

# **Mitral Valve Annuloplasty plus CABG versus CABG alone in moderate Functional Ischemic Mitral Regurgitation: final results of the Randomized Ischemic Mitral Evaluation (RIME) Trial**

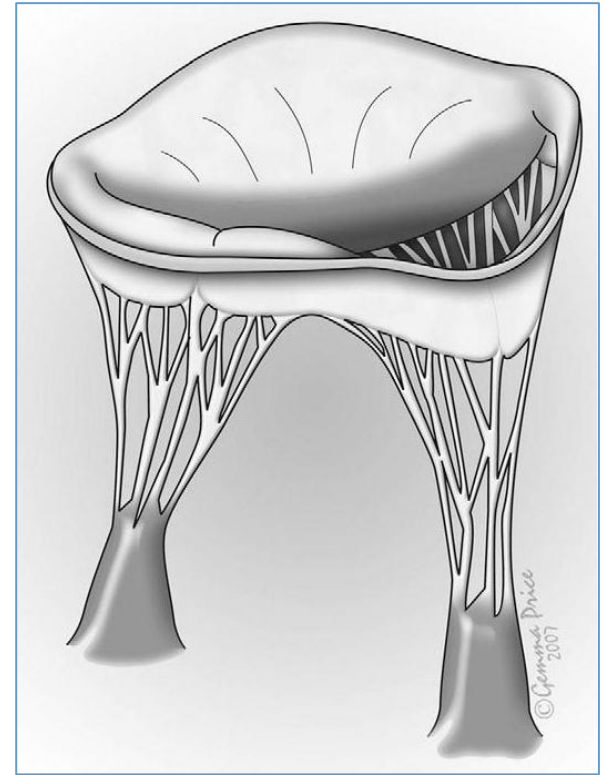
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## Background: Functional Ischemic MR

- Occurs in up to 40% of patients following myocardial infarction.
- Result of LV remodeling & dilatation.
- Mitral valve tethered and pulled apart.
- MR usually mild or moderate in severity.
- Heart failure and death increased up to 3x.
- Most have 3-vessel coronary artery disease, benefit from CABG.



Chan KMJ, et al. Prog Cardiovasc Dis 2009; 51(6):460-471

## Background: Functional Ischemic MR

- Persistent increased risk of heart failure and death (up to 1.5x) with coronary artery revascularization alone.
- Efficacy of adding mitral valve repair to CABG uncertain: reduction in MR severity reported in observational, non-randomized studies, but no improvement in functional capacity, heart failure or survival.
- Significant recurrence rates of MR reported in studies due to suboptimal surgical techniques (use of flexible annuloplasty bands, inadequate downsizing, incomplete coronary revascularization).

## Methods: Study design

- Single blinded randomized controlled trial: 7 centers.
- Randomization into two groups (1:1 ratio):
- **Group 1: CABG only**
  - Complete coronary artery revascularization.
  - Pedicled left internal mammary artery grafted to the LAD.
- **Group 2: CABG + Mitral Valve Repair**
  - Complete rigid or semi-rigid mitral annuloplasty ring used.
  - Carpentier-McCarthy-Adams IMR ETlogix ring recommended.
  - Sized by measurement of anterior mitral valve leaflet.
  - Downsized by 2 sizes if alternative complete ring used.
  - Aim: coaptation length of at least 8 mm between the anterior and posterior mitral valve leaflets with no more than trace MR.

## Methods: Eligibility

- **Inclusion criteria**
  - Patients referred for elective CABG.
  - Moderate functional ischemic MR as defined by the AHA/ACC/ASE criteria measured at rest or peak exercise by echocardiography:
    - Effective Regurgitant Orifice Area (EROA) 0.20–0.39 cm<sup>2</sup>
    - Regurgitant Volume 30-59 ml/beat
    - Regurgitant Fraction 30-49%
    - Vena Contracta Width 0.3-0.69 cm

## Methods: Eligibility

- **Main exclusion criteria**

- Severe LV dysfunction: EF < 30%.
- Structural abnormalities of the mitral valve (including papillary muscle rupture).
- Significant aortic valve disease.
- Previous or active endocarditis.
- Significant co-morbidities: severe renal, liver or respiratory impairment.
- NYHA class IV, unstable angina, acute pulmonary edema, cardiogenic shock.
- Previous cardiac surgery.

## Methods: Hypothesis

- **Primary hypothesis**
  - Adding mitral valve annuloplasty to CABG in patients with moderate functional ischemic MR improves functional capacity.
  
- **Secondary hypothesis**
  - Adding mitral valve annuloplasty to CABG in patients with moderate functional ischemic MR improves LV reverse remodelling, MR severity, and BNP levels.

## Methods: Endpoints

- **Primary endpoint (one year):**
  - Functional capacity (Peak oxygen consumption)
- **Secondary endpoints (one year):**
  - LV reverse remodeling (LVESVI)
  - Mitral regurgitation (MR volume)
  - BNP levels.

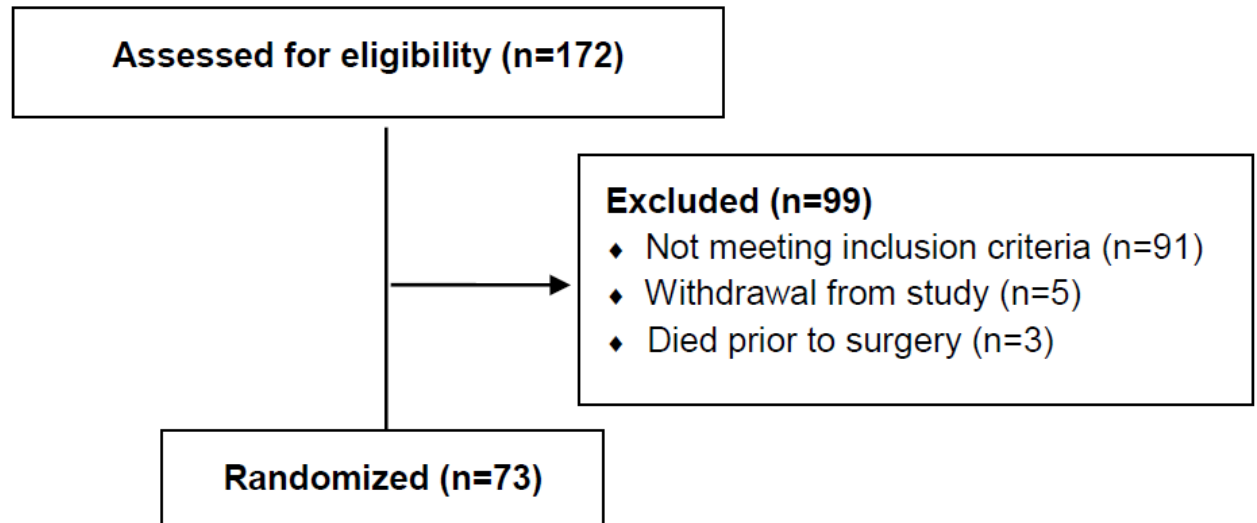


## Methods: Statistics

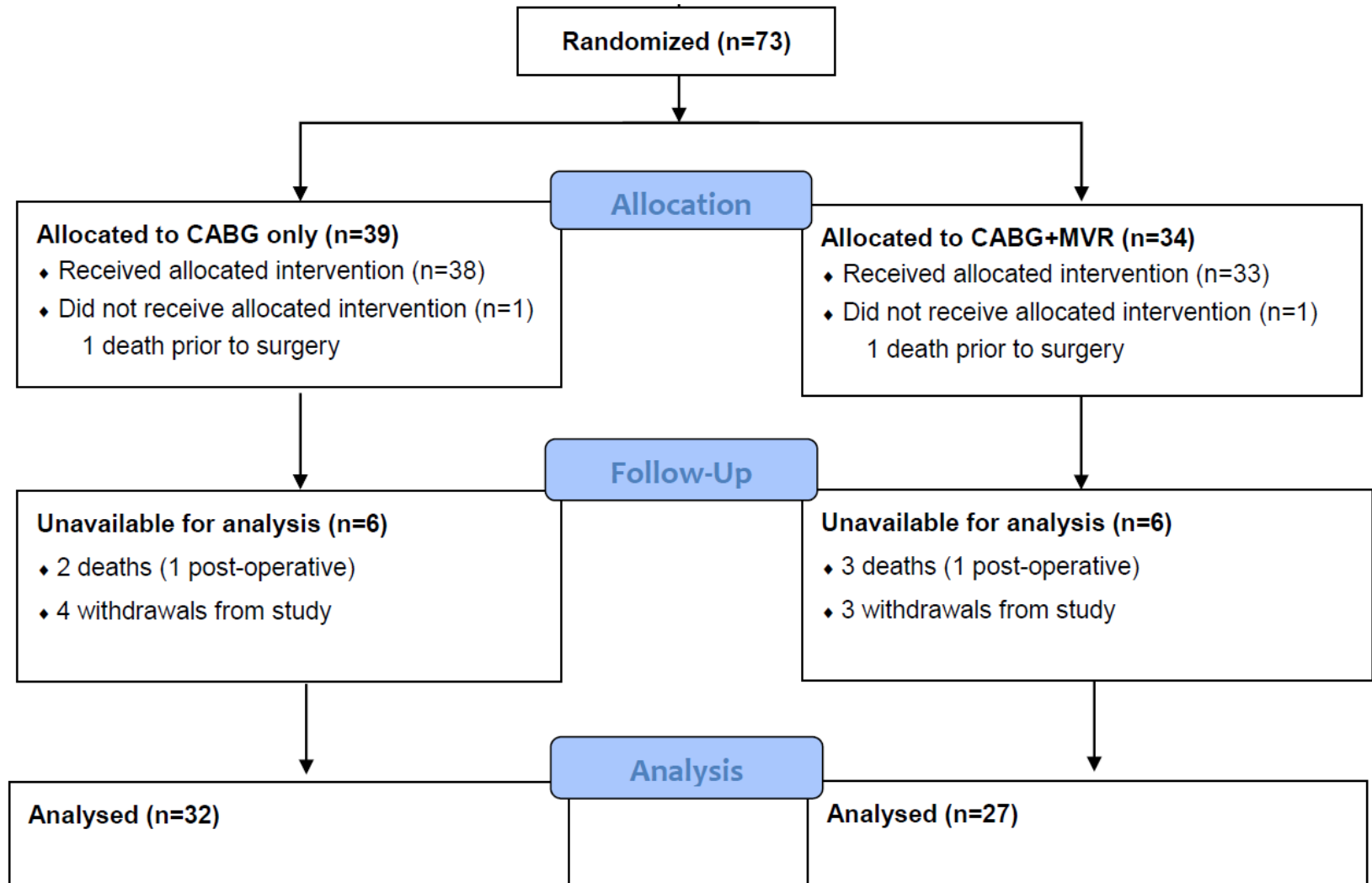
- **Power calculations**
  - Using 90% power,  $\alpha = 0.05$ , and S.D. = 3.5, 82 patients required to detect difference of  $\geq 2.5$  ml/kg/min in primary endpoint, peak  $\text{VO}_2$ .
  - Two planned interim analysis performed.
  - Benefit demonstrated for CABG + MVR group, ( $P=0.008$  for primary endpoint).
  - Recruitment stopped after results of second interim analysis (73 patients randomised).

# Results: Enrollment

## Enrollment



# Results: Treatment Allocation & Follow-up



## Results: Baseline

|                              | CABG        | CABG + MVR  |
|------------------------------|-------------|-------------|
| Age (years) – mean (range)   | 70 (51-83)  | 71 (47-86)  |
| Female sex (%)               | 26          | 26          |
| NYHA class (%)               |             |             |
| I                            | 3           | 3           |
| II                           | 64          | 65          |
| III                          | 33          | 32          |
| <b>Mitral regurgitation</b>  |             |             |
| EROA (cm <sup>2</sup> )      | 0.18 ± 0.10 | 0.21 ± 0.09 |
| Regurgitant volume (ml/beat) | 30.3 ± 13.8 | 35.5 ± 13.3 |
| <b>Left ventricle</b>        |             |             |
| LVEDD (mm)                   | 43.3 ± 9.5  | 45.7 ± 7.4  |
| LVEDD (mm)                   | 56.5 ± 12.0 | 56.5 ± 12.6 |
| LV Ejection fraction (%)     | 40.3 ± 16.1 | 40.0 ± 17.3 |

## Results: Surgery

|   | CABG        | CABG + MVR    | P-value |
|---|-------------|---------------|---------|
| Number of bypass grafts (%)             |             |               |         |
| 2                                       | 8           | 9             |         |
| 3                                       | 74          | 70            |         |
| 4                                       | 18          | 21            |         |
| CPB time (min) – median (Q1-Q3)         | 84 (70-106) | 147 (133-169) | <0.001  |
| Cross clamp time (min) – median (Q1-Q3) | 51 (41-55)  | 95 (90-110)   | <0.001  |
| <b>Mitral Annuloplasty ring</b>         |             |               |         |
| • CMA IMR ETlogix (%)                   |             | 85            |         |
| • CE Physio (%)                         |             | 15            |         |
| • Mean ring size (mm)                   |             | 28            |         |

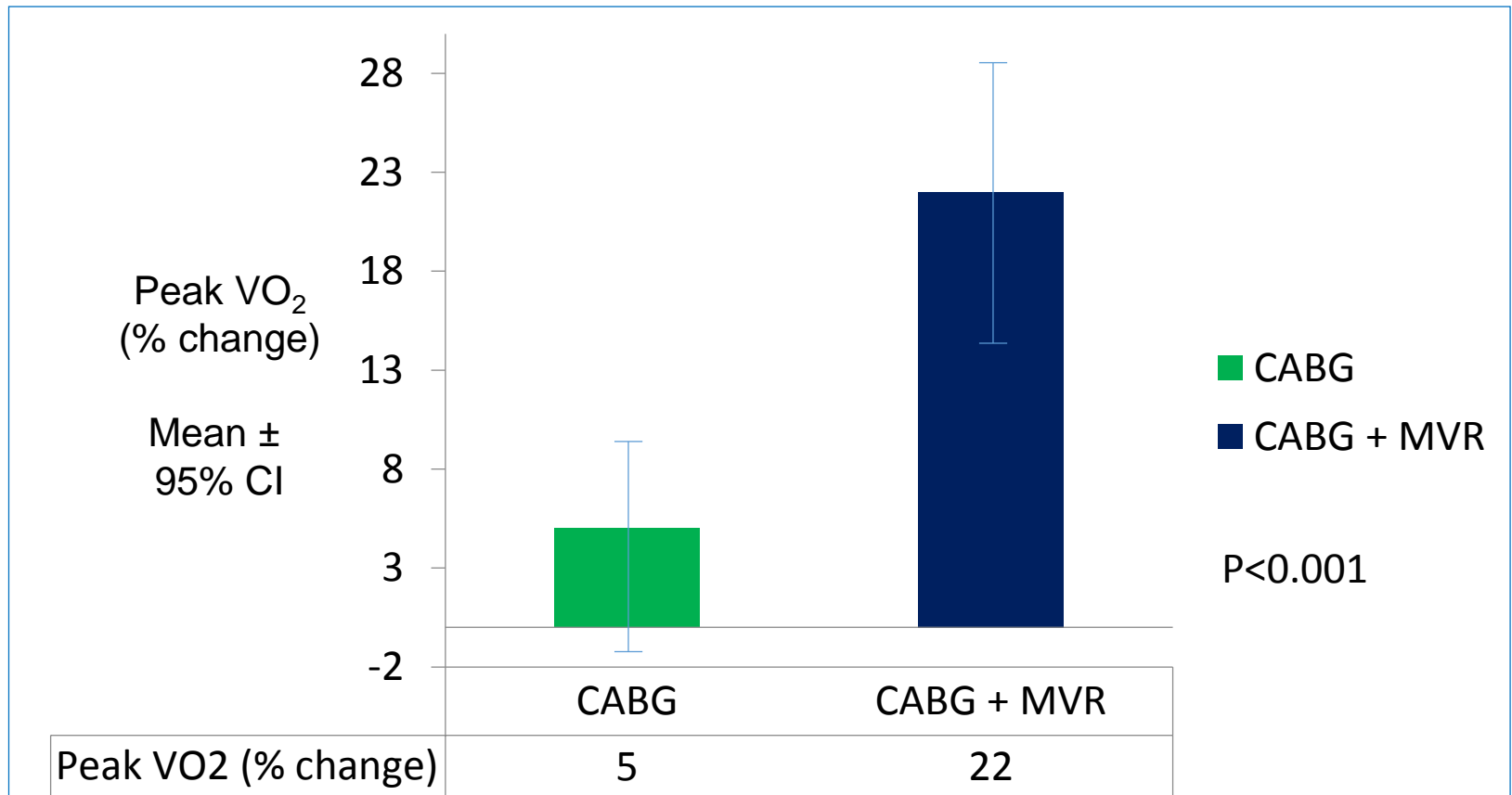
## Results: Post-operative

|   | CABG          | CABG + MVR     | P-value |
|---|---------------|----------------|---------|
| <b><i>Intensive care</i></b>                                |               |                |         |
| IABP use (%)  | 29            | 33             | 0.57    |
| Intubation time (hours) – median (Q1-Q3)                    | 17 (12-20)    | 28 (17-102)    | 0.004   |
| <b><i>Blood loss &amp; transfusion – median (Q1-Q3)</i></b> |               |                |         |
| Blood loss (ml)   | 755 (479-933) | 672 (511-1006) | 0.89    |
| Blood transfused (ml)                                       | 153 (0-818)   | 900 (225-1439) | 0.016   |
| Platelet transfused (ml)                                    | 0 (0-0)       | 0 (0-306)      | 0.08    |
| Fresh frozen plasma transfused (ml)                         | 0 (0-0)       | 0 (0-636)      | 0.42    |

## Results: Post-operative

|  | CABG     | CABG + MVR | P-value |
|--|----------|------------|---------|
| <b><i>Complications</i></b>                |          |            |         |
| Hemofiltration (%)                         | 8        | 12         | 0.70    |
| Re-operation for bleeding or tamponade (%) | 5        | 12         | 0.41    |
| Stroke (%)                                 | 0        | 3          | 0.47    |
| 30 day mortality (%)                       | 3        | 3          | 1.00    |
| <b><i>Hospital stay</i></b>                |          |            |         |
| Length of hospital stay – median (Q1-Q3)   | 9 (7-12) | 15 (11-16) | 0.05    |
| <b><i>Clinical events</i></b>              |          |            |         |
| One year survival (%)                      | 95       | 91         | 0.66    |
| Hospital admission for heart failure (%)   | 8        | 3          | 0.62    |

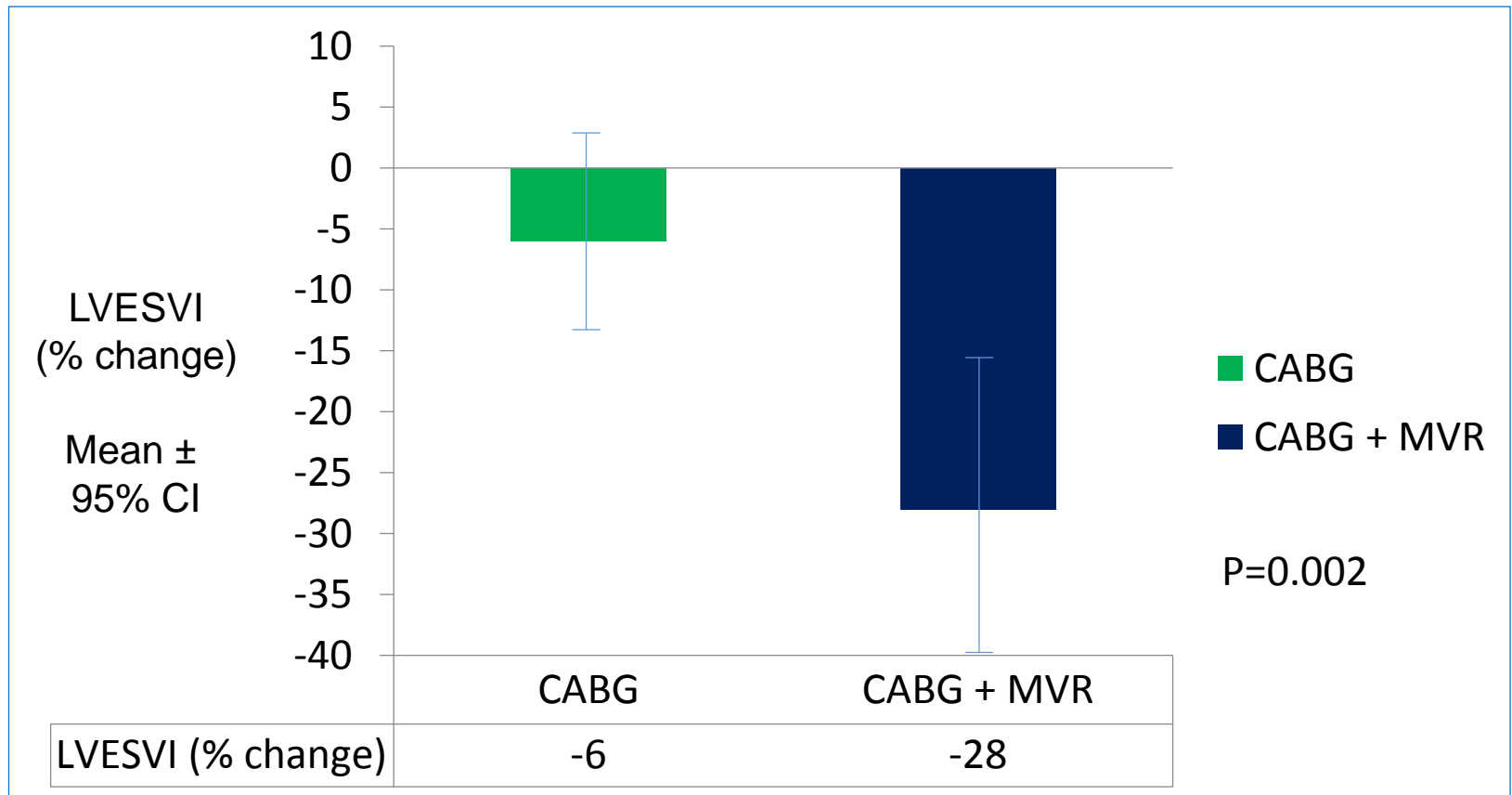
## Results: Primary endpoint Functional Capacity at 1 Year



Improvement in functional capacity was greater following CABG + MV repair compared to CABG alone.

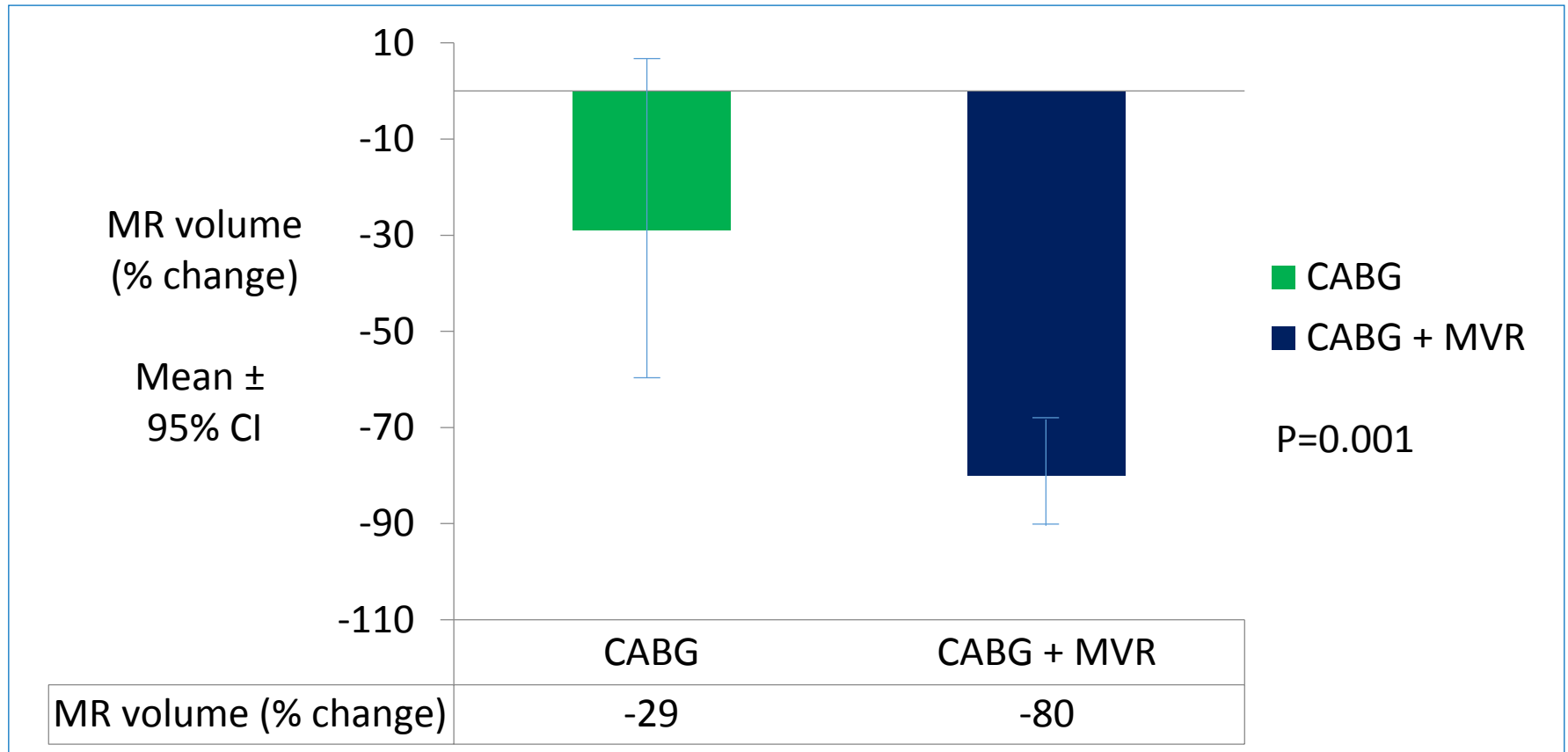


## Results: Secondary endpoints LV reverse remodelling at 1 Year



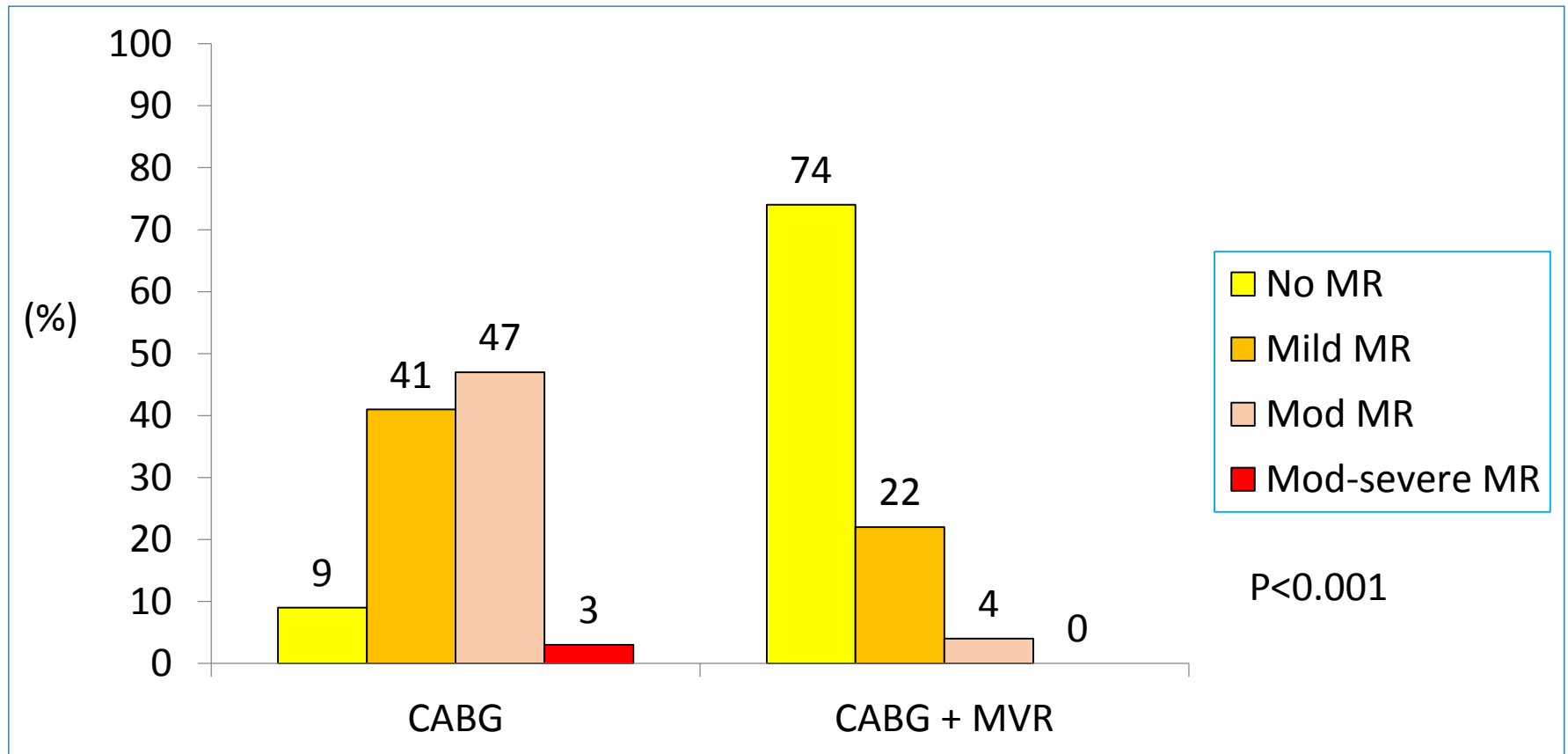
LV reverse remodelling was greater following CABG + MV repair compared to CABG alone.

## Results: Secondary endpoints Mitral regurgitation at 1 Year



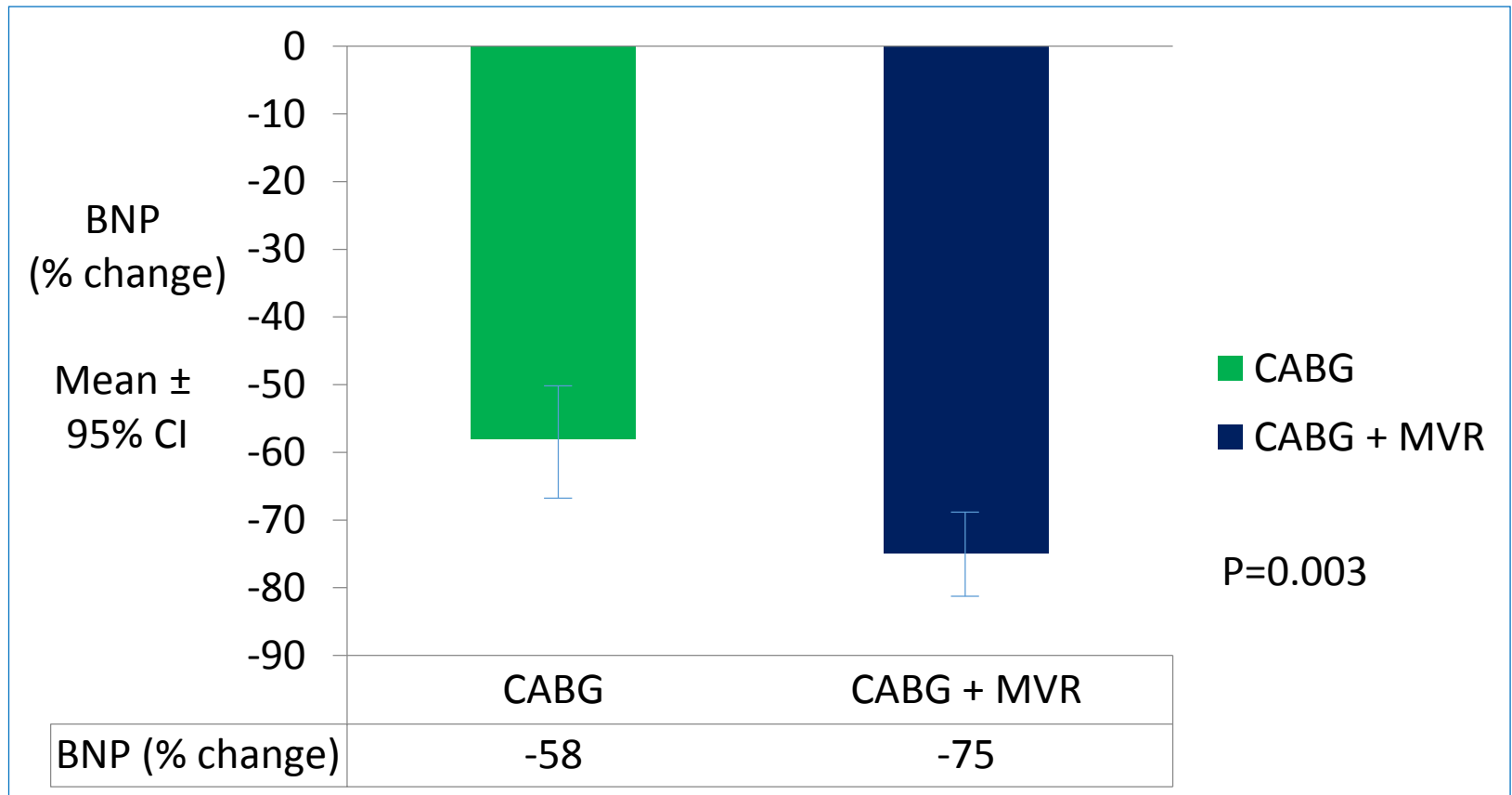
Reduction in mitral regurgitation was greater following CABG + MV repair compared to CABG only.

## Results: Secondary endpoints Mitral regurgitation at 1 Year



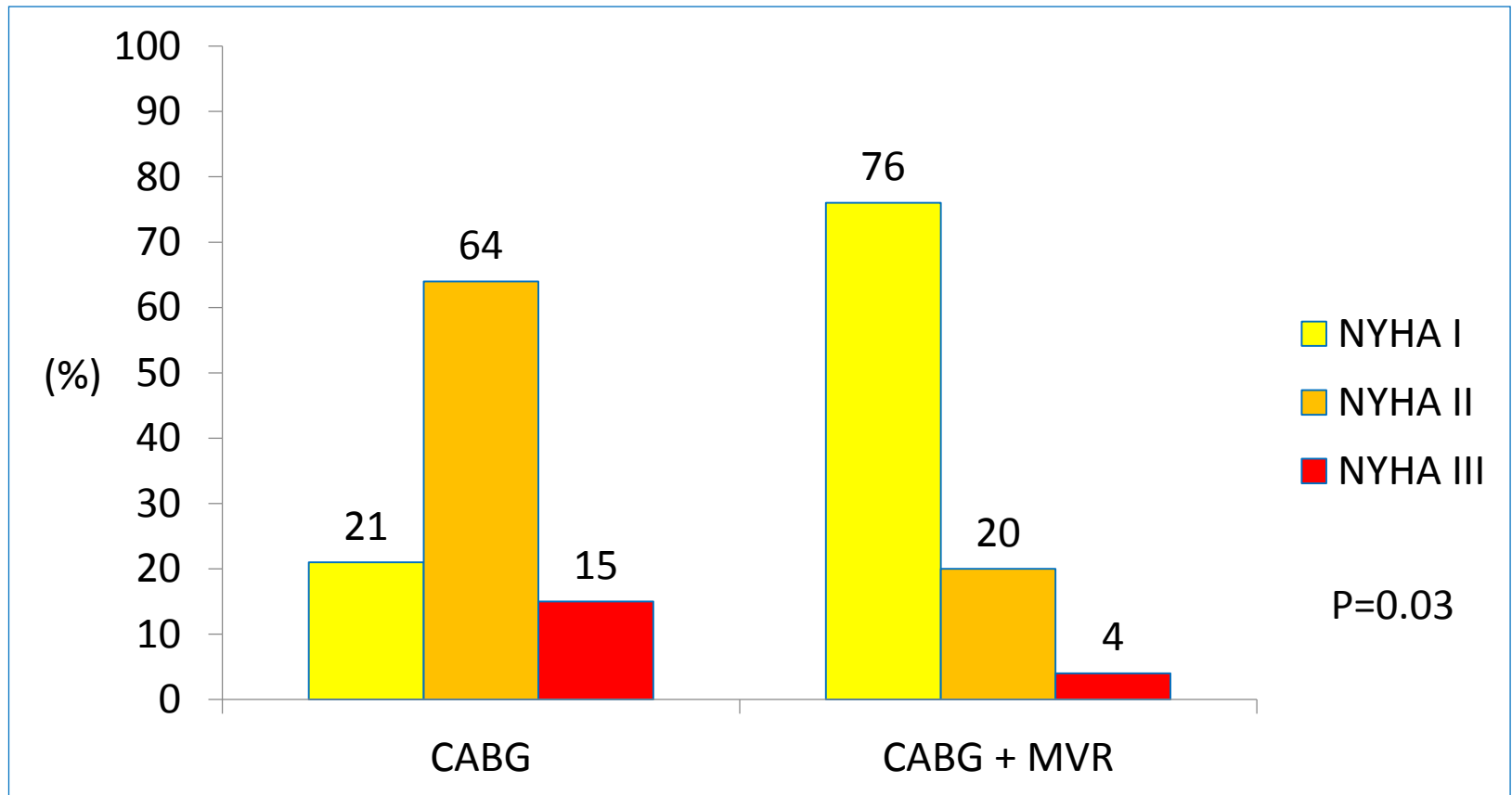
Mitral regurgitation was less following CABG + MV repair compared to CABG only.

## Results: Secondary endpoints BNP at 1 Year



Reduction in BNP was greater following CABG + MV repair compared to CABG only.

## Results: Symptoms at 1 Year



NYHA class was better following CABG + MV repair compared to CABG only.

## Limitations

- Study stopped early for benefit after review of interim results.
- Single (not double) blinded study.
- Endpoints determined at one year; longer follow-up necessary.
- Study not designed and not powered to evaluate clinical events and survival.

## Conclusions

- Compared to CABG alone, addition of MV annuloplasty to CABG in patients with moderate functional ischemic MR improves:
  - Functional capacity and symptoms
  - LV reverse remodelling
  - Mitral regurgitation
  - BNP levels
- The impact of these benefits on longer term clinical outcomes remain to be defined.
- CABG plus MV annuloplasty required longer operation times, increased intubation and hospital stay duration, and blood transfusion.
- Concomitant CABG plus MV annuloplasty should be considered in patients with moderate functional ischemic MR.

# Acknowledgement

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