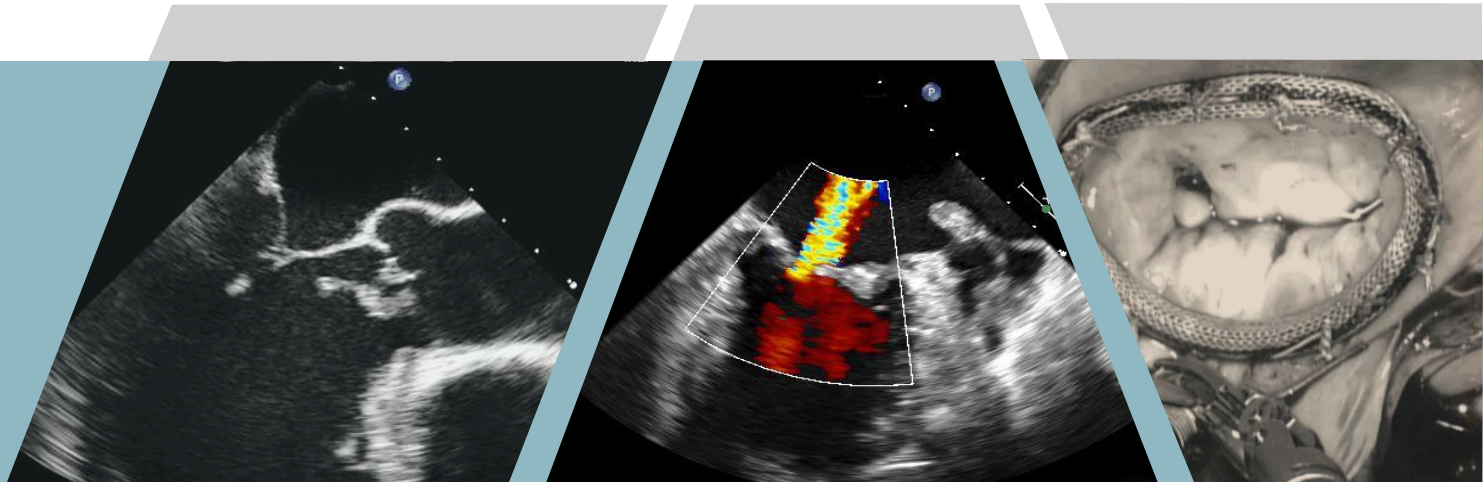


# Randomized Trial of *Early Surgery* Versus Conventional Treatment for Infective *Endocarditis (EASE)*



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# Introduction

- ***Infective endocarditis (IE)*** remains a serious disease that carries considerable mortality and morbidity
- The role of surgery has been expanding in complicated IE
- Due to lack of randomized clinical trials, **the optimal timing and indications for surgical intervention** to prevent systemic embolism in IE remain unclear

# EASE Trial Design

- **Design**

a prospective, open-label, randomized trial at 2 centers in Korea between 2006 and 2011

- **Purpose**

To evaluate the effect of early surgery on embolic events compared with conventional treatment in IE patients with high embolic risks

# Study Patients

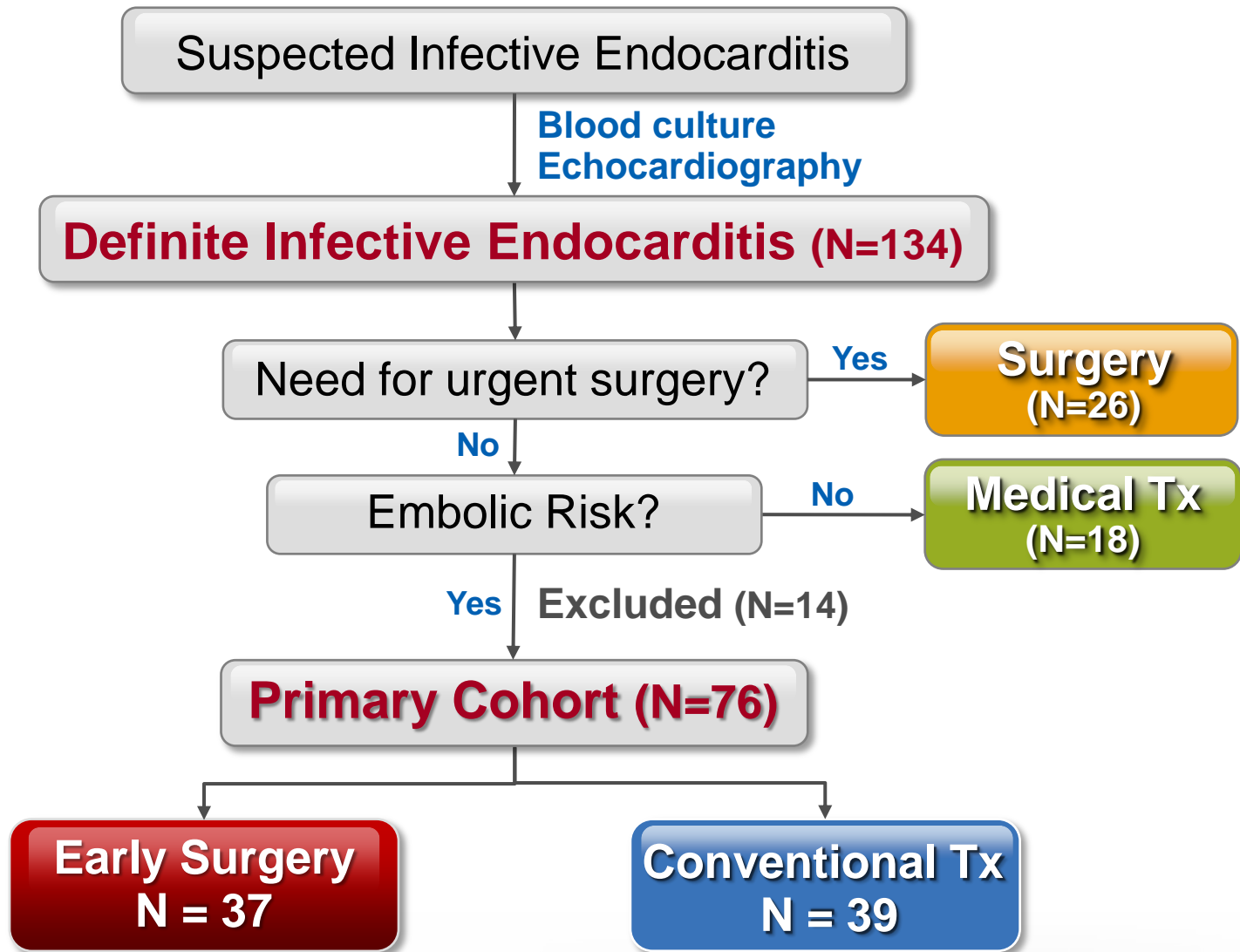
- All patients suspected of IE underwent **blood cultures and echocardiography** within 24 hrs after hospitalization

## Inclusion Criteria

- Age: 15-80 years
- Definite **left-sided native valve IE** according to Duke criteria
- Severe mitral or aortic valve disease
- **Vegetation length > 10mm**

## Exclusion Criteria

- **Pts with urgent indication of surgery** moderate to severe CHF, heart block, annular or aortic abscess, penetrating lesions, fungal endocarditis
- **Pts not candidates for early surgery** age > 80 yrs, coexisting major embolic stroke or poor medical status
- Prosthetic valve IE
- Right-sided vegetations
- Small vegetations  $\leq 10\text{mm}$



**Primary end point:**

In-hospital death and clinical embolic events at 6 weeks

# Study Procedures

- All pts screened for eligibility underwent transesophageal echo and CT
- Pts were randomly assigned on a 1:1 basis to **early surgery** or **conventional treatment** using an interactive web response system
- **In the early surgery group**, surgery was performed **within 48 hours** of randomization
- **Pts in the conventional treatment group** were treated according to the current guidelines

# End Points

- **Primary End Point**

A composite of in-hospital death and clinical embolic events\* within 6 weeks from randomization

- **Secondary End Point**

The rate of all-cause death, embolic events, recurrence of IE, repeated hospitalization at 6 month follow-up

\* **embolic events:** acute onset of embolism with occurrence of new lesions



# Statistical Analysis

- **Primary hypothesis**

To show the superiority of early surgery over conventional treatment with respect to primary end point

- **Power calculation**

- Assuming event rate 23% in the conventional treatment group<sup>1,2</sup> and 3% in the early surgery group<sup>2</sup>
- Intended sample size: 74 pts for  $\geq 80\%$  power

- **Primary analysis on intention-to-treat principle**

<sup>1</sup> Chan et al *J Am Coll Cardiol* 2003 42:775-780

<sup>2</sup> Kim et al *Circulation* 2010 122:S17-S22



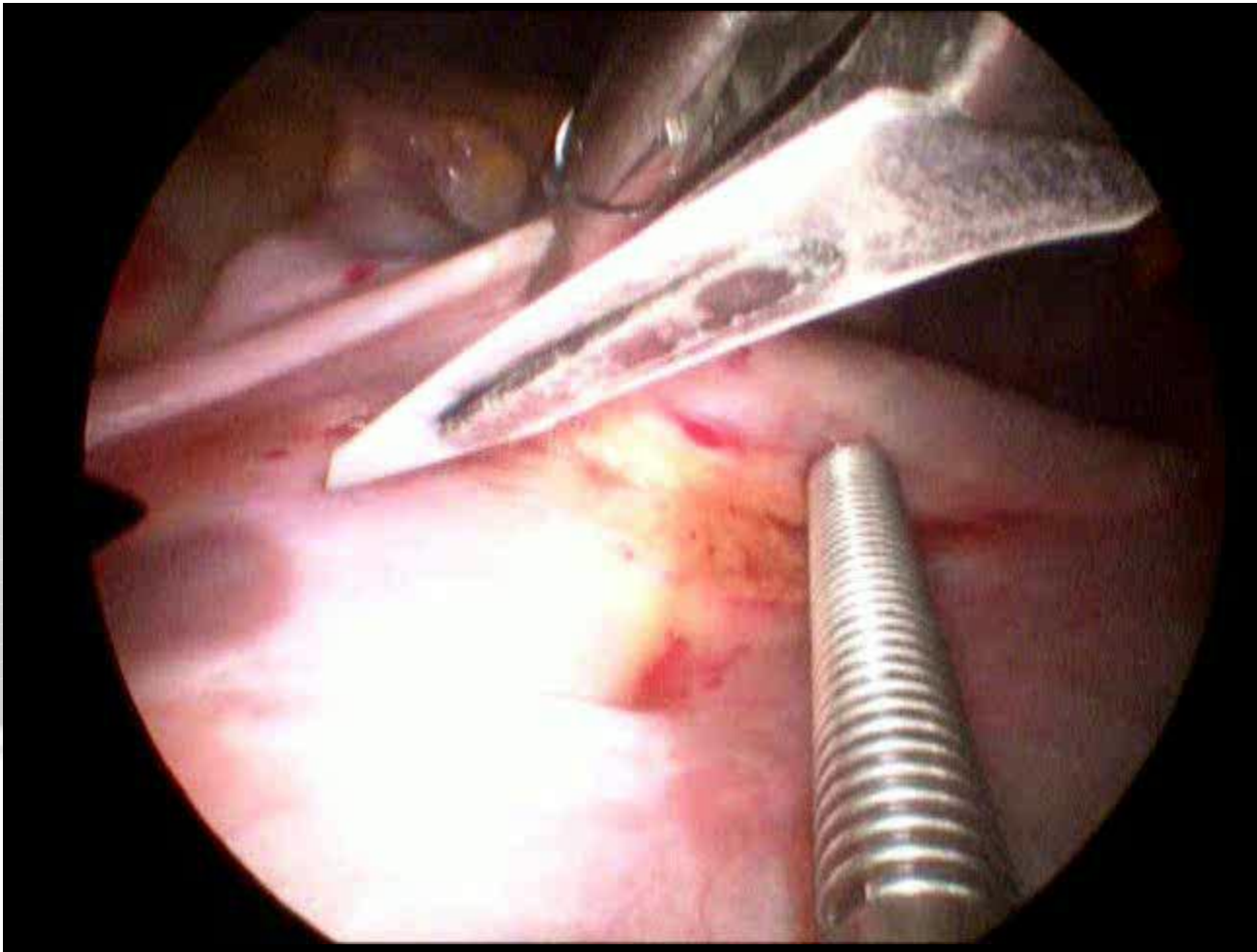
# Patient Characteristics (1)

| Characteristics          | CONV Tx<br>(n=39) | Early Surgery<br>(n=37) | p-value |
|--------------------------|-------------------|-------------------------|---------|
| Age, years               | 48±18             | 46±15                   | 0.54    |
| Male sex                 | 27 (69%)          | 24 (65%)                | 0.69    |
| Diabetes                 | 4 (10%)           | 8 (22%)                 | 0.17    |
| Hypertension             | 7 (18%)           | 11 (30%)                | 0.23    |
| Coronary artery disease  | 1 (3%)            | 3 (8%)                  | 0.35    |
| Immunocompromised status | 1 (3%)            | 2 (5%)                  | 0.61    |
| Serum creatinine, mg/dL  | 0.9±0.7           | 1.3±1.9                 | 0.31    |
| EuroSCORE                | 6.7±1.7           | 6.4±1.6                 | 0.49    |
| Embolism on admission    | 17 (44%)          | 19 (51%)                | 0.50    |
| Brain                    | 11 (28%)          | 11 (30%)                |         |
| Kidney                   | 7 (18%)           | 6 (16%)                 |         |
| Spleen                   | 9 (23%)           | 14 (38%)                |         |

# Patient Characteristics (2)

| Characteristics                       | CONV Tx<br>(n=39) | Early Surgery<br>(n=37) | p-value |
|---------------------------------------|-------------------|-------------------------|---------|
| <b><i>Valve involved</i></b>          |                   |                         | 0.96    |
| Mitral                                | 23 (59%)          | 22 (59%)                |         |
| Aortic                                | 11 (28%)          | 11 (30%)                |         |
| Aortic and mitral                     | 5 (13%)           | 4 (11%)                 |         |
| <b><i>Valvular disease</i></b>        |                   |                         | 0.62    |
| Severe stenosis                       | 3 (8%)            | 1 (3%)                  |         |
| Severe regurgitation                  | 36 (92%)          | 36 (97%)                |         |
| <b><i>LV ejection fraction</i></b>    | 61±7              | 62±5                    | 0.52    |
| <b><i>Vegetation diameter, mm</i></b> | 14±4              | 14±3                    | 0.41    |
| <b><i>Blood microorganism</i></b>     |                   |                         | 0.50    |
| Streptococcus                         | 25 (64%)          | 21 (57%)                |         |
| Staphylococcus                        | 5 (13%)           | 3 (8%)                  |         |
| Enterococcus and other                | 2 (6%)            | 3 (8%)                  |         |
| Culture negative                      | 7 (18%)           | 10 (27%)                |         |

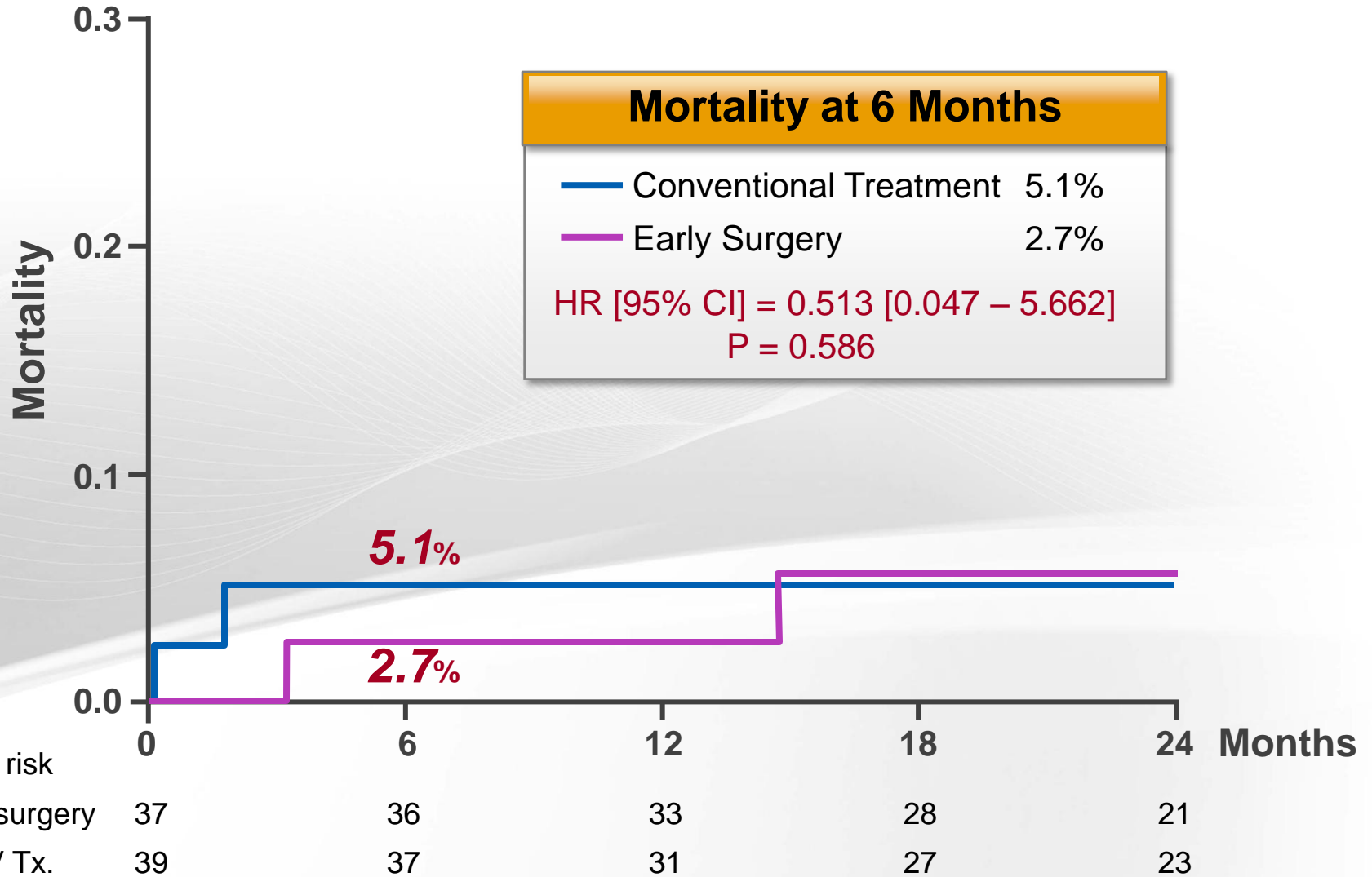
# Early Mitral Valve Repair



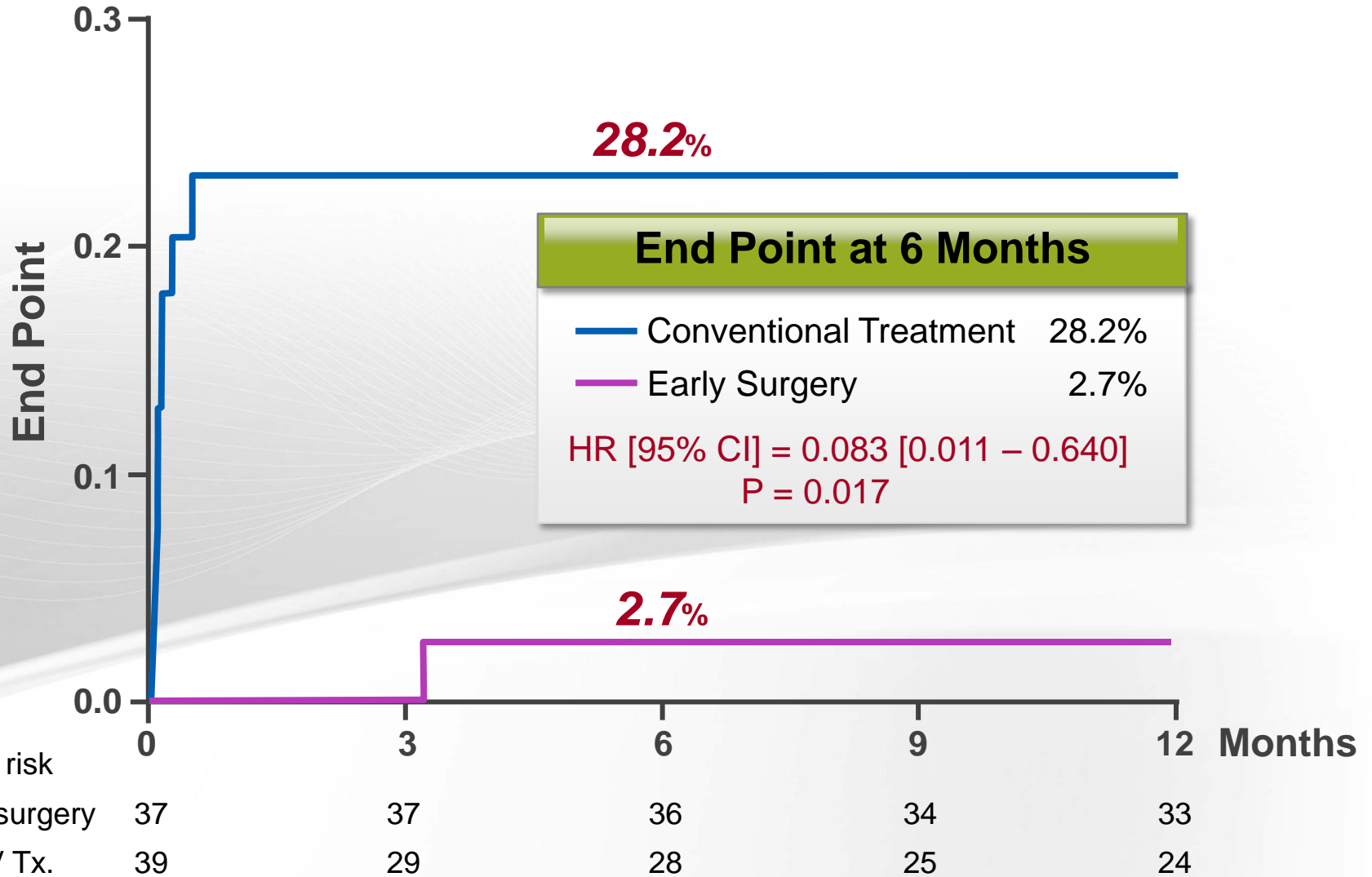
# End Point

| End Point                               | CONV Tx<br>(n=39) | Early Surgery<br>(n=37) | p-value      |
|---|-------------------|-------------------------|--------------|
| <b><i>Primary end point</i></b>         | <b>9 (23%)</b>    | <b>1 (3%)</b>           | <b>0.014</b> |
| In-hospital death                       | 1 (3%)            | 1 (3%)                  | 1.000        |
| Embolic event at 6 wks                  | 8 (21%)           | 0 (0%)                  | 0.005        |
| Cerebral                                | 5                 | 0                       |              |
| Coronary                                | 1                 | 0                       |              |
| Popliteal                               | 1                 | 0                       |              |
| Spleen                                  | 1                 | 0                       |              |
| <b><i>Secondary end point at 6M</i></b> | <b>11 (28%)</b>   | <b>1 (3%)</b>           | <b>0.003</b> |
| Mortality                               | 2 (5%)            | 1 (3%)                  | 1.000        |
| Embolic event                           | 8 (21%)           | 0 (0%)                  | 0.005        |
| Relapse of IE                           | 1 (3%)            | 0 (0%)                  | 1.000        |

# All Cause Mortality



# End Point



# Conclusions

- The EASE randomized trial showed that **early surgery significantly reduced the primary end point** of death and embolic events in IE patients with large vegetations
- Additional randomized trials are needed in complicated IE



Thank you  
for your attention

