             | 119 (74.4)                       | 0.21    |
| De novo CRT              | 92 (74.8)                    | 60 (70.6)             | 151 (94.4)                       | <0.001  |
| LV lead (RAO) non-apical | 119 (96.7)                   | 80 (94.1)             | 151 (94.4)                       | 0.58    |
| LV lead (LAO) lateral    | 123 (100.0)                  | 85 (100.0)            | 152 (95.0)                       | 0.005   |



# Primary endpoint

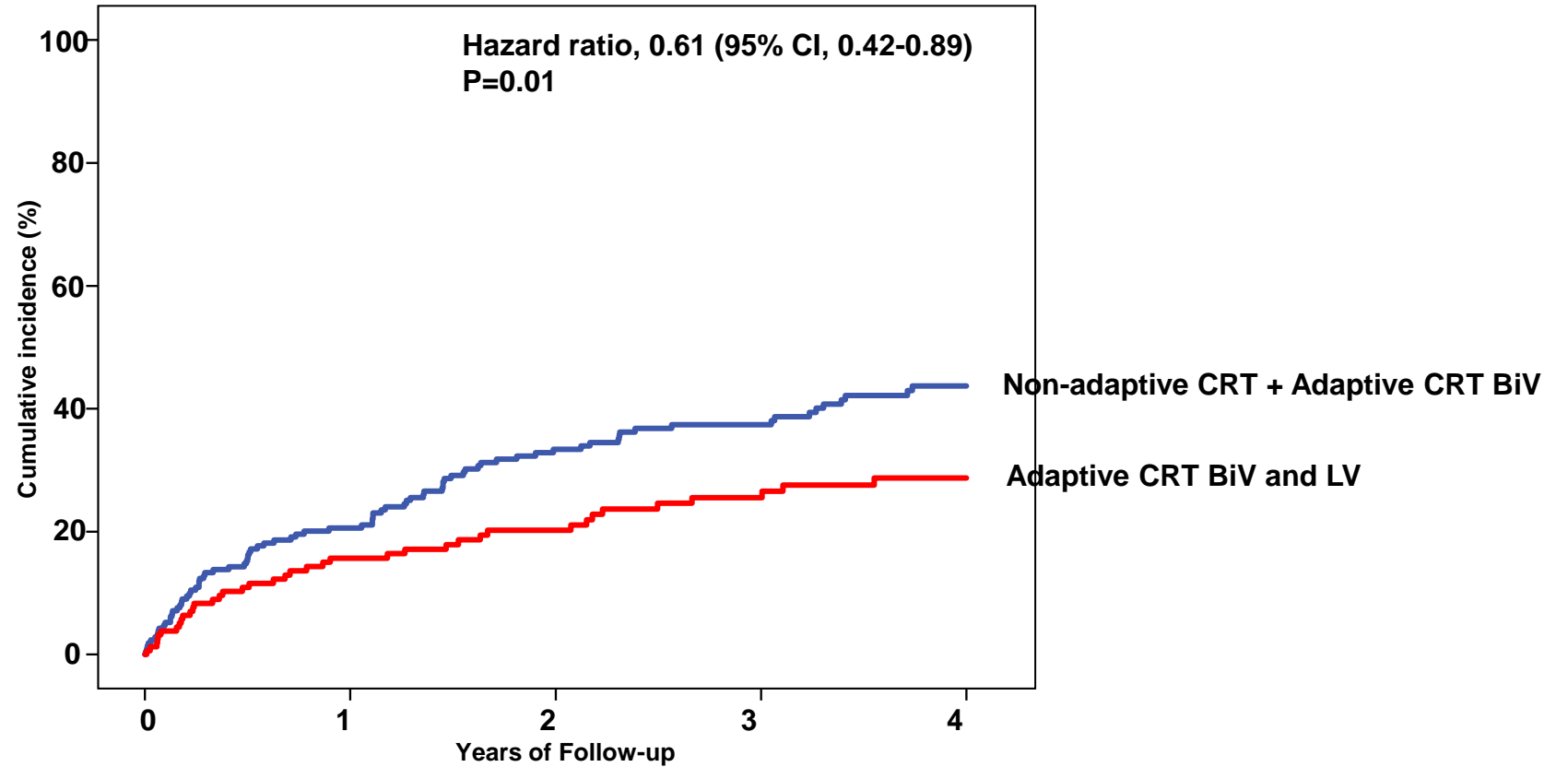
A composite of death, hospitalization due to heart failure, and defibrillator therapy for ventricular arrhythmia



## No. at Risk

|                         | 0   | 1   | 2  | 3  | 4  |
|-------------------------|-----|-----|----|----|----|
| Non-adaptive CRT        | 118 | 93  | 72 | 55 | 45 |
| Adaptive CRT BiV        | 93  | 69  | 53 | 40 | 26 |
| Adaptive CRT BiV and LV | 157 | 118 | 93 | 74 | 55 |

# Primary endpoint (two groups)



## No. at Risk

|                                     | 0   | 1   | 2   | 3  | 4  |
|-------------------------------------|-----|-----|-----|----|----|
| Non-adaptive CRT + Adaptive CRT BiV | 211 | 162 | 125 | 95 | 71 |
| Adaptive CRT BiV and LV             | 157 | 118 | 93  | 74 | 55 |

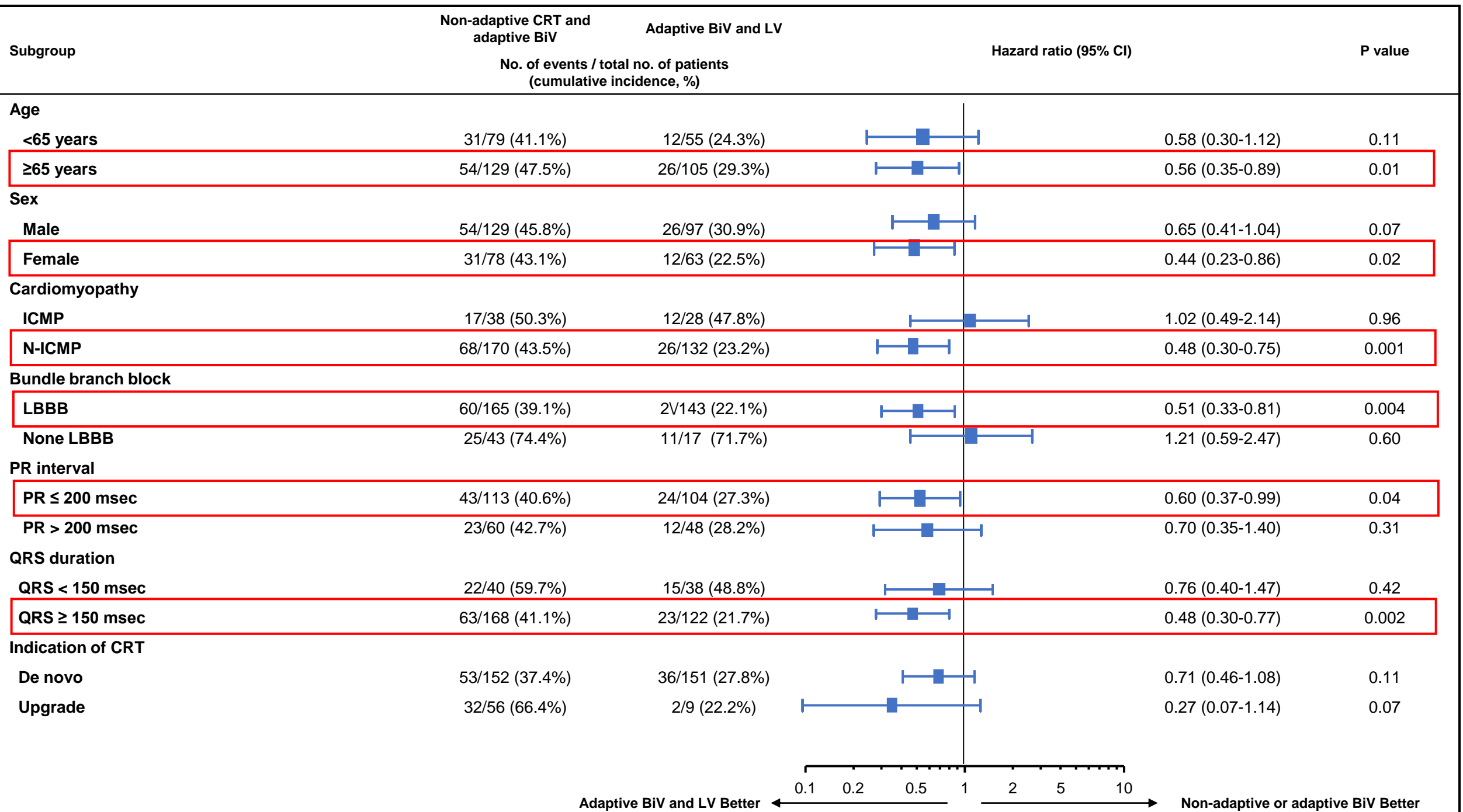
# Primary and secondary end point

| End point   | Non-adaptive +<br>Adaptive BiV<br>(n= 211) | Adaptive BiV and<br>LV (n = 157) | Hazard ratio     | P value |
|---|--|----------------------------------|------------------|---------|
| <b>Primary end point</b><br>Composite of death, hospitalization<br>due to heart failure, and<br>defibrillator therapy for ventricular<br>arrhythmia | 84 (43.7)                                  | 39 (28.7)                        | 0.60 (0.42-0.89) | 0.010   |
| <b>Secondary end point</b>  |  |                                  |                  |         |
| All-cause death   | 30 (17.9)                                  | 9 (7.2)                          | 0.40 (0.19-0.84) | 0.016   |
| Cardiac death   | 20 (11.9)                                  | 4 (3.3)                          | 0.27 (0.09-0.78) | 0.016   |
| Hospitalization due to HF   | 58 (30.9)                                  | 33 (24.9)                        | 0.77 (0.50-1.18) | 0.22    |
| Defibrillator therapy for ventricular<br>arrhythmia   | 32 (16)                                    | 10 (7.1)                         | 0.41 (0.20-0.83) | 0.014   |

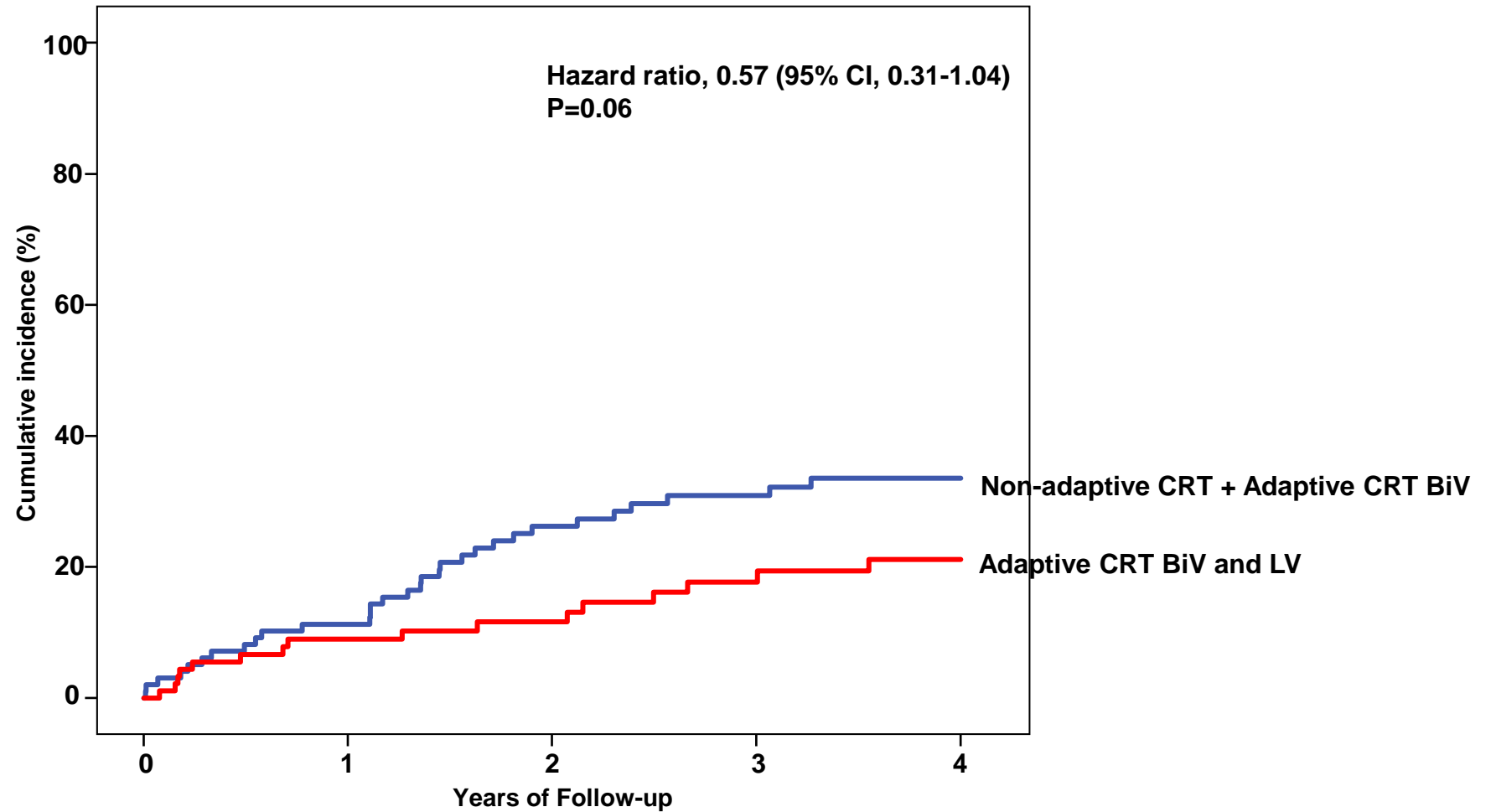
Data presented as n (%). Percentages are 4-year Kaplan–Meier estimates.

# Predictive factors for a composite outcome

| Variable                            | Univariate analysis |           |         | Multivariate analysis |           |         |
|-------------------------------------|---------------------|-----------|---------|-----------------------|-----------|---------|
|                                     | Hazard ratio        | 95% CI    | P value | Hazard ratio          | 95% CI    | P value |
| <b>Age</b>                          | 1.01                | 0.99-1.01 | 0.70    | 0.99                  | 0.98-1.01 | 0.83    |
| <b>Sex (male)</b>                   | 1.22                | 0.84-1.76 | 0.30    |                       |           |         |
| <b>Hypertension</b>                 | 1.01                | 0.70-1.43 | 0.98    |                       |           |         |
| <b>Diabetes</b>                     | 0.94                | 0.66-1.35 | 0.75    |                       |           |         |
| <b>Ischemic CMP</b>                 | 1.68                | 1.11-2.55 | 0.02    | 1.44                  | 0.93-2.24 | 0.10    |
| <b>Paroxysmal AF</b>                | 2.19                | 1.46-3.30 | <0.001  | 1.97                  | 1.31-2.98 | 0.001   |
| <b>QRS duration ≥ 150</b>           | 0.52                | 0.35-0.76 | 0.001   | 0.57                  | 0.39-0.85 | 0.006   |
| <b>Reprogramming</b>                | 1.53                | 0.97-2.40 | 0.07    |                       |           |         |
| <b>Adaptive LV only pacing "on"</b> | 0.61                | 0.42-0.89 | 0.01    | 0.65                  | 0.44-0.95 | 0.03    |



# LBBB and $PR \leq 200$ patient (subgroup)



## No. at Risk

Non-adaptive CRT +  
Adaptive CRT BiV

99

85

67

53

42

Adaptive CRT BiV and LV

92

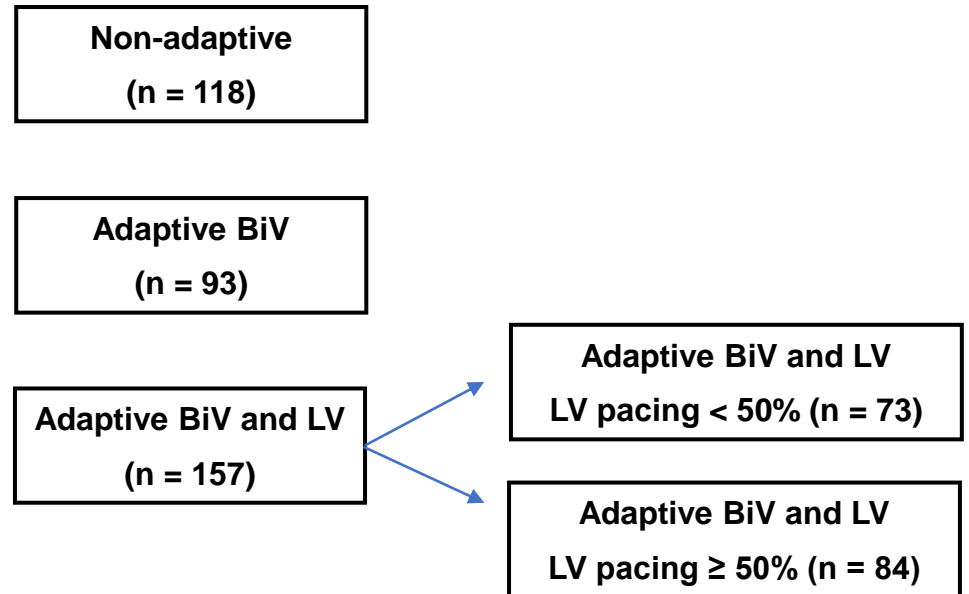
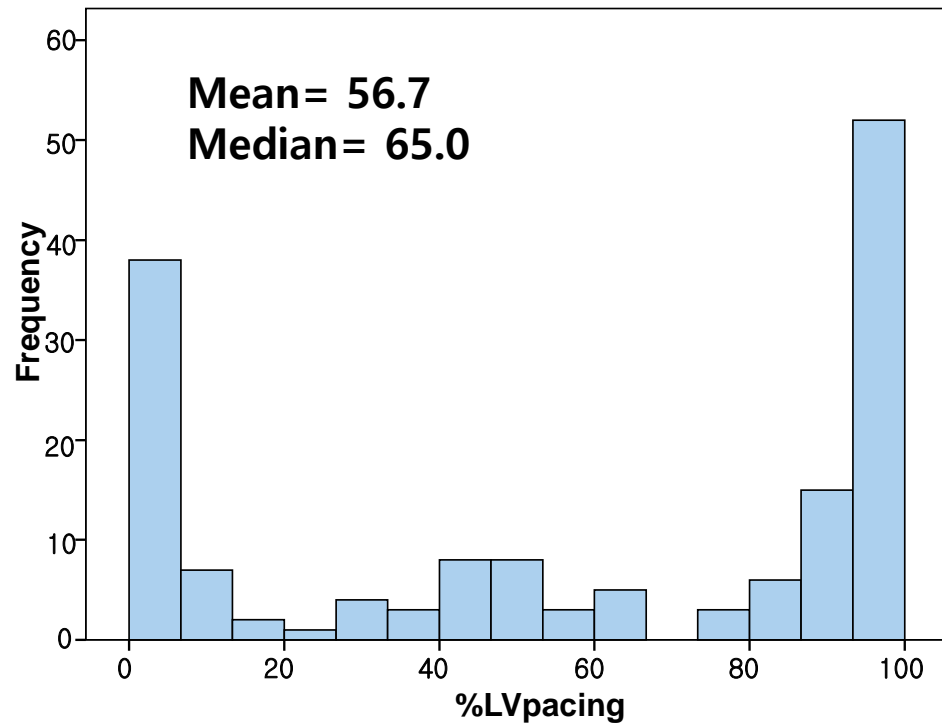
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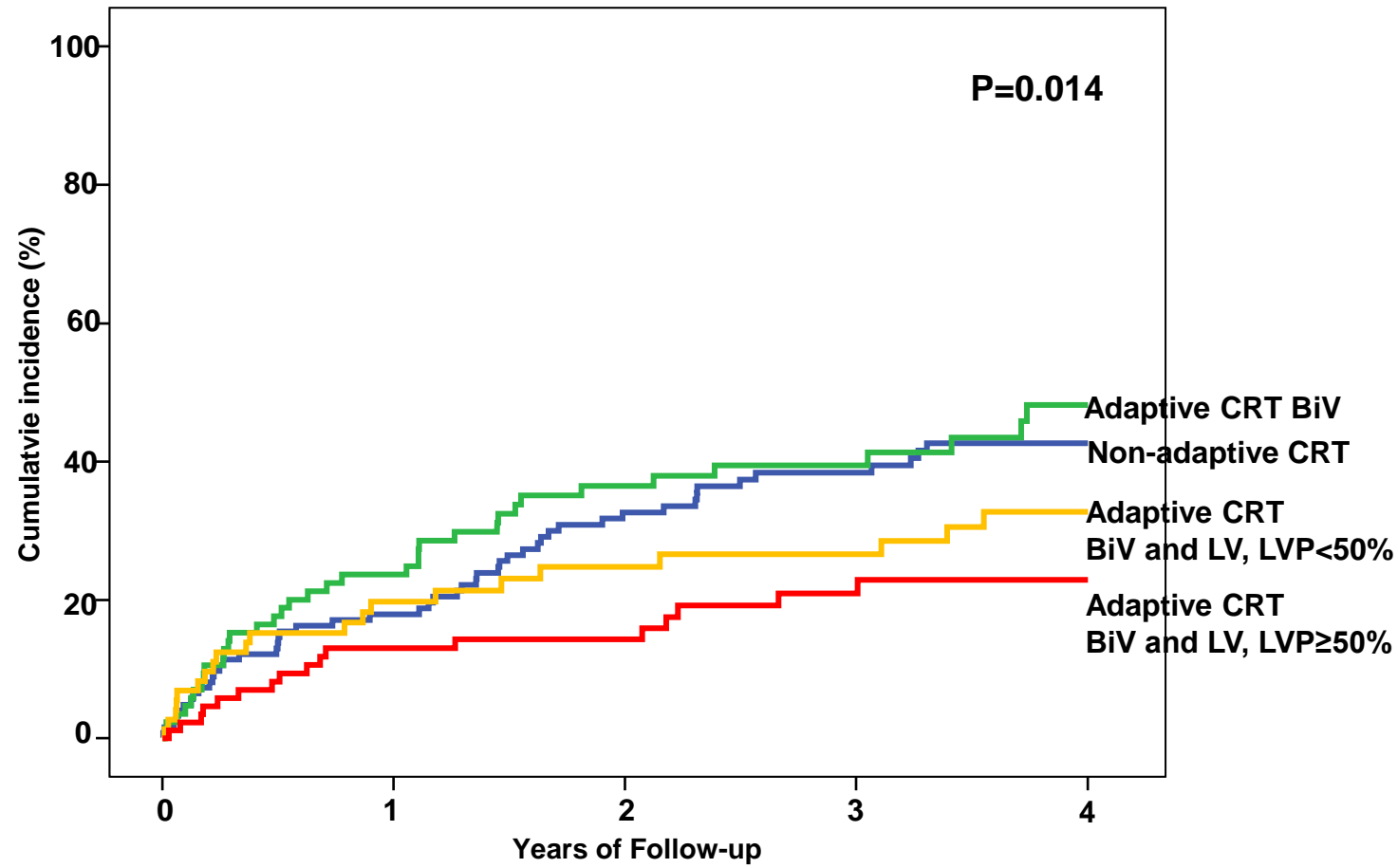
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# How did the LV-only pacing% effect?



A higher LV-only pacing percentage ( $\geq 50\%$ ) showed better clinical outcomes.





# Limitation

- Retrospective study
- Echocardiographic LV volume measurements for CRT response rate (definition LVESV reduction  $>15\%$ ) were not collected and not available for analysis.
- Soft endpoint (HF hospitalization) is not significant compared to hard endpoint (Death)
- Some patients (n=45, 12%) have changed the device programming mode during follow-up period.

# Conclusion

- **Dynamic algorithm-based optimisation with adaptive CRT with-only pacing showed better clinical outcomes compared to conventional or adaptive BiV CRT.**
- LV-only pacing is an established alternative to BiV pacing and may be considered in BiV non-responders with intact AV conduction and LBBB maximising individual response.
- There are still gaps in the use of optimisation in non-LBBB conduction delay, AV block, persistent AF.