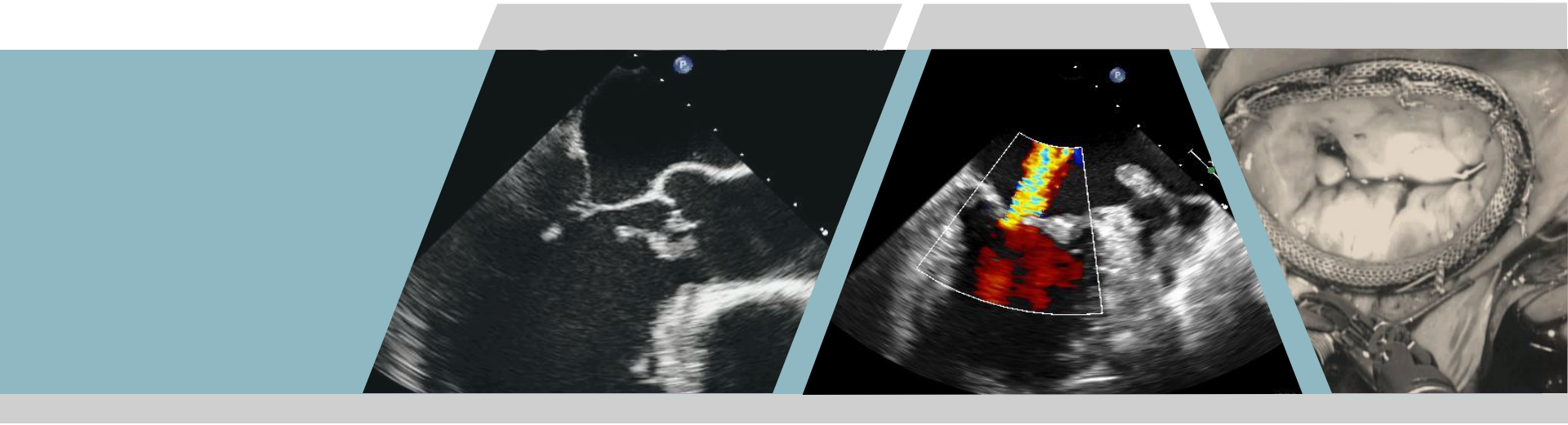
Randomized Trial of *Ea*rly *S*urgery Versus Conventional Treatment for Infective *E*ndocarditis *(EASE)*



Duk-Hyun Kang, MD, PhD

on behalf of The EASE Trial Investigators

Asan Medical Center, Seoul, Korea

UNIVERSITY OF ULSAN
COLLEGE OF MEDICINE

Asan Medical Center

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

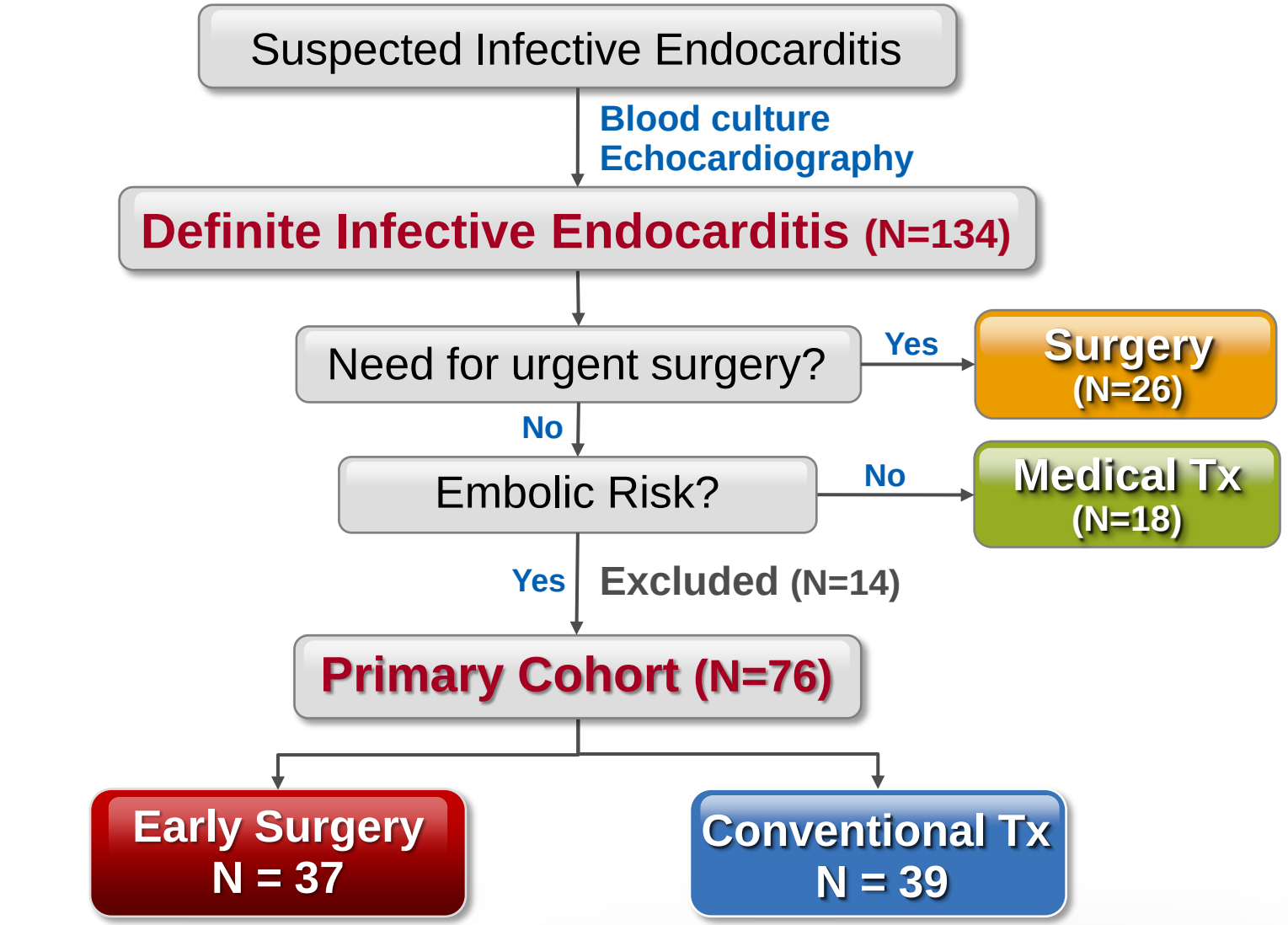
- All patients suspected of IE underwent blood cultures and echocardiography within 24 hrs after hospitalization

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 ≤ 10mm



Primary end point:

In-hopital 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[1,2] and 3% in the early surgery group[2]
  - Intended sample size: 74 pts for ≥ 80% power

- Primary analysis on intention-to-treat principle

[1] *Chan et al J Am Coll Cardiol* 2003 42:775-780

[2] *Kim et al Circulation* 2010 122:S17-S22

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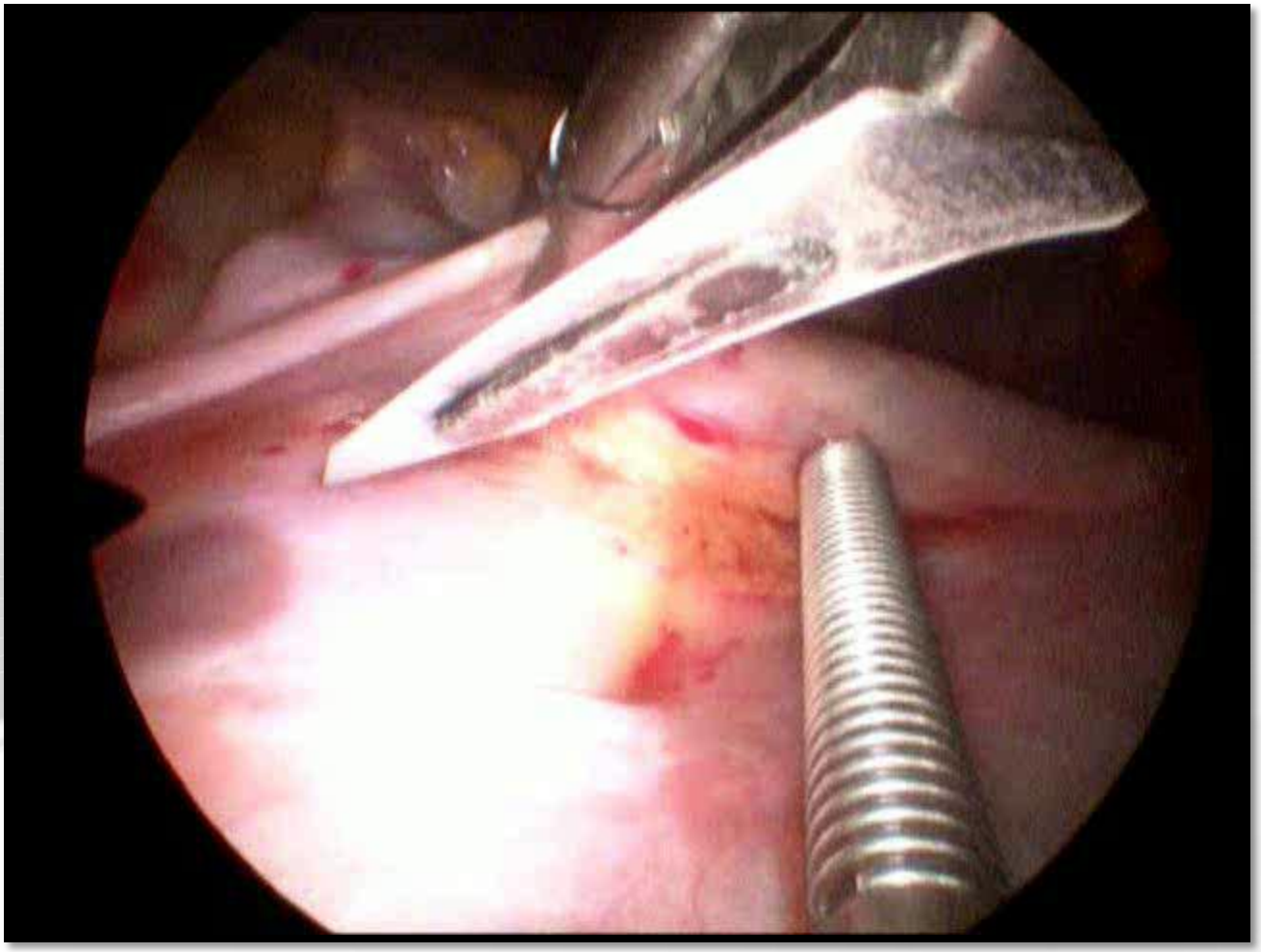
Patient Characteristics (1)

Characteristics	CONV Tx (n=39)	Early Surgery (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 (n=39)	Early Surgery (n=37)	p-value
Valve involved			0.96
Mitral	23 (59%)	22 (59%)	
Aortic	11 (28%)	11 (30%)	
Aortic and mitral	5 (13%)	4 (11%)	
Valvular disease			0.62
Severe stenosis	3 (8%)	1 (3%)	
Severe regurgitation	36 (92%)	36 (97%)	
LV ejection fraction	61±7	62±5	0.52
Vegetaion diameter, mm	14±4	14±3	0.41
Blood microorganism			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%)	

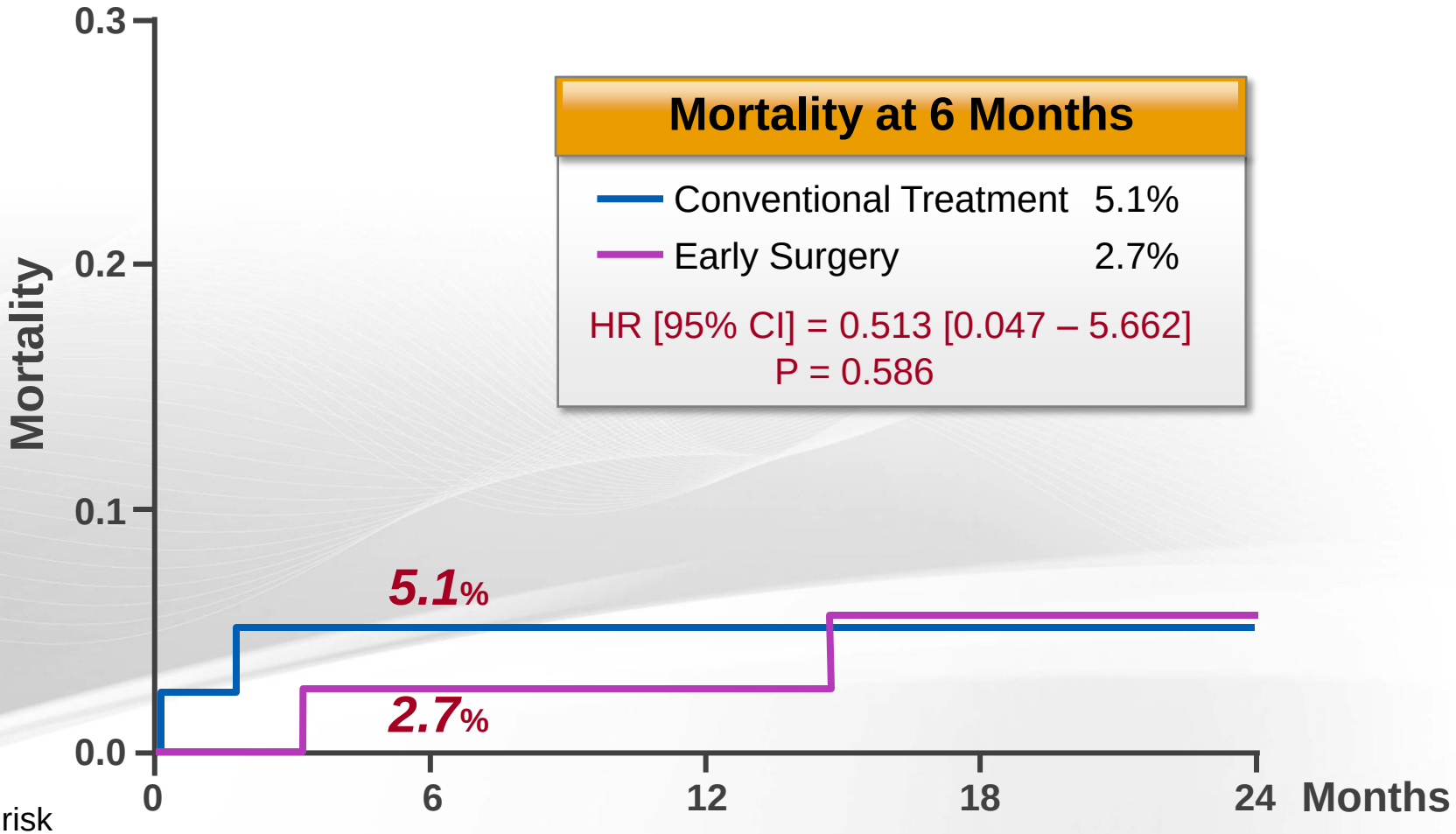
Early Mitral Valve Repair



End Point

End Point	CONV Tx (n=39)	Early Surgery (n=37)	p-value
Primary end point	***9 (23%)***	***1 (3%)***	***0.014***
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	
Secondary end point at 6M	***11 (28%)***	***1 (3%)***	***0.003***
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



No. at risk					
Early surgery	37	36	33	28	21
CONV Tx.	39	37	31	27	23

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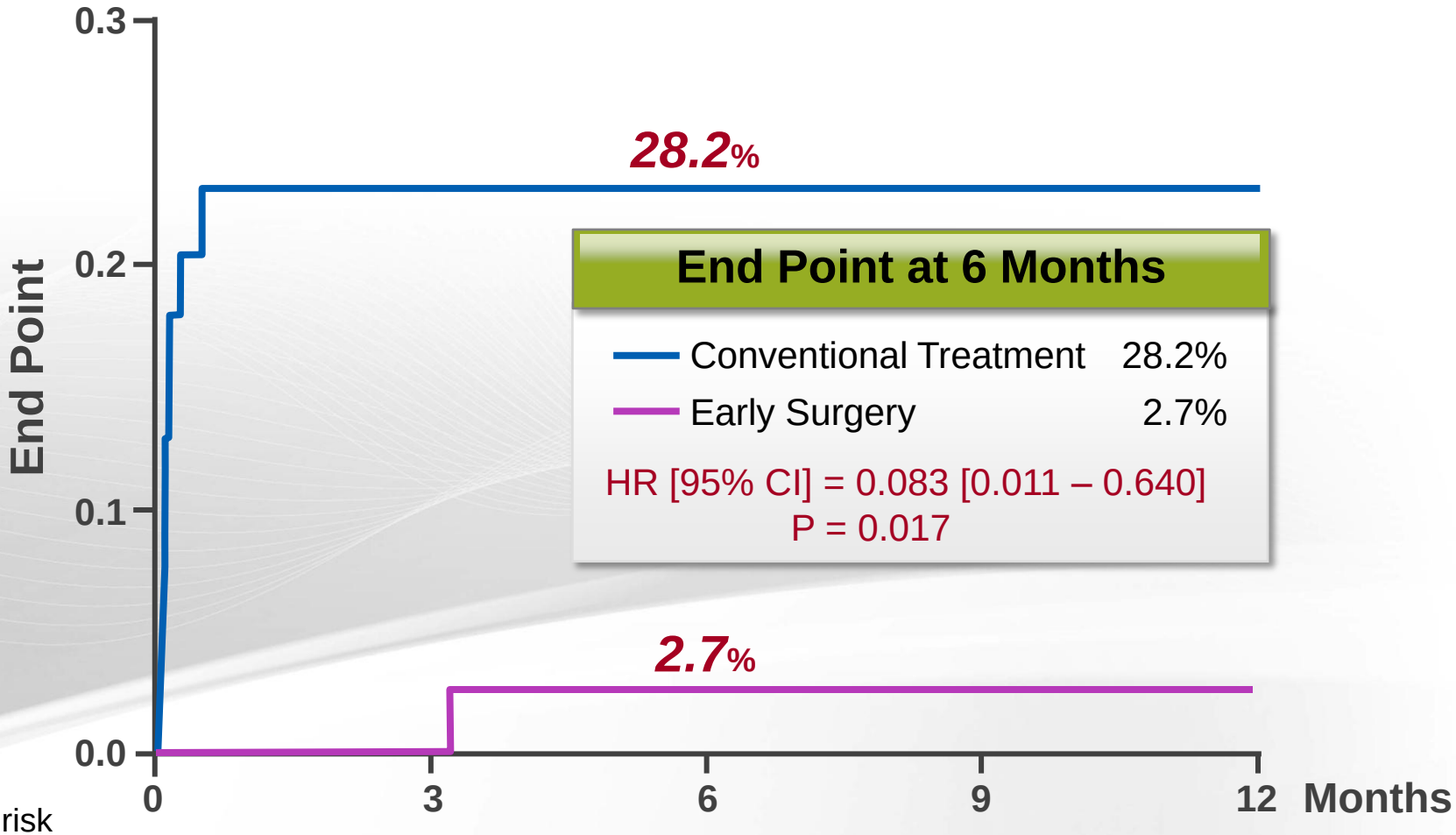
End Point



No. at risk					
Early surgery	37	37	36	34	33
CONV Tx.	39	29	28	25	24

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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