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LBCTs: Overview of Arrhythmia & Anticoagulation

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Re-Dual Trial

Randomized Evaluation of Dual Antithrombotic Therapy With Dabigatran vs. Triple Therapy With Warfarin in Patients With Non-valvular Atrial Fibrillation Undergoing Percutaneous Coronary Intervention

NEJM, 27 August 2017

- The goal of the trial was to evaluate dual therapy compared with triple therapy among patients with atrial fibrillation undergoing coronary revascularization. Triple therapy usually consists of aspirin, an ADP receptor antagonist, and warfarin; however, this approach is associated with increased bleeding.

Re-Dual:BACKGROUND

- The goal of the trial was to evaluate dual therapy compared to triple therapy among patients with atrial fibrillation undergoing coronary revascularization.
- Triple therapy is ASA, an ADP antagonist and warfarin.
- Dual therapy group, participants received an ADP antagonist in addition to one of two doses of dabigatran

Re-Dual Trial Design

- 2,725 patients with atrial fibrillation undergoing coronary revascularization (stable or unstable CAD) were randomized to dual therapy with dabigatran at dose of 110mg (n=981) vs. Dual therapy with dabigatran at a dose of 150mg (n=763) vs. Triple therapy with warfarin (n=981)
- In the dual therapy group, participants received clopidogrel or ticagrelor in addition to one of two doses of dabigatran.
- In the triple therapy group, participants received aspirin plus clopidogrel or ticagrelor in addition to warfarin. The duration of aspirin was 1 month after a bare-metal stent and 3 months after a drug-eluting stent.
- Outside the United States, elderly participants were not eligible for the dabigatran 150 mg dose.
- Duration of follow-up- 6months
- Mean pt age- 72 years, 26% female, 37% diabetics

Re-Dual: Trial Design

Inclusion criteria:

- Patients with stable or unstable coronary artery disease undergoing coronary revascularization
- Non-valvular atrial fibrillation

Exclusion criteria:

- Bioprosthetic or mechanical heart valve
- Severe renal insufficiency

Other salient features/characteristics:

- Acute coronary syndrome: 52%
- Drug-eluting stent: 82%
- Approximately 10% received ticagrelor as their ADP receptor antagonist

Re- Dual: Results

- Primary safety outcome- incidence of major or clinically relevant non-major bleeding occurred in 15.4% of the dual therapy with dabigatran 110mg vs 26.9% of the triple therapy group.
- Primary safety outcome- incidence of major or clinically relevant non-major bleeding occurred in 20.2% of the dual therapy with dabigatran 150mg vs 25.7% of the triple therapy group.
- TIMI major bleeding was also lower in the dual vs triple therapy group.
- Primary efficacy outcome, incidence of death, MI, stroke, systemic embolism or revascularization occurred in 13.7 % dual therapy vs 13.4% of the triple therapy group.

Re-Dual Results

- The secondary outcomes:
- MI: 4.5% with dual therapy-110mg vs 3.0% triple therapy
- MI: 3.4% with dual therapy- 150mg vs 2.9% triple therapy
- Definite stent thrombosis:
- 1.5% with dual therapy- 110mg vs 0.8% with triple therapy
- 0.9% with dual therapy 150mg vs 0.9% with triple therapy

Re-Dual Conclusions

- Among patients with atrial fibrillation undergoing coronary revascularization, dual therapy compared with triple therapy was effective at reducing bleeding events.
- Dual therapy consisted of an ADP receptor antagonist (clopidogrel or ticagrelor) and dabigatran (110 mg or 150 mg).
- Dual therapy was noninferior to triple therapy with respect to risk of thromboembolic events.
- Adverse cardiac events were similar between treatment groups; however, there was a numerical increase in MI and definite stent thrombosis in the dual therapy dabigatran 110 group vs. the triple therapy group.
- Growing body of evidence now suggest that it is safe to treat atrial fibrillation patients who undergo coronary revascularization with anticoagulation (warfarin studied in WOEST, rivaroxaban studied in PIONEER AF-PCI, dabigatran studied in RE-DUAL PCI) and clopidogrel monotherapy.

The CASTLE-AF Trial

Catheter Ablation versus Standard Conventional Treatment In Patients With Left Ventricular Dysfunction And Atrial Fibrillation

- Atrial fibrillation (AF) and heart failure are commonly seen together

- Study the effectiveness of catheter ablation of atrial fibrillation in patients with heart failure in improving primary endpoints of mortality and heart failure progression when compared to conventional standard treatment

Castle-AF

Primary Endpoint

All-cause mortality

Worsening heart failure admissions

Secondary Endpoints

All cause mortality
Worsening of heart failure admissions
Cerebrovascular accidents
Cardiovascular mortality
Unplanned hospitalization due to cardiovascular reason
All cause hospitalization
Quality of Life: Minnesota Living with Heart Failure and EuroQoL EQ5D
Exercise tolerance (6 minutes walk test)
Number of delivered ICD shocks, and ATPs (appropriate/inappropriate)
LVEF
Time to first ICD shock, and time to first ATP
Number of device detected VT/VF
AF burden: cumulative duration of AF episodes
AF free interval: time to first AF recurrence after 3 months blanking period post ablation

CASTLE-AF: Inclusion Criteria

- Symptomatic paroxysmal or persistent AF
- Failure or intolerance to ≥ 1 or unwillingness to take Antiarrhythmic tx
- LVEF ≤ 35%
- NYHA class ≥ II
- ICD/CRTD already implanted for primary or secondary prevention and who has home monitoring capabilities

Study Design— CASTLE-AF

Investigator initiated, Prospective, Multicenter (31 sites, 9 countries), Randomized, Controlled

397 patients enrolled and randomized
179 patients underwent ablation
184 pts underwent conventional therapy

Conventional therapy

Efforts to maintain sinus rhythm were recommended

In case of rate control strategy:
60 and 80 beats per minute at rest, 90 and 115 beats per minute during moderate exercise

Anticoagulation was initiated and maintained throughout the study. The INR was maintained between 2.0 and 3.0

Ablation Protocol

Pulmonary Vein Isolation

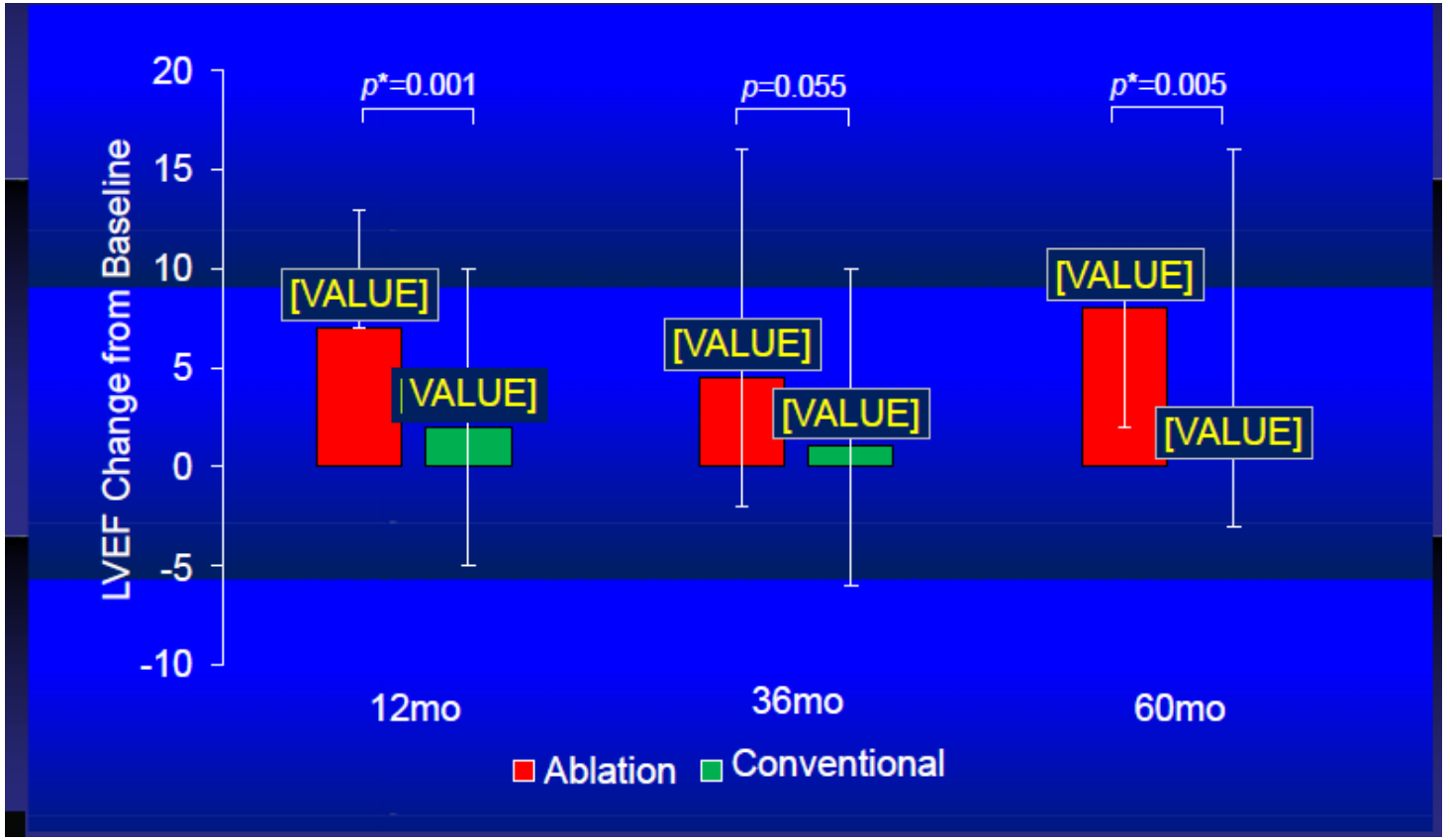
Additional lesions
at discretion of operator

Repeat ablation after blanking period

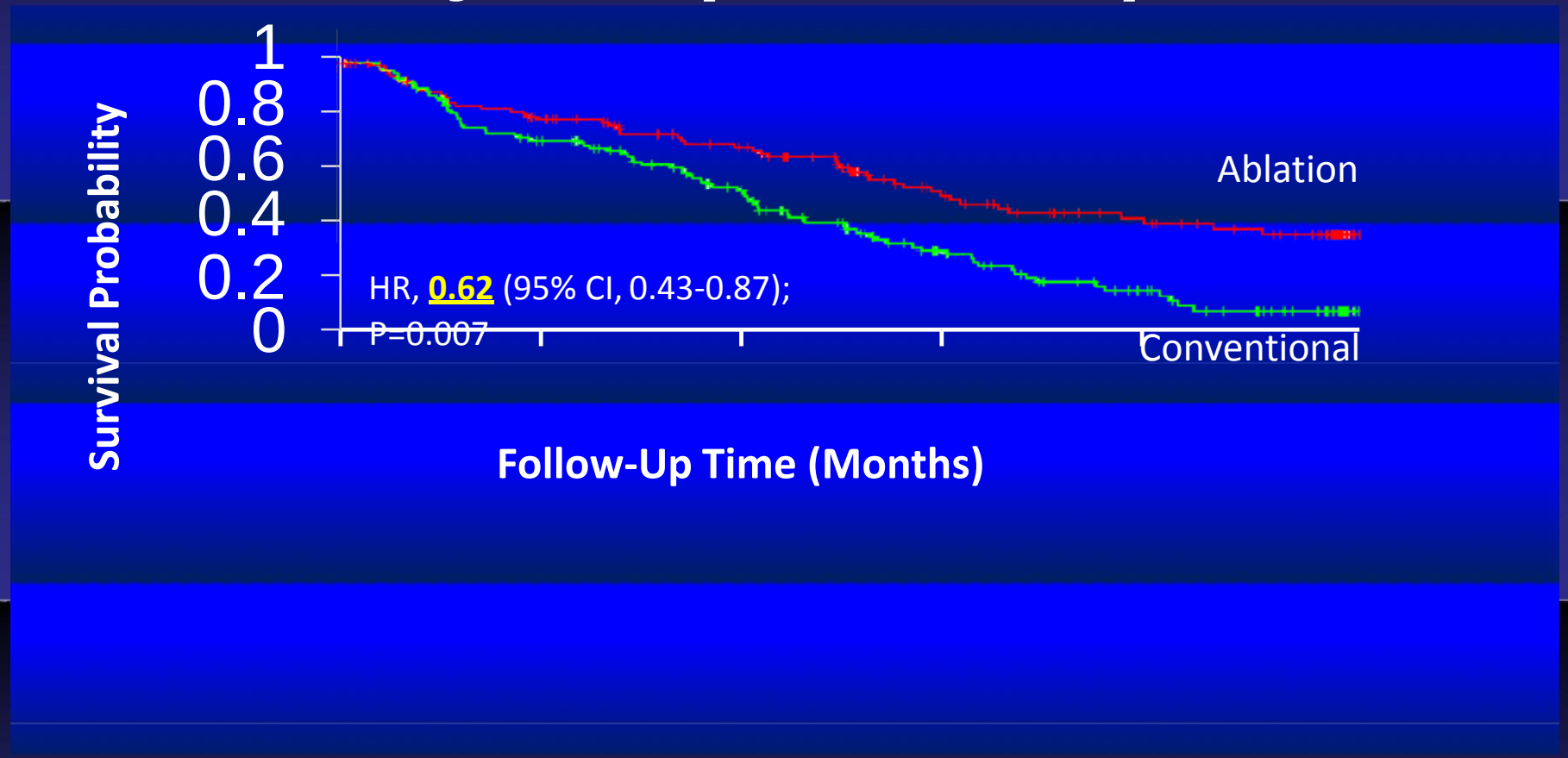
Baseline CharacteristicsCASTLE AF

	Ablation group (179 patients)	Conventional group (184 patients)
• Age – years	64 (5671)	64 (5673.5)
• New York Heart Association class		
• I	11%	11%
• II	58%	61%
• III	29%	27%
• IV	2%	1%
• Left ventricular ejection fraction	32.5%	31.5%
Atrial fibrillation		
Paroxysmal	30%	35%
Persistent	70%	65%
• CRTD implanted	27%	28%
• ICD implanted	73%	72%

Change in the LVEF from Baseline

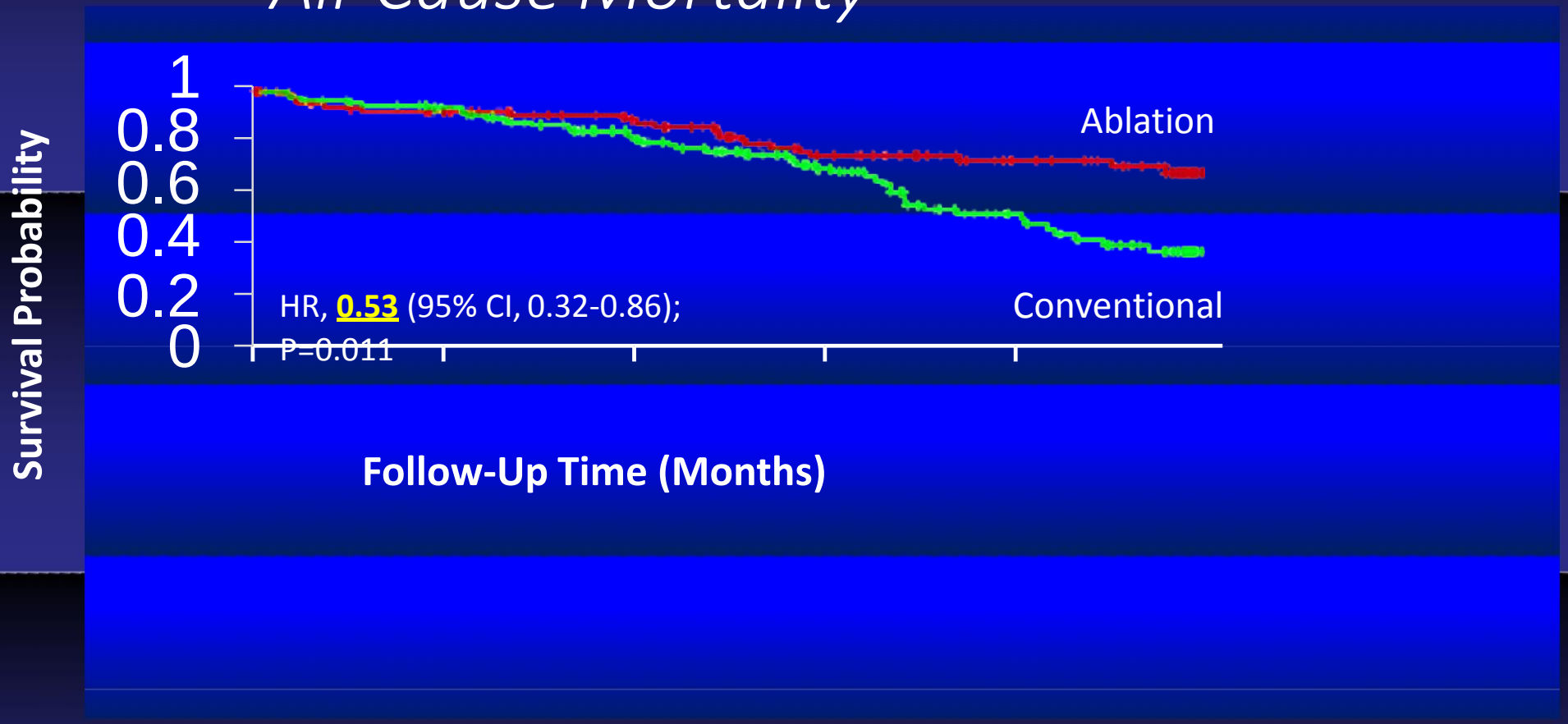


Primary Composite Endpoint

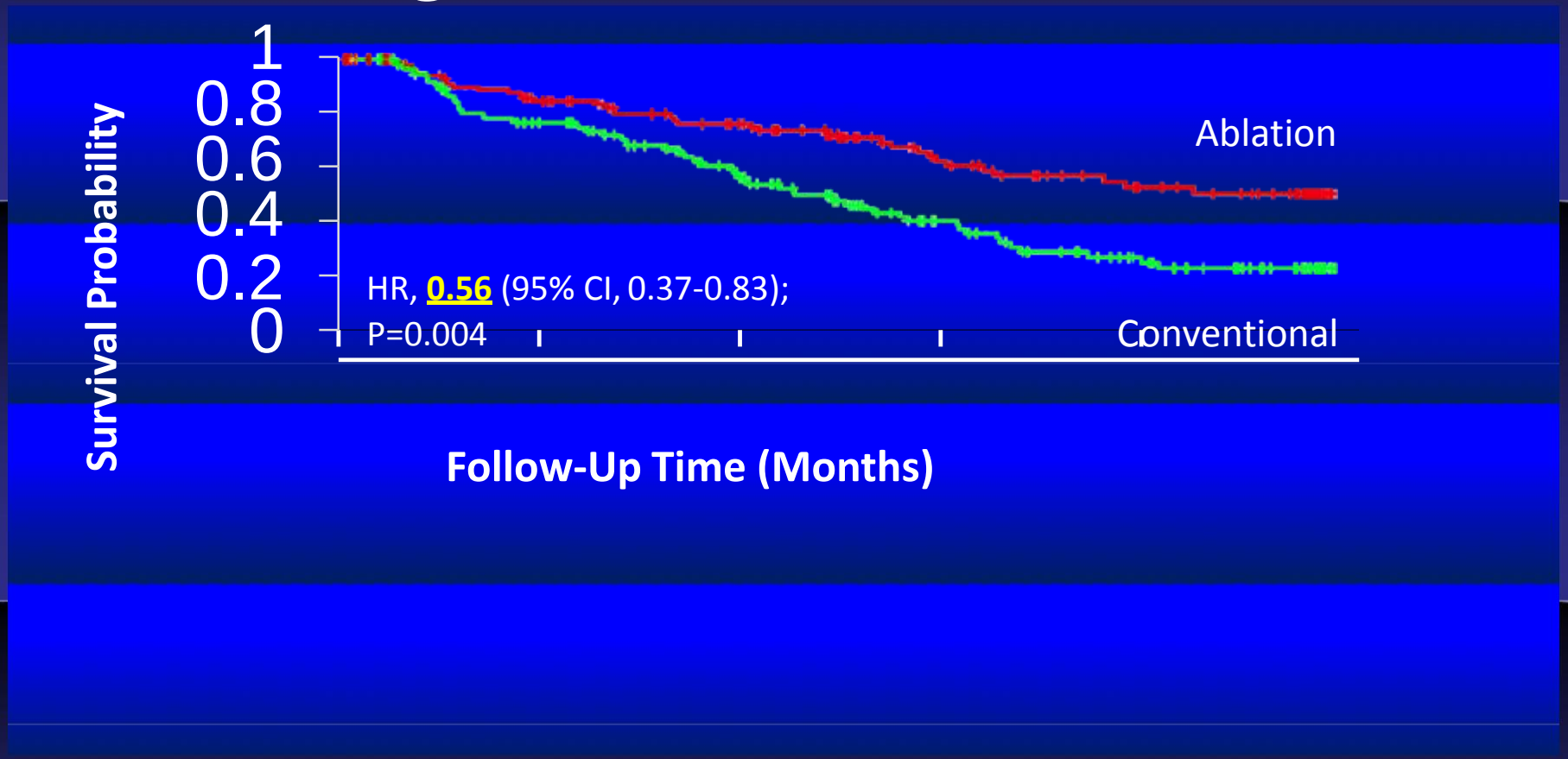


ResultsCASTLE AF

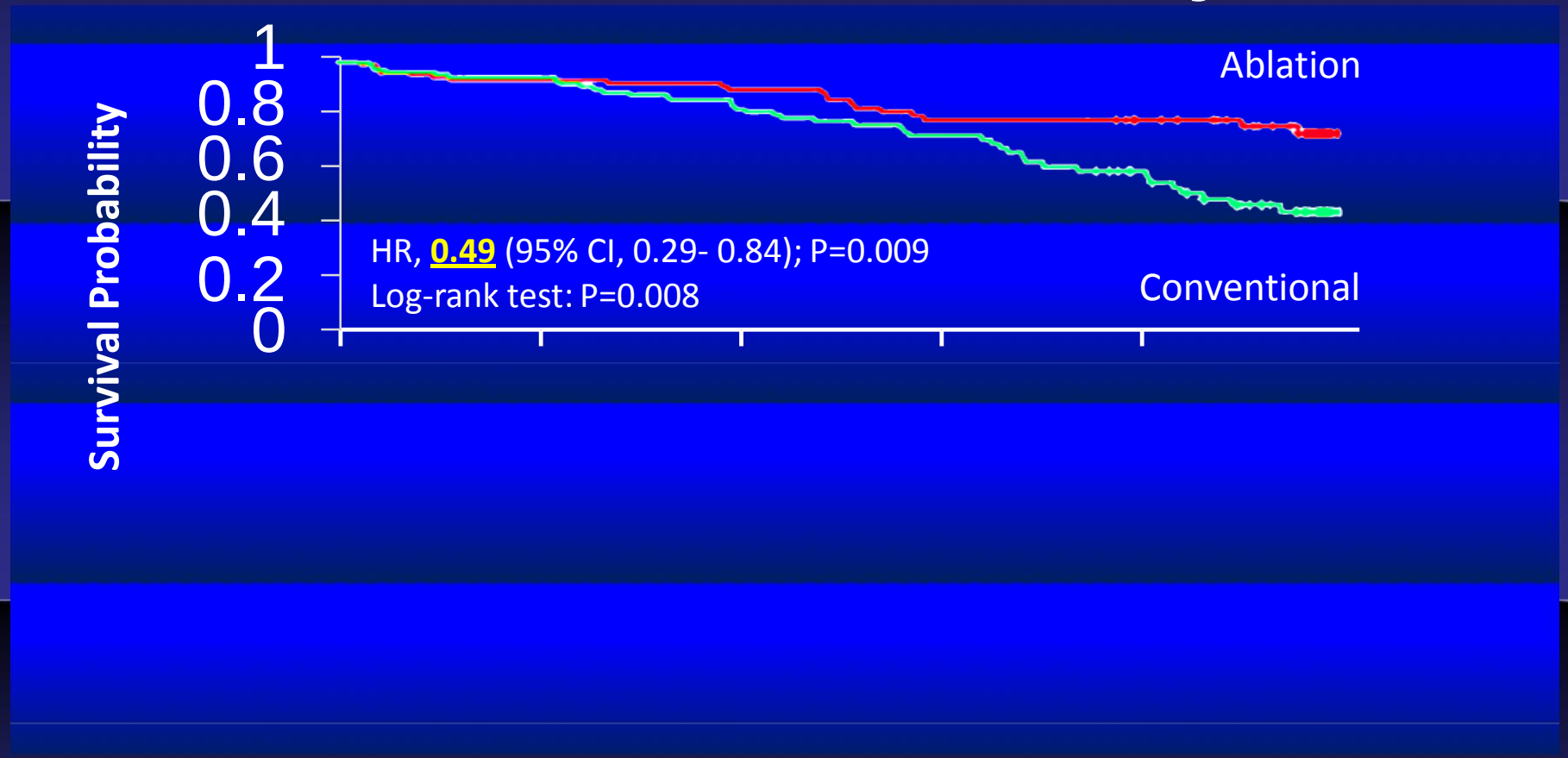
All-Cause Mortality



Worsening Heart Failure Admissions



Cardiovascular Mortality



Conclusion CASTLE- AF

- **Catheter ablation of atrial fibrillation in patients with heart failure was associated with improved all-cause mortality, improved cardiovascular mortality and decreased hospitalization due to fewer admissions for worsening heart failure when compared to conventional standard of care treatment**

Reference :

- Cannon CP, Bhatt DL, Oldgren J, et al., on behalf of the RE-DUAL PCI Steering Committee and Investigators. Dual Antithrombotic Therapy with Dabigatran after PCI in Atrial Fibrillation. *N Engl J Med* 2017;Aug 27:[Epub ahead of print].
- Re-Dual PCI Presented by Dr. Christopher P. Cannon at the European Society of Cardiology Congress, Barcelona, Spain, August 27, 2017.
- Castle-HF- Presented by Dr. Nassir Marrouche at the European Society of Cardiology Congress, Barcelona, Spain, August 27, 2017.