



慢性左心衰的治疗进展

南方医科大学南方医院心血管内科
— 许顶立 曾庆春

- 2016 ESC心衰指南和2017 ACC/AHA心衰管理指南发布
- 慢性心力衰竭治疗进展

2016 ESC心衰指南对心衰的定义

强调 “无症状，无心衰”

2012 ESC心衰指南

心衰被定义为一种由于心脏结构或功能异常所致的临床综合征，患者具有典型的症状(如气短、踝部水肿和疲乏)和体征(如颈静脉压升高、肺部湿啰音和心尖异位搏动)

2016 ESC心衰指南

心衰被定义为一种由于心脏结构或功能异常所致的临床综合征，患者具有典型的症状(如气短、踝部水肿和疲乏)，伴有颈静脉压升高、肺部湿啰音和**外周性水肿等体征。可导致患者静息/应激状态下心输出量减少和(或) 心腔内压力升高**

1. McMurray JJ , et al. Eur Heart J. 2012 Jul;33(14):1787-847.
2. Ponikowski P, et al. Eur Heart J. 2016 May 20. pii: ehw128.

HFmrEF约占心衰群体的10-20%

2016 ESC心衰指南中新增了HFmrEF分类

心衰的分类	HFrEF	HFmrEF	HFpEF
分类标准	症状±体征*	症状±体征*	症状±体征*
	LVEF <40%	LVEF 40-49%	LVEF ≥50%
	——	• 利钠肽水平升高[#] • 至少包含以下任意一项 1. 相关的结构性心脏病 (LVH和/或LAE) 2. 舒张功能障碍	• 利钠肽水平升高[#] • 至少包含以下任意一项 1. 相关的结构性心脏病 (LVH和/或LAE) 2. 舒张功能障碍

* HF早期阶段(尤其是HFpEF)患者以及经利尿剂治疗的患者可不出现体征

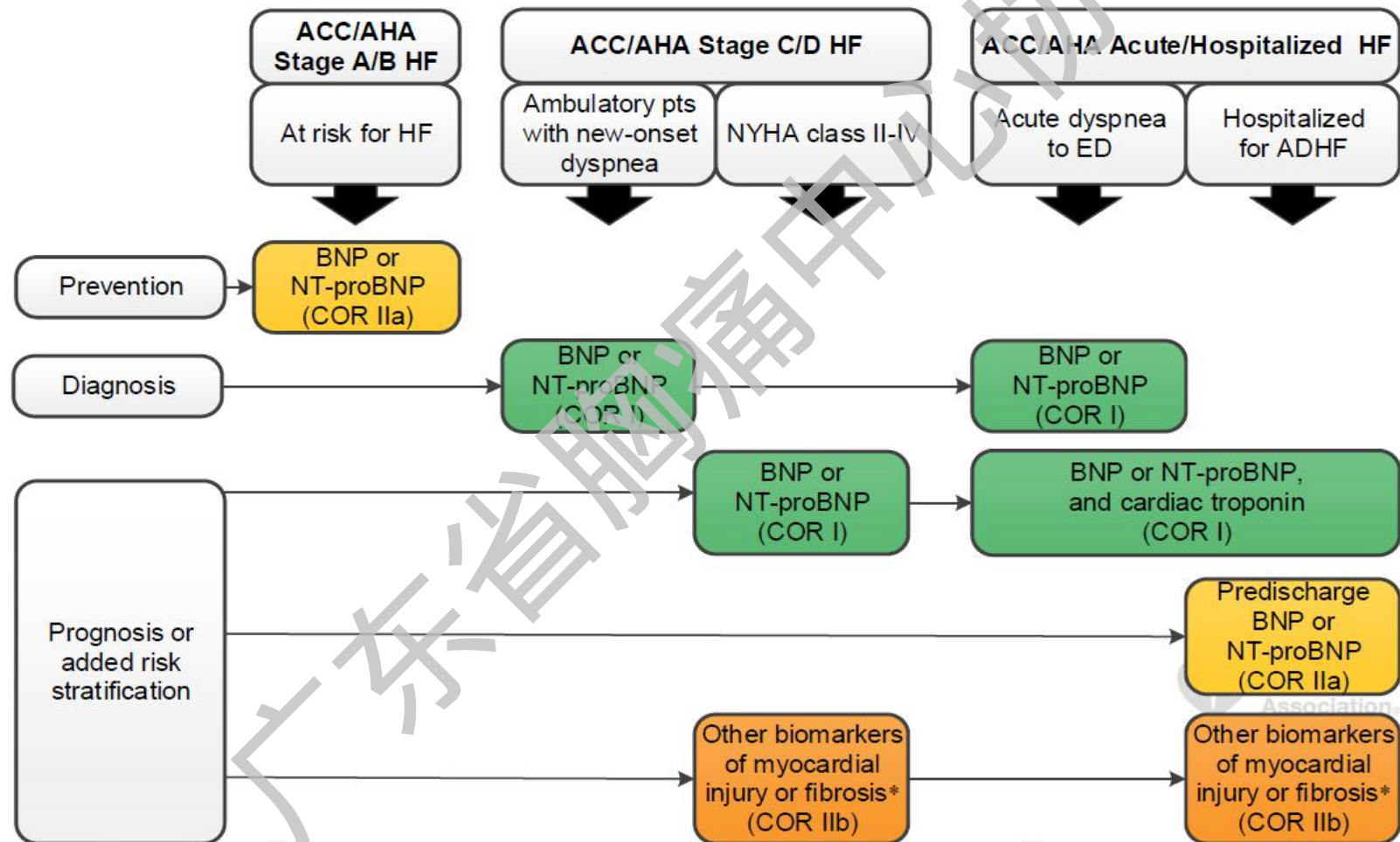
[#]BNP>35 pg/mL和(或)NT-proBNP>125 pg/mL

LVH：左心室肥大；LAE：左心房扩大

Ponikowski P, et al. Eur Heart J. 2016 May 20. pii: ehw128.

2017 ACC/AHA/HFSA Heart Failure Focused Update

Figure 1. Biomarkers Indications for Use



2017 ACC/AHA/HFSA Heart Failure Focused Update

9.5.2. Treating Hypertension in Stage C HFrEF: Recommendation

Recommendation for Hypertension in Stage C HFrEF			
COR	LOE	Recommendation	Comment/Rationale
I	C-EO	Patients with HFrEF and hypertension should be prescribed GDMT titrated to attain systolic blood pressure <u>less than 130 mm Hg</u> (191).	NEW: Recommendation has been adapted from recent clinical trial data but not specifically tested per se in a randomized trial of patients with HF.
See Online Data Supplements E and F.		Clinical trials evaluating goal blood pressure reduction and optimal blood pressure-lowering agents in the setting of HFrEF and concomitant hypertension have not been done. However, it is apparent that in those patients at higher risk, blood pressure lowering is associated with fewer adverse cardiovascular events. GDMT for HFrEF with agents known to lower blood pressure should consider a goal blood pressure reduction consistent with a threshold now associated with improved clinical outcomes but not yet proven by RCTs in a population with HF.	

Biomarker-Guided HF Drug Management: No Advantage in Large Randomized Trial

Steve Stiles

August 25, 2017

生物标志物指导心力衰竭药物治疗的结果令人失望

Patients in the two groups hit the NT-proBNP target of <1000 pg/mL at 12 months at similar rates, 46% in the guided-therapy group and 40% in the usual-care group ($P=0.21$).

Adjusted HR (95% CI) for Outcomes in Biomarker-Guided Group vs Usual-Care Group

End points	HR (95% CI)	<i>P</i>
Primary end point*	0.98 (0.79–1.22)	0.88
CV death	0.94 (0.65–1.37)	0.75
Death by any cause	0.86 (0.62–1.20)	0.37

*First HF hospitalization or CV death

Coverage from the
European Society of Cardiology (ESC) Congress 2017

High Salt Intake Linked to Increased Heart-Failure Risk

高盐摄入将增加患心力衰竭的风险

Liam Davenport
August 28, 2017

National health records were then examined to determine the rate of incident heart failure over a mean 12-year follow-up, based on causes of death, hospital discharge summaries, and drug reimbursements.

Hazard Ratios for Incident Heart Failure

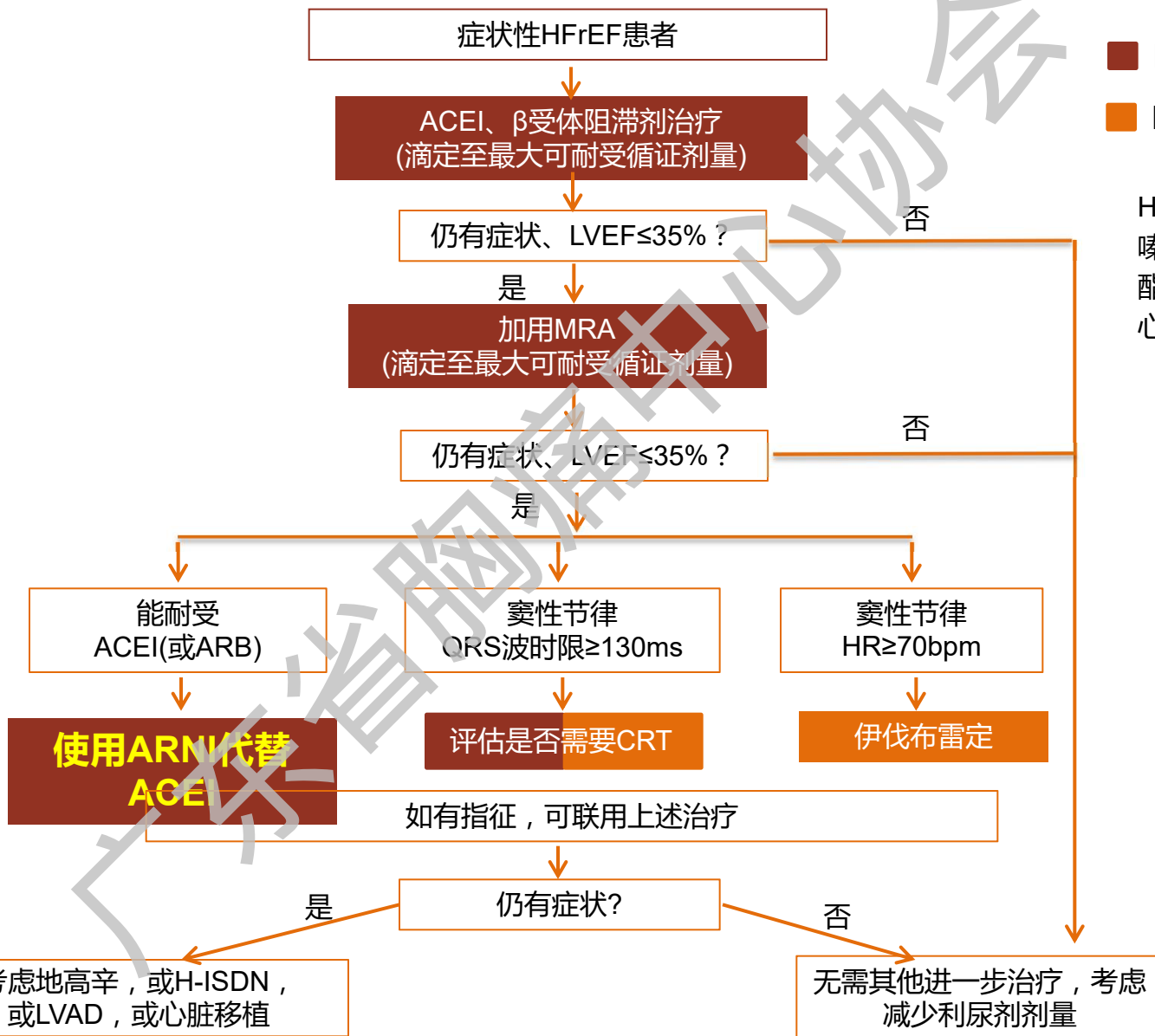
Salt intake (quintiles)	Fully adjusted hazard ratio
<6.77 g/day	1.0 (reference)
6.77–8.80 g/day	1.13
8.81–10.95 g/day	1.45
10.96–13.73 g/day	1.56
>13.73 g/day	1.75
<i>P</i> for trend	0.009

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HFrEF的治疗流程

使用利尿剂减轻充血症状和体征

若经OMT后 LVEF≤35%
或有VT/VF症状史，考虑植入ICD



(一) DANISH研究

The NEW ENGLAND JOURNAL of MEDICINE

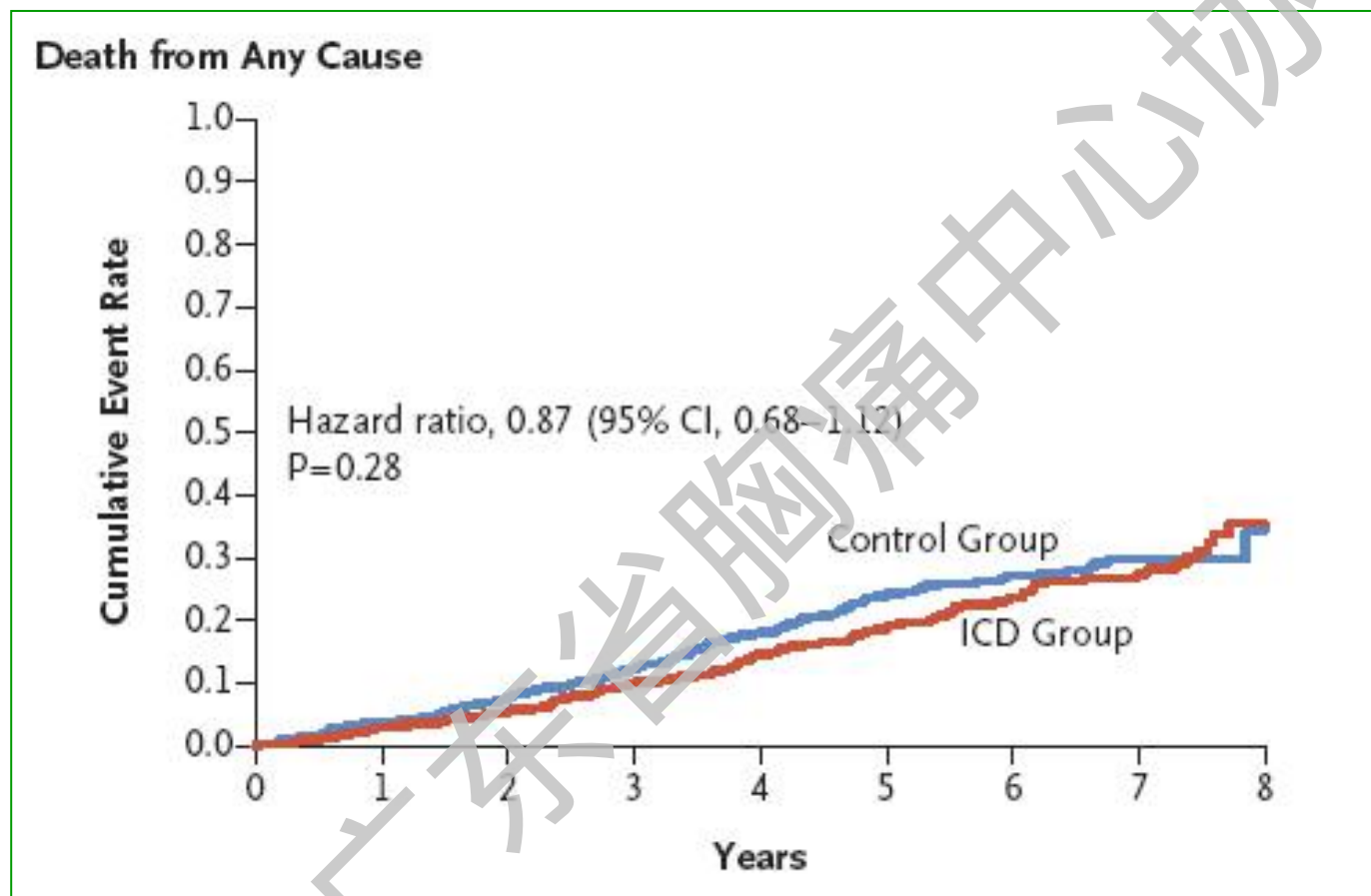
ORIGINAL ARTICLE

Defibrillator Implantation in Patients with Nonischemic Systolic Heart Failure

- 研究分为两组
 - 556例非冠状动脉疾病引起的症状性收缩性心衰患者（左室射血分数 $\leq 35\%$ ）接受ICD治疗
 - 560例患者接受常规诊疗
- 两组中均有58%的患者接受CRT
- 主要终点：全因死亡
- 次要终点：猝死、心血管死亡

(一) DANISH研究

主要终点结果：两组全因死亡率无显著差异



全因死亡在ICD组和常规诊疗组中的发生率分别为21.6% (n=120) 和23.4% (n=131 ; 风险比：0.87 ; P=0.28) 。

(一) DANISH研究结论

- 在非冠状动脉疾病引起的症状性收缩性心衰患者中，相较于常规临床诊疗，预防性使用ICD并不显著降低远期全因死亡率。
- 主要研究者，Copenhagen University Hospital的Lars Kober 说：
 - 美国和欧洲的指南推荐所有左室射血分数减少的心衰患者接受预防性ICD治疗（I类推荐），但对于非缺血性心衰患者来说，相关证据比较薄弱。该研究填补了非缺血性心衰患者相关数据的空白，其结果给大家‘提了个醒儿’。

(二) REM-HF和MORE-CARE研究

Remote management of heart failure using implanted devices and formalized follow-up procedures (REM-HF)

Martin R Cowie

Professor of Cardiology, Imperial College London (Royal B
London, UK
&

John M Morgan

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On behalf of the REM-HF investigators



European Journal of Heart Failure (2016)
doi:10.1002/ehf.626

Effects of remote monitoring on clinical outcomes and use of healthcare resources in heart failure patients with biventricular defibrillators: results of the MORE-CARE multicentre randomized controlled trial

Giuseppe Boriani^{1,2*}, Antoine Da Costa³, Aurelio Quesada⁴, Renato Pietro Ricci⁵,
Stefano Favale⁶, Gabriele Boscolo⁷, Nicolas Clementy⁸, Valentina Amori⁹,
Lorenza Mangoni di S. Stefano⁹, Haran Burri¹⁰, on behalf of the MORE-CARE Study
Investigators

¹University of Modena and Reggio Emilia, Policlinico di Modena, Modena, Italy; ²University of Bologna, S. Orsola-Malpighi University Hospital, Bologna, Italy; ³University Hospital, St. Etienne, France; ⁴University General Hospital, Valencia, Spain; ⁵San Filippo Neri Hospital, Rome, Italy; ⁶University Hospital, Bari, Italy; ⁷Chioggia ULSS 14, Chioggia, Italy; ⁸Tours University Hospital, Tours, France; ⁹Medtronic EMEA Regional Clinical Center, Rome, Italy; and ¹⁰University Hospital of Geneva, Geneva, Switzerland

Received 5 July 2016; revised 27 July 2016; accepted 27 July 2016

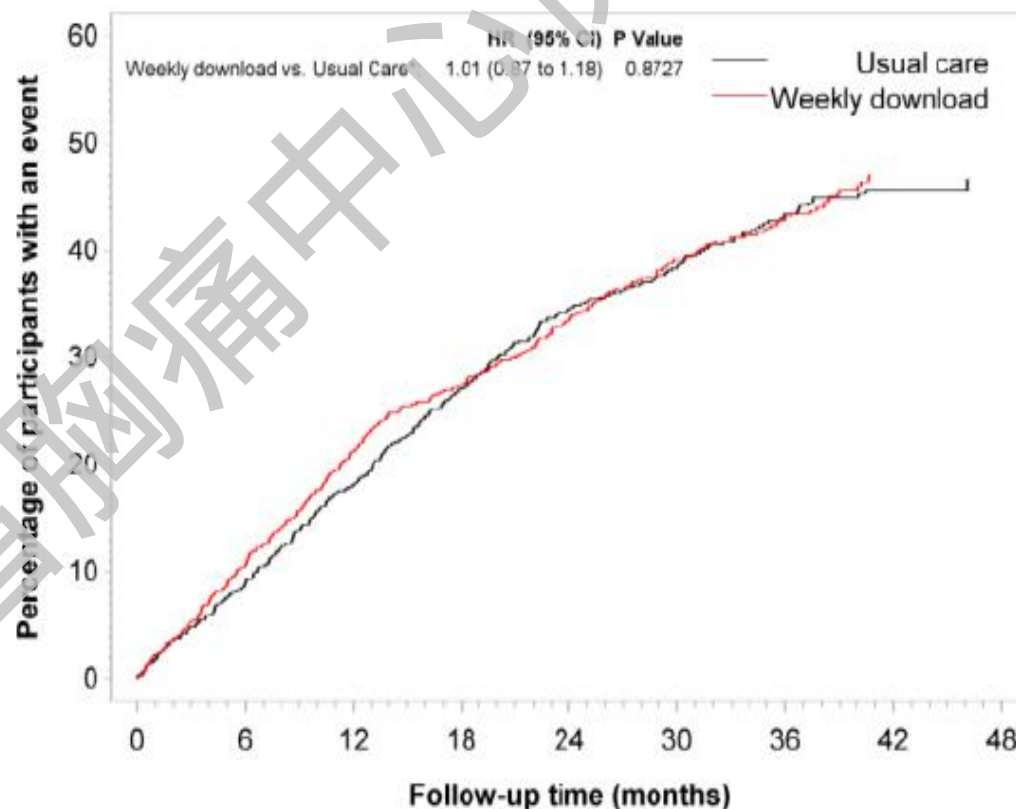
REM-HF 和 MORE-CARE 两项研究试图评价在植入 ICD/CRT 或 CRT-D 的心衰患者中，应用设备内置的远程监测系统报告患者病情变化，并采取相应治疗，是否能进一步改善患者的远期预后。

(二) REM-HF研究结果：

对置入CIEDs的患者使用远程监测并不能改善患者结局

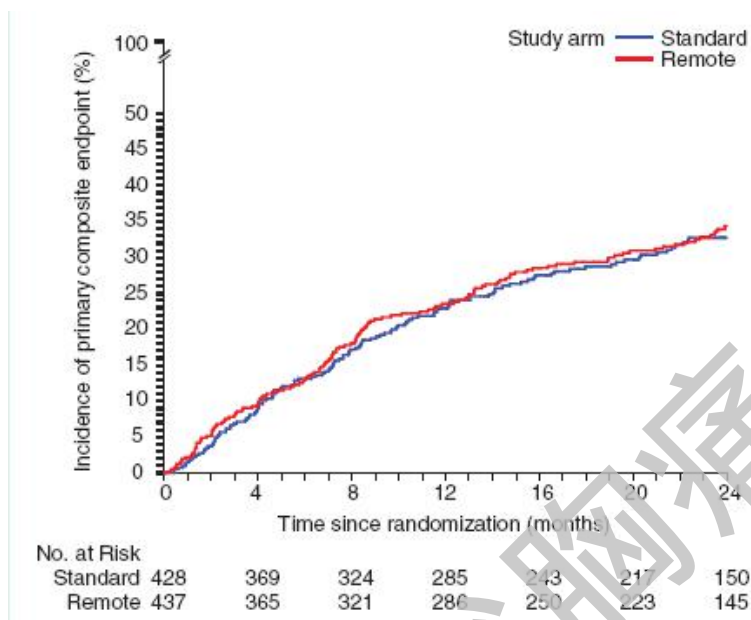
- REM-HF研究搜集了英国9个中心的1650例平均年龄70岁的心衰患者数据
- 随访2.8年
- 未观察到远程监测组患者全因死亡或心血管再住院风险的降低 (HR 1.01, 95% CI 0.87-1.18, P=0.87)
- 次要终点——全因死亡、心血管死亡和非计划住院依然无显著差异。

Primary End Point



(二) MORE-CARE研究主要结果：

使用心脏置入器械的远程监测并未带来显著临床获益



- 入选 917 例植入CRT-D的慢性心衰患者
- 最终随访中位数为24个月
- 未能观察到远程监测对于全因死亡或再入院风险的改善作用

HR 1.02

95% CI 0.80-1.30

P=0.89

Table 2 Results of the primary outcome and its components

	Remote (n = 437)	Standard (n = 428)	Hazard ratio (95% CI)	P-value
Primary composite endpoint, n (%)				
Death or first CV or device-related hospitalization (≥48 h stay)	130 (29.7)	123 (28.7)	1.02 (0.80–1.30)	0.889
Components, n (%)				
Death from any cause	40 (9.2)	34 (7.9)	1.13 (0.71–1.80)	0.594
First CV hospitalization	100 (22.9)	97 (22.7)	0.96 (0.73–1.28)	0.796
First device-related hospitalization	17 (3.9)	18 (4.2)	0.89 (0.44–1.79)	0.742

CI, confidence interval; CV, cardiovascular.

(三) LEVO-CTS研究



ACC.17

66th Annual Scientific Session & Expo

Levosimendan In Patients With Left Ventricular Systolic Dysfunction Undergoing Cardiac Surgery With Cardiopulmonary Bypass PRIMARY RESULTS OF THE LEVO-CTS TRIAL

John H. Alexander, MD, MHS, FACC

Rajendra H. Mehta, Jeffrey D. Leimberger, Stephen Fremes, John Luber, Wolfgang Toller, Matthias Heringlake, Jerrold H. Levy, Robert A. Harrington, Kevin J. Anstrom

on behalf of the LEVO-CTS Investigators



Duke Clinical Research Institute

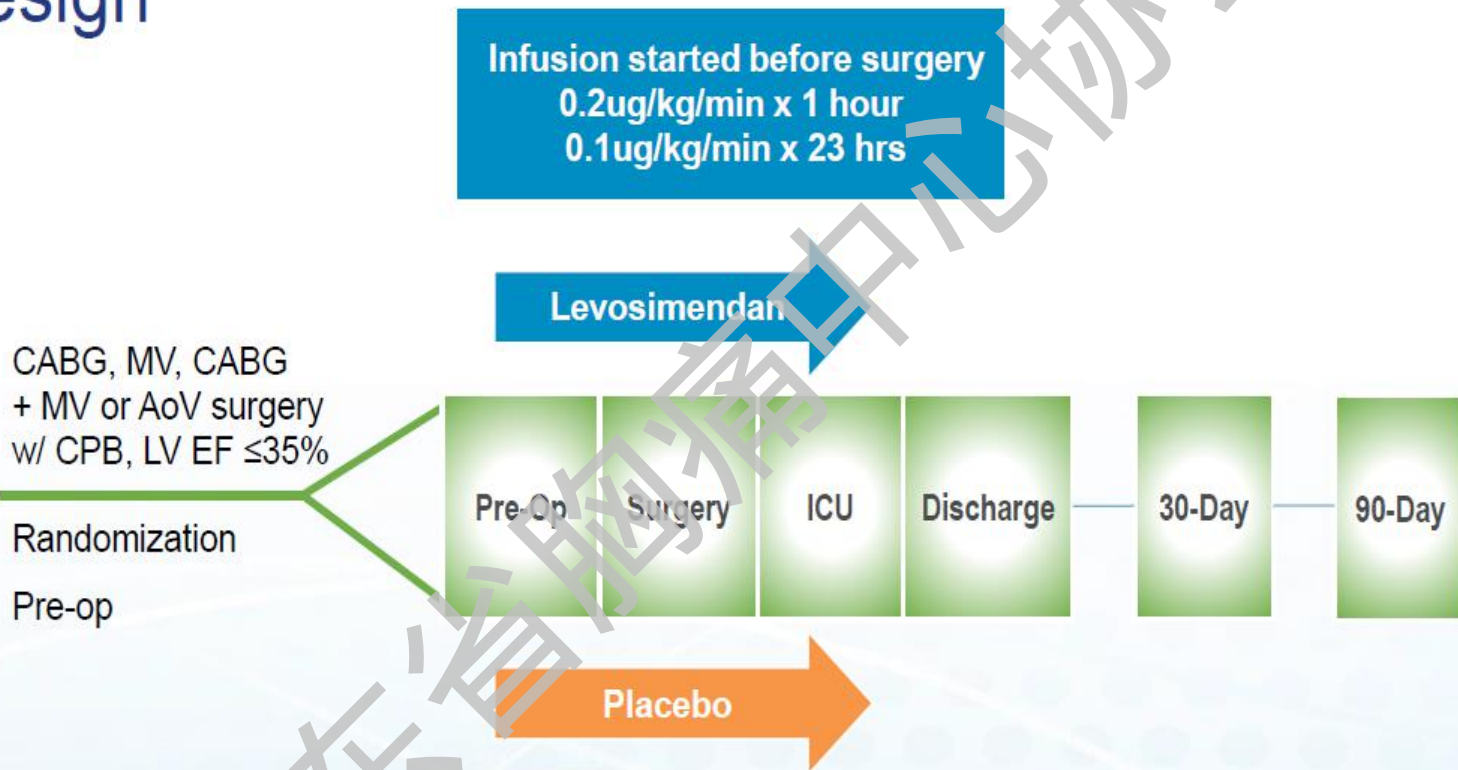
FROM THOUGHT LEADERSHIP
TO CLINICAL PRACTICE

TENAX
THERAPEUTICS



(三) LEVO-CTS研究

Design



(三) LEVO-CTS研究

Cardiac Output

Cardiac Index (mls/min/m²) Mean (SD)

Levosimendan (n=359) 2.86 (0.61)

Placebo (n=340) 2.68 (0.65)

p<0.0001

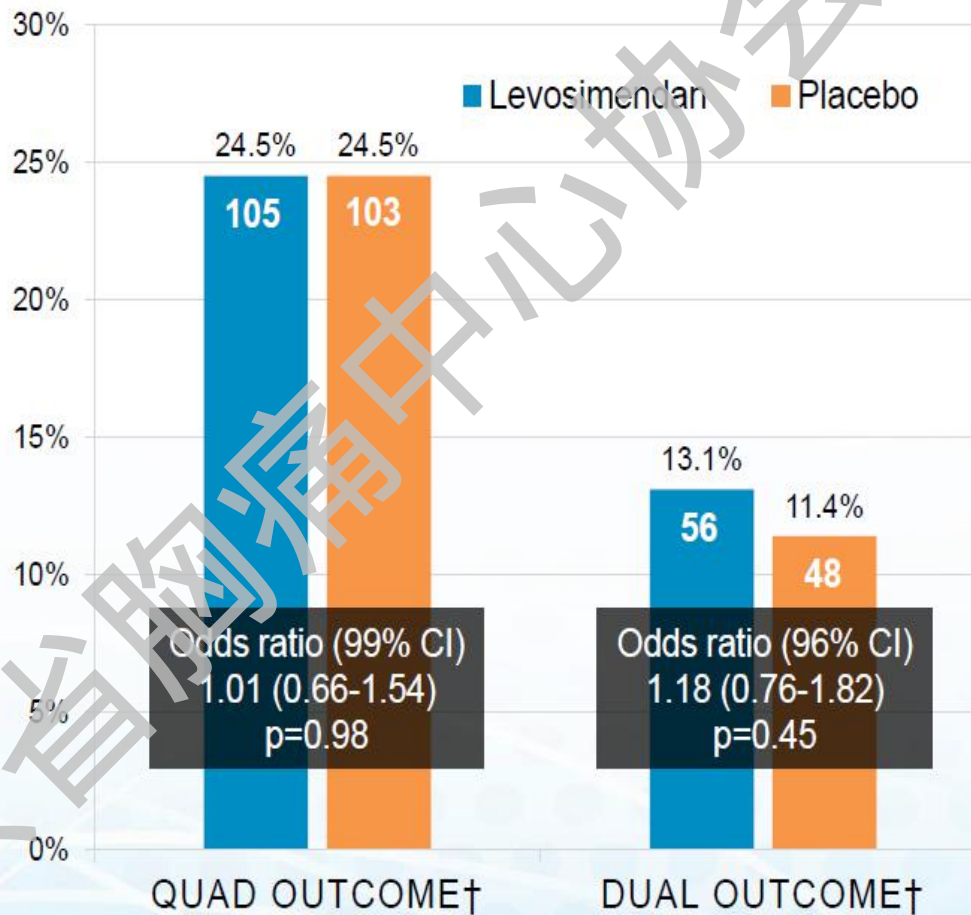
(三) LEVO-CTS研究

Co-Primary Outcomes

Quad Outcome = death, dialysis, MI or mechanical assist device use

Dual Outcome = death or mechanical assist device use

LEVO CTS
levosimendan in cardio thoracic surgery



†Adjusted for covariates: type of surgery, LVEF, age, sex

(三) LEVO-CTS研究解读

◆ **LEVO-CTS**研究结果显示：对体外循环下行心脏外科手术的有左室射血分数降低（ $\leq 35\%$ ）患者提前应用左西孟旦治疗并未能降低患者的主要终点事件（包括30天内死亡或使用肾脏替代治疗、围术期心肌梗死、5天内使用机械辅助装置），但可增加患者心脏排量（心脏指数CI），减少术后低心排综合征的发生和减少其它正性肌力药物的使用。

◆ 研究结果再次提示（1）左西孟旦对存在围手术期低心排综合征患者是安全有效的正性肌力药；（2）正性肌力药物在有低血压和/或低灌注的心力衰竭患者是有效安全的治疗方法，但左室射血分数降低（ $\leq 35\%$ ）患者提前预防应用左西孟旦并不能带来降低患者的主要终点事件的获益。

(四) 心衰房颤的射频消融治疗获益

Coverage from the
European Society of Cardiology (ESC) Congress 2017

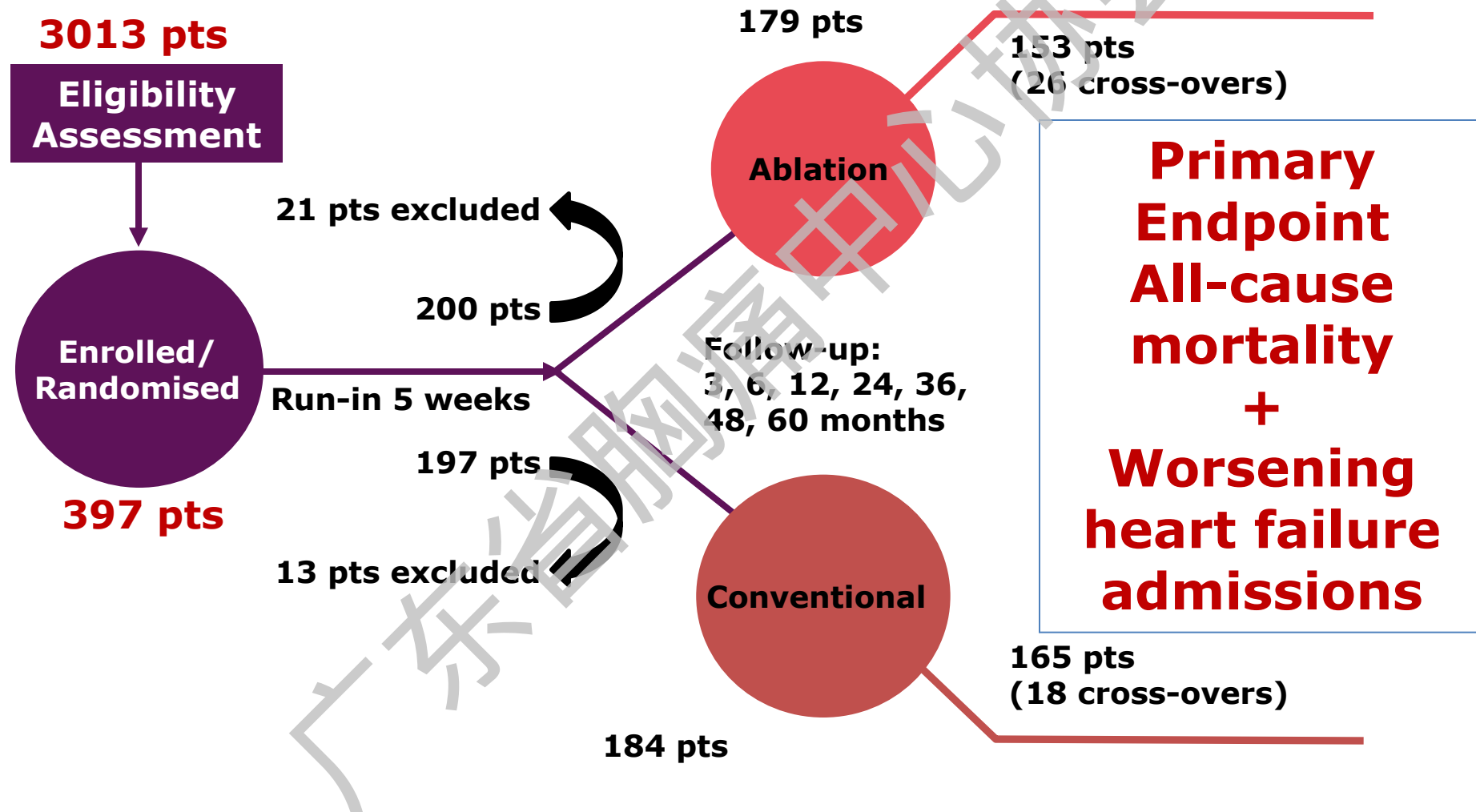
CASTLE-AF: Ablation Reduces Mortality in LV Dysfunction, AF

Susan Jeffrey
August 29, 2017

CASTLE-AF: Primary and Secondary End Points

End point	Hazard ratio	95% CI	P
All-cause mortality and worsening heart failure	0.62	0.43–0.87	0.007
All-cause mortality	0.53	0.32–0.86	0.011
Worsening heart-failure admissions	0.56	0.37–0.83	0.0004
Cardiovascular mortality	0.49	0.29–0.84	0.008
Cardiovascular hospitalization	0.72	0.52–0.99	0.041

CASTLE-AF



CASTLE-AF

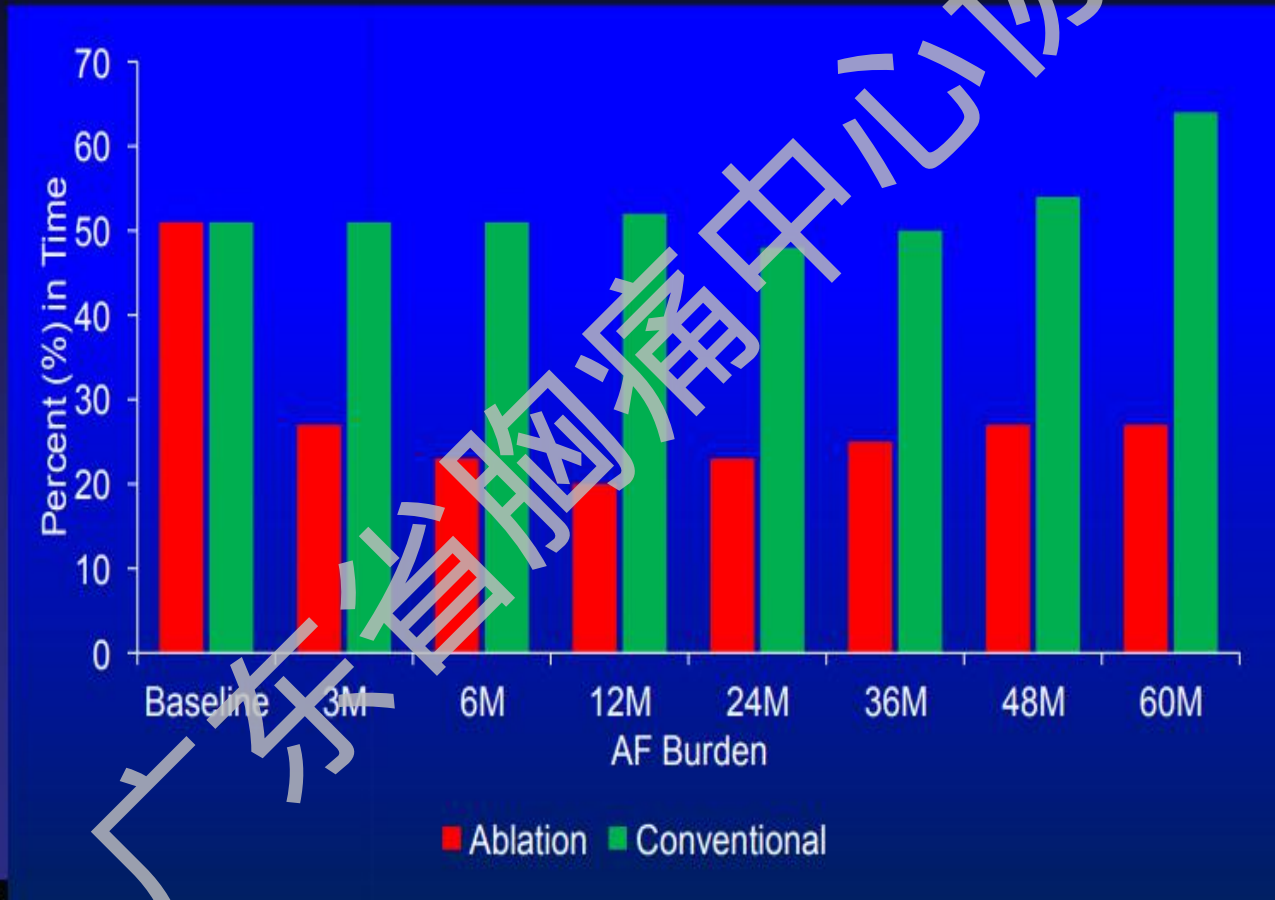
Inclusion Criteria



- Symptomatic paroxysmal or persistent AF
- Failure or intolerance to ≥ 1 or unwillingness to take AAD
- LVEF $\leq 35\%$
- NYHA class $\geq II$
- ICD/CRT-D with Home Monitoring capabilities already implanted due to primary or secondary prevention

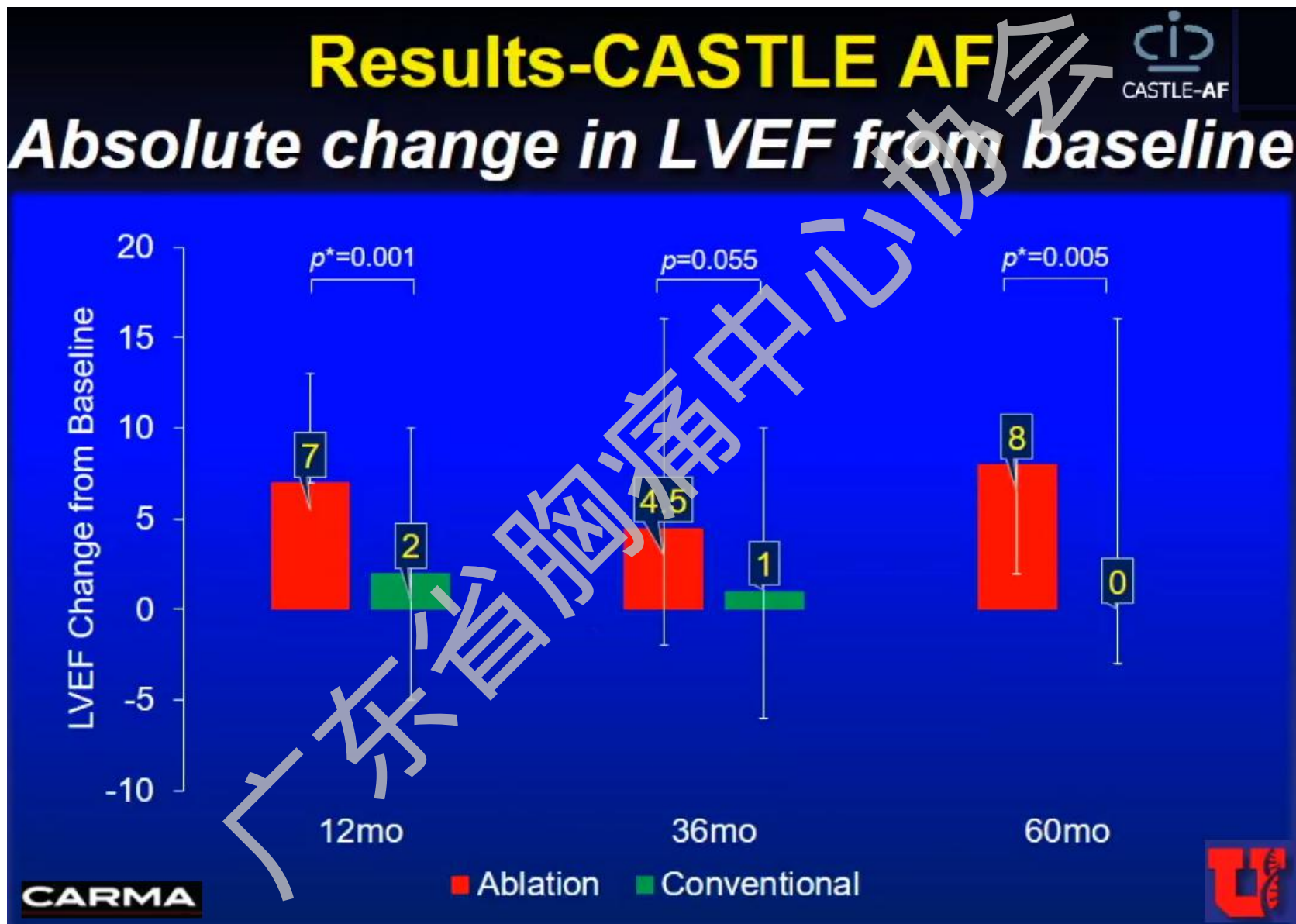
Results-CASTLE AF

AF Burden Derived from Memory of Implanted Devices



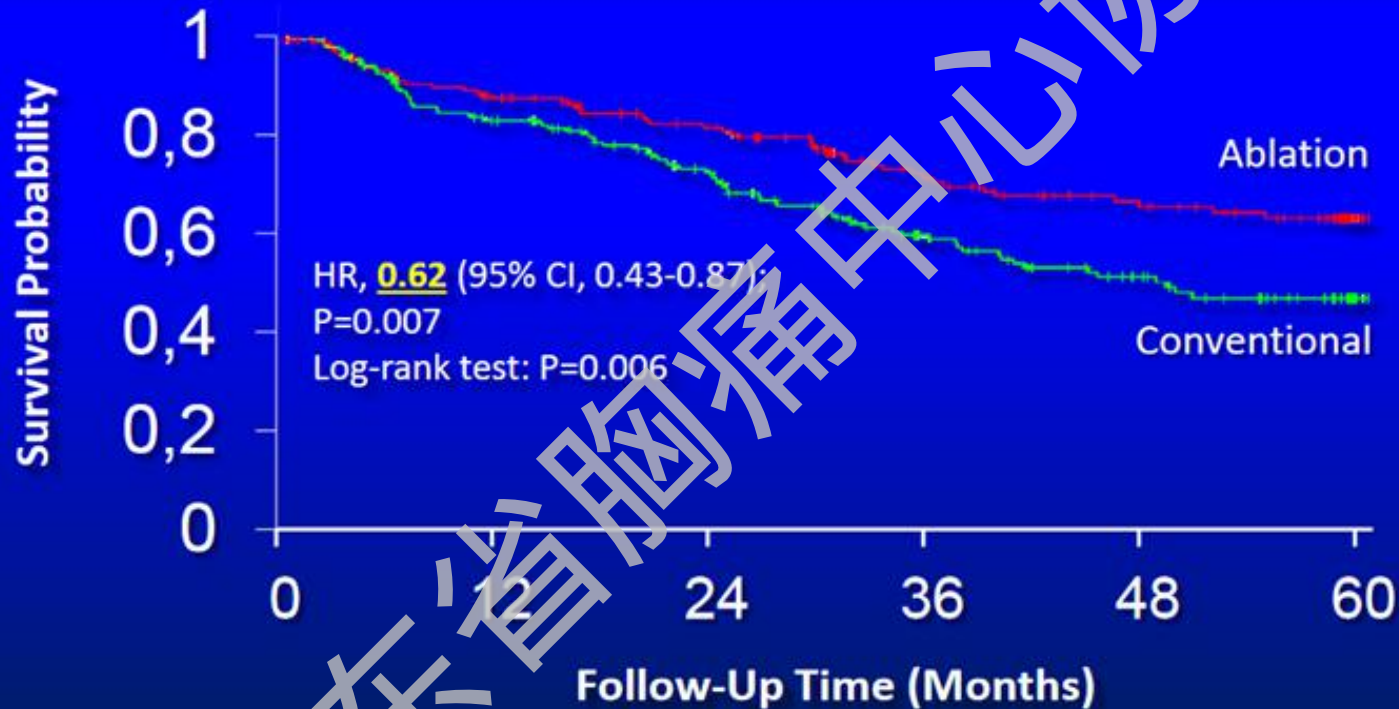
CARMA





Results-CASTLE AF

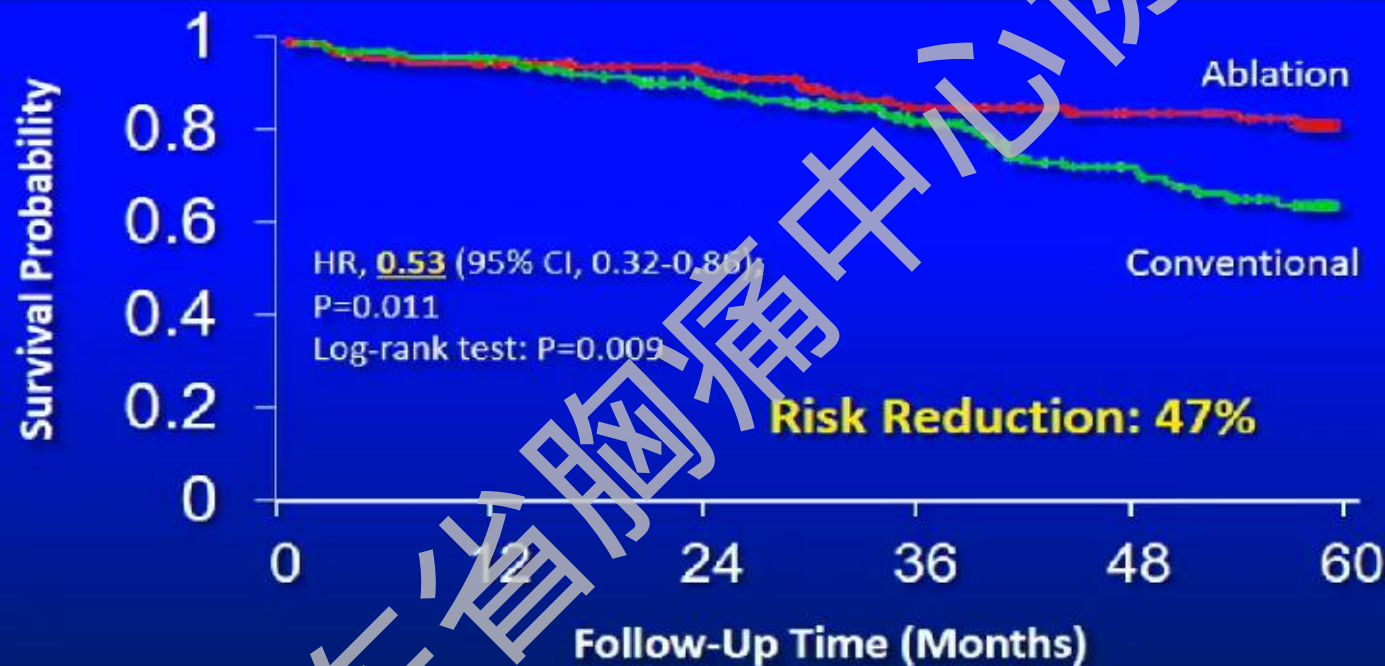
Primary Composite Endpoint



Patients at Risk

Ablation	179	141	114	76	58	22
Conventional	184	145	111	70	48	12

Results-CASTLE AF All-Cause Mortality

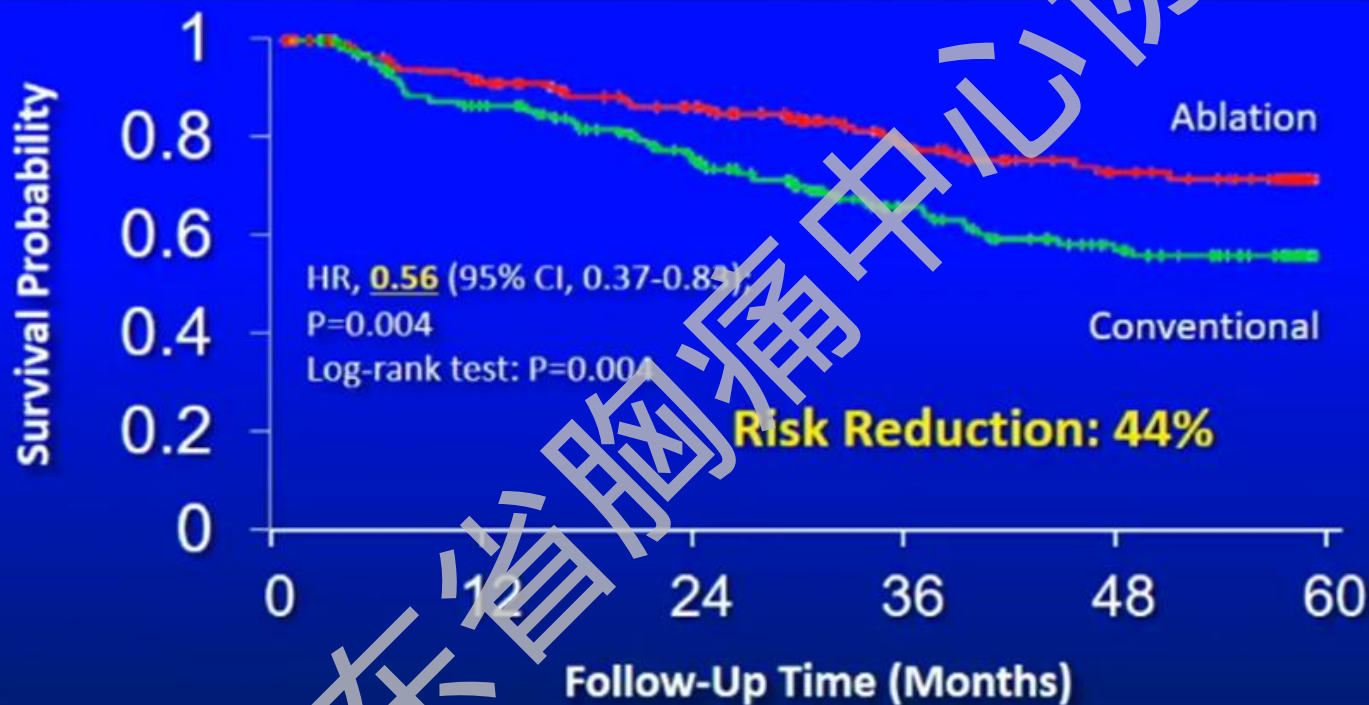


Patients at Risk

Ablation	179	154	130	94	71	27
Conventional	184	168	138	97	63	19

Results-CASTLE AF

Worsening Heart Failure Admissions



Patients at Risk

Ablation	179	141	114	76	58	22
Conventional	184	145	111	70	48	12

CARMA

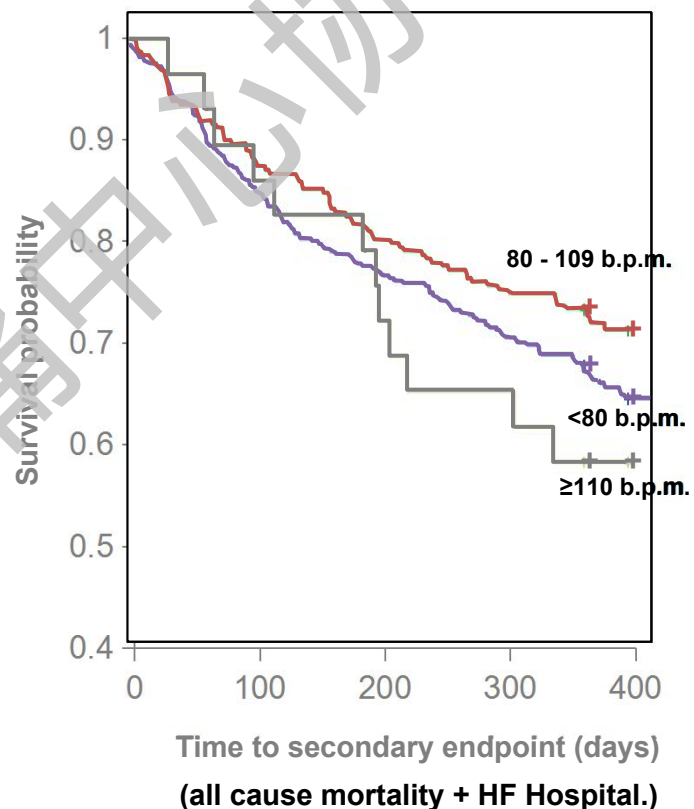
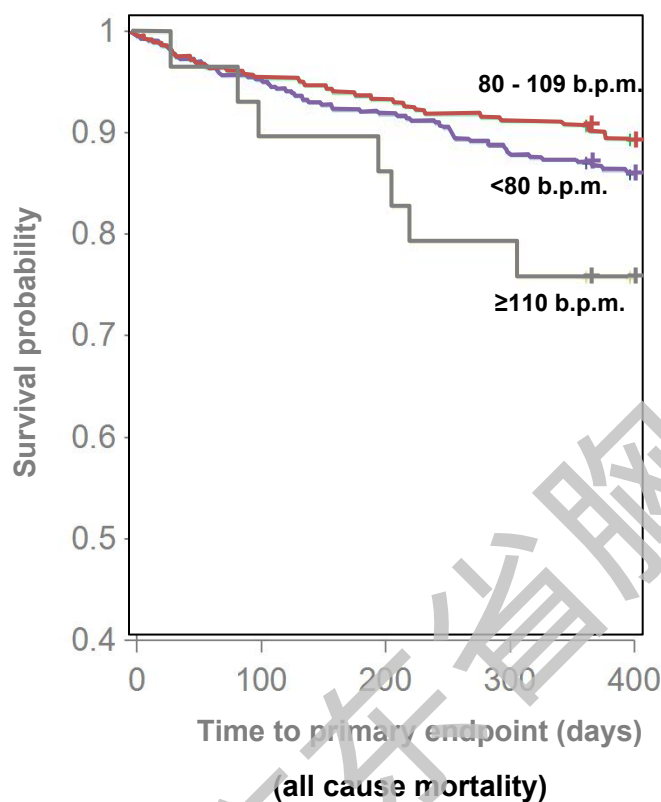


(五)

BETA BLOCKERS, HEART RATE AND ATRIAL FIBRILLATION (B受体阻滞剂与房颤)



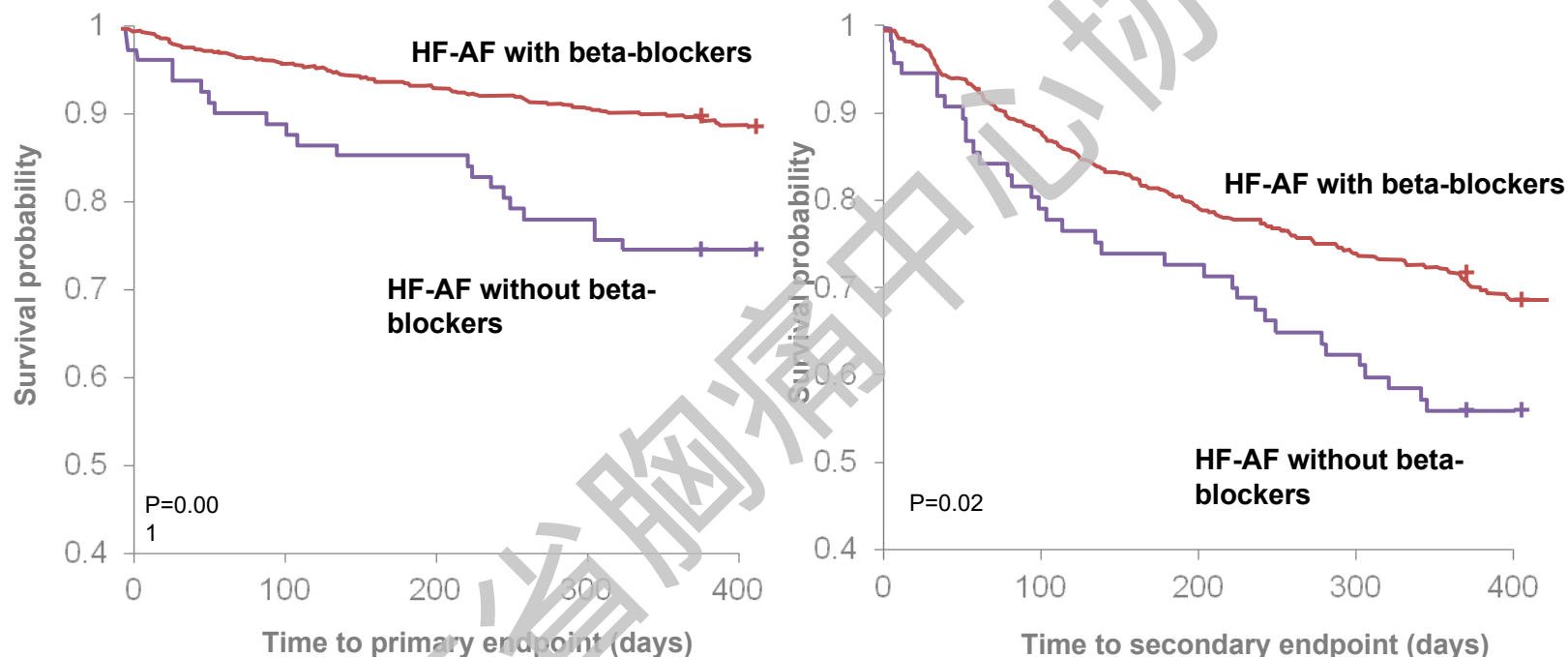
DO BETA-BLOCKERS IMPROVE ONE-YEAR SURVIVAL IN HEART FAILURE PATIENTS WITH ATRIAL FIBRILLATION? – RESULTS FROM THE ESC-HF REGISTRY



b.p.m. – beats per minute

K. Ozieranski (Warsaw, PL) 4899

DO BETA-BLOCKERS IMPROVE ONE-YEAR SURVIVAL IN HEART FAILURE PATIENTS WITH ATRIAL FIBRILLATION? – RESULTS FROM THE ESC-HF REGISTRY



Beta-blockers	0.52 (0.31-0.89)	0.02	0.74 (0.49-1.11)	0.14
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AF – atrial fibrillation, HF – heart failure

K. Ozieranski (Warsaw, PL) 4899

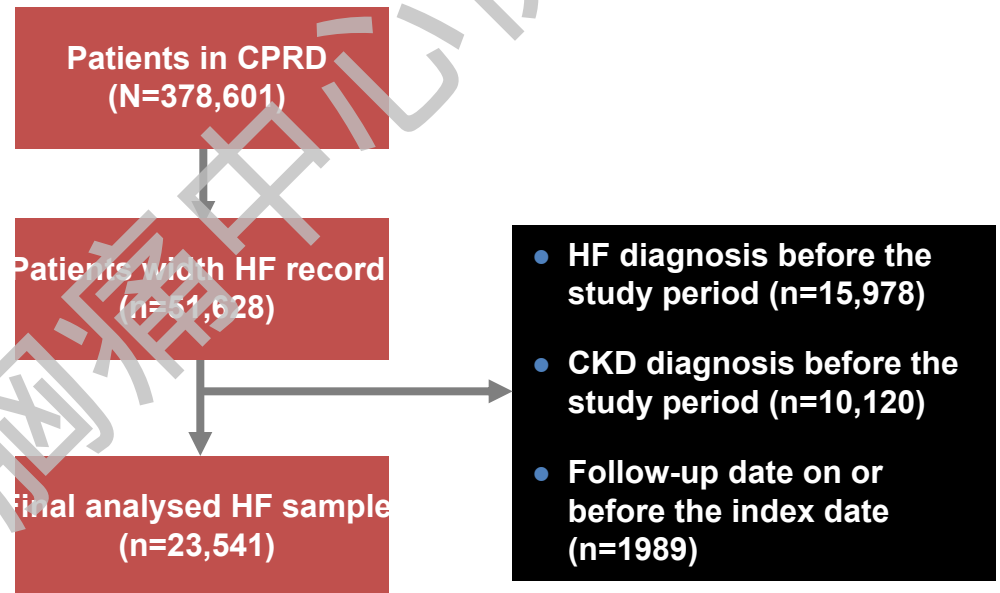
(六)

POTASSIUM (血钾)

ASSOCIATION BETWEEN SERUM POTASSIUM AND CLINICAL OUTCOMES IN UK PATIENTS WITH HEART FAILURE

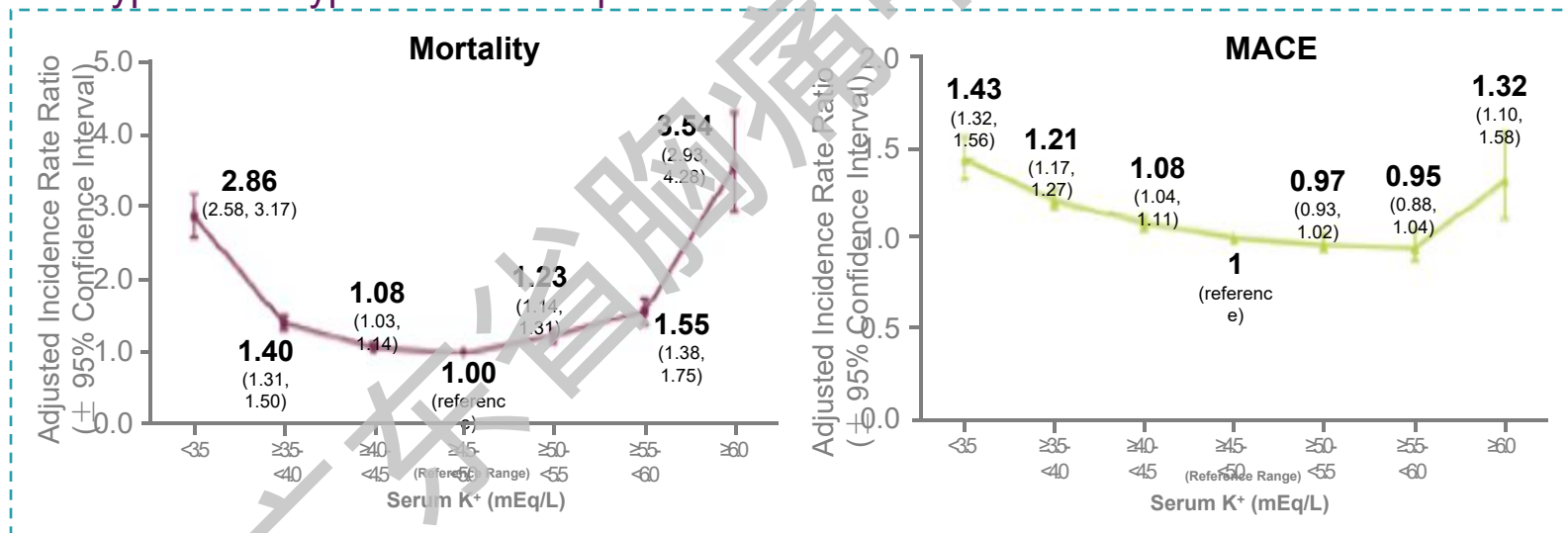
- Primary care data for 2006-2015 extracted from the Clinical Practice Research Datalink (CPRD)

→ Electronic database of anonymous longitudinal records for >11m patients from 674 primary care practices across UK



ASSOCIATION BETWEEN SERUM POTASSIUM AND CLINICAL OUTCOMES IN UK PATIENTS WITH HEART FAILURE

- This real-world analysis indicates U-shaped patterns of association between K⁺ and incidence of mortality and MACE
 - ➔ K⁺ levels outside the normal range were associated with greater risks of mortality and MACE
 - ➔ Results support the need for close monitoring of K⁺ and prompt treatment of hypo- and hyperkalaemia in patients with HF



Risk of mortality is 3.5 times greater for patients with K⁺ ≥6 mEq/L compared to those with normokalaemia



谢谢!

广东省胸科中心协作