争分夺秒优化流程
STEMI患者再灌注策略选择

首都医科大学附属北京朝阳医院心脏中心

王乐丰

无论何种再灌注方式，都应强调：

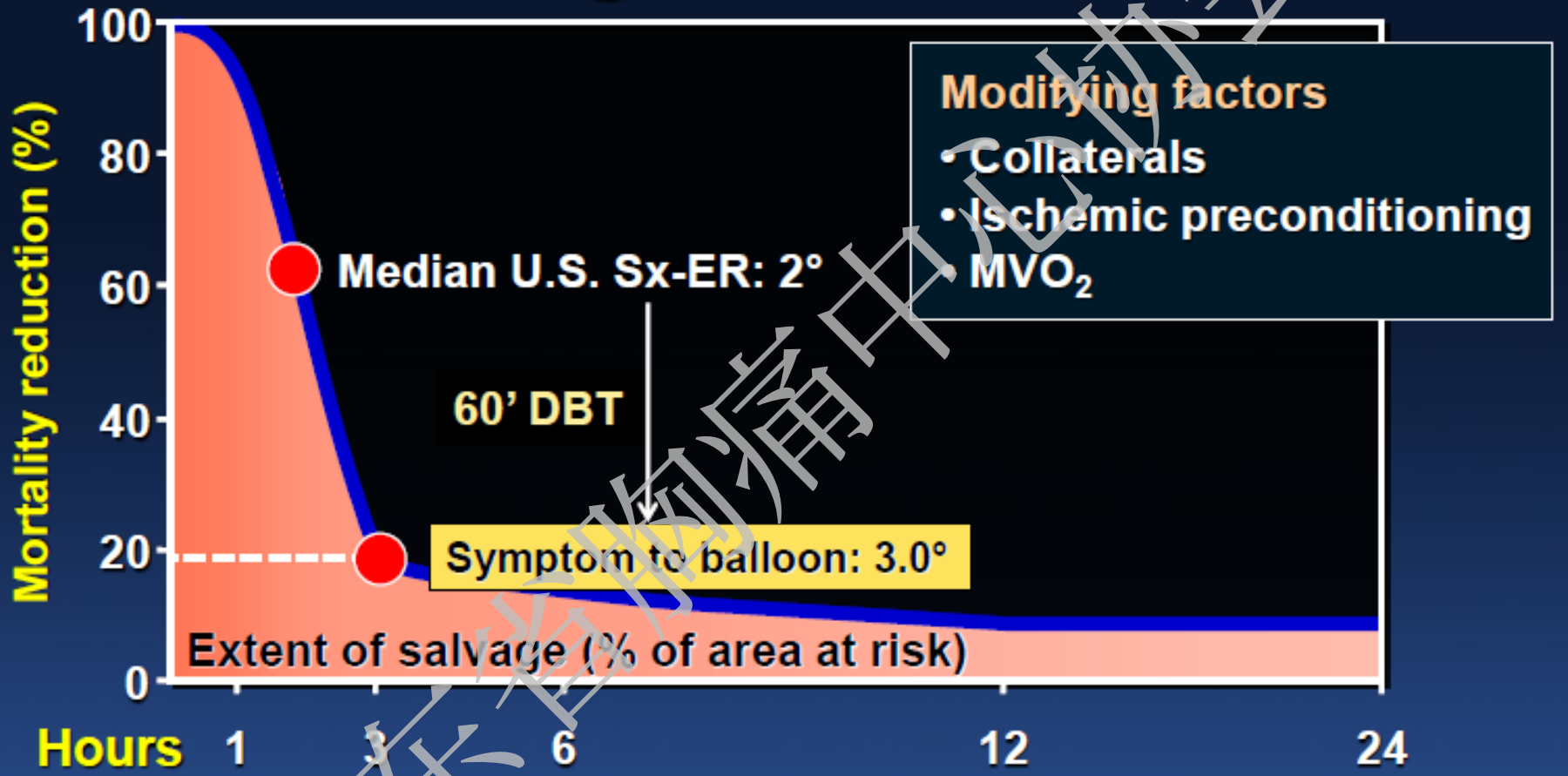
时间就是心肌，

时间就是生命

Time Dependent

Wavefront of Necrosis

Relationship Between Myocardial Salvage and Survival



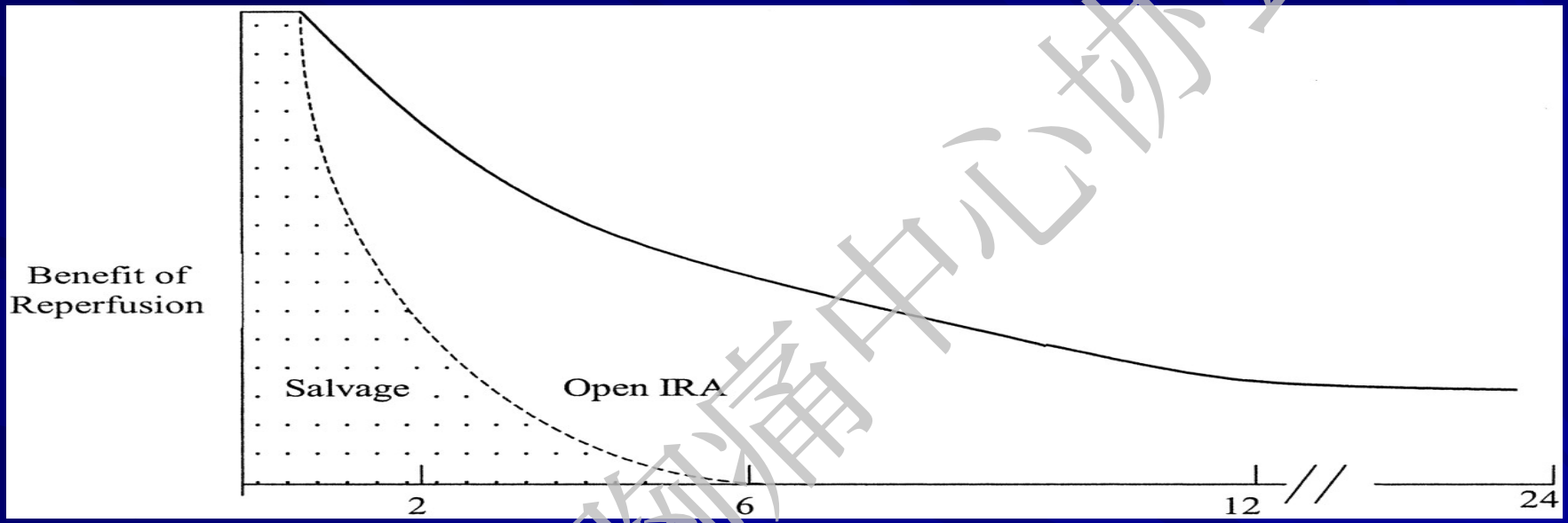
Treatment objectives

Time to treatment is critical

Opening the IRA (PCI > lysis)

Gersh, Stone, Holmes. *JAMA* 2005

时间对再灌注抢救的意义



0 – 1 hrs　预防心肌梗死，使梗死“流产”
1 – 3 hrs　大量抢救心肌，获益 PCI=溶栓
3 – 6 hrs　心肌挽救降低，溶栓效果开始不如急诊PCI
6 – 12 hrs　基本不挽救心肌, 但可防止梗死扩大
>12hrs　如有症状也可PCI干预，可以改善左室重构

第一部分 ECG法

一、患者基线资料分析

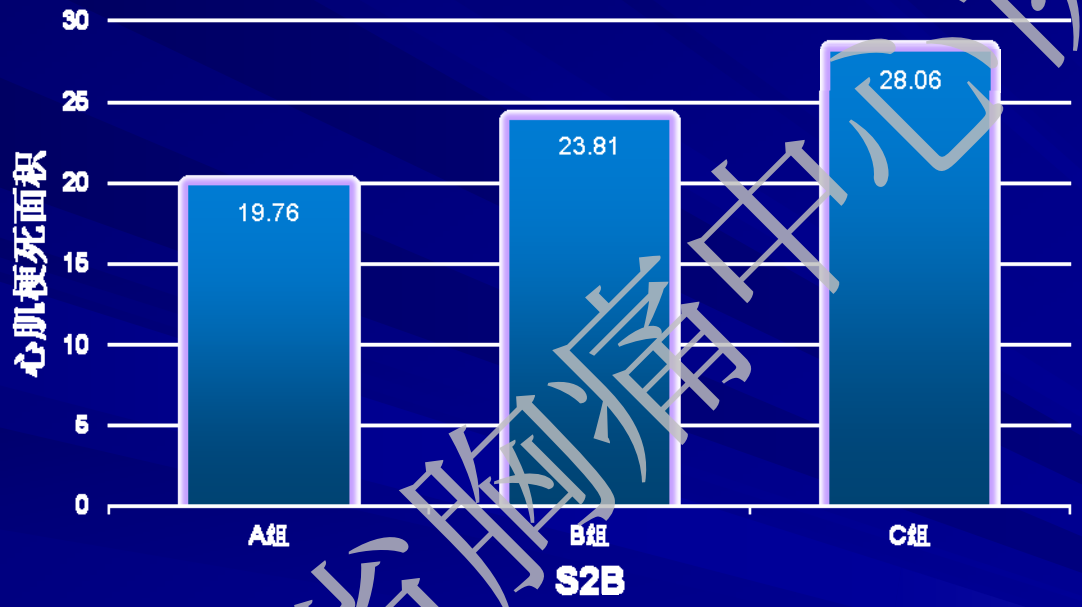
- 纳入2015年3月至2015年12月共计124人，A组：≤3小时（n=37）；B组：>3-6小时（n=50）；C组：>6小时（n=37）。
- 三组临床基本资料、冠脉造影结果、药物治疗无统计学差异。

表1 A、B、C三组基本临床料资分析

临床基本资料	A组 (n=37)	B组 (n=50)	C组 (n=37)	P
年龄（岁）	57±11	58±14	56±16	0.781
男性（%）	27（73.0）	45（90.0）	31（83.3）	0.111
高血压（%）	20（54.1）	25（50.0）	19（51.4）	0.932
高脂血症（%）	31（83.3）	40（80.0）	32（86.5）	0.721
糖尿病（%）	11（29.7）	18（36.0）	5（13.5）	0.063
吸烟史（%）	18（48.6）	33（66.0）	20（54.1）	0.242
冠心病家族史（%）	9（24.3）	10（20.0）	4（10.8）	0.308
梗死前心绞痛（%）	6（16.2）	9（18.0）	7（18.9）	0.238

第一部分 ECG法

三、三组心肌梗死面积比较

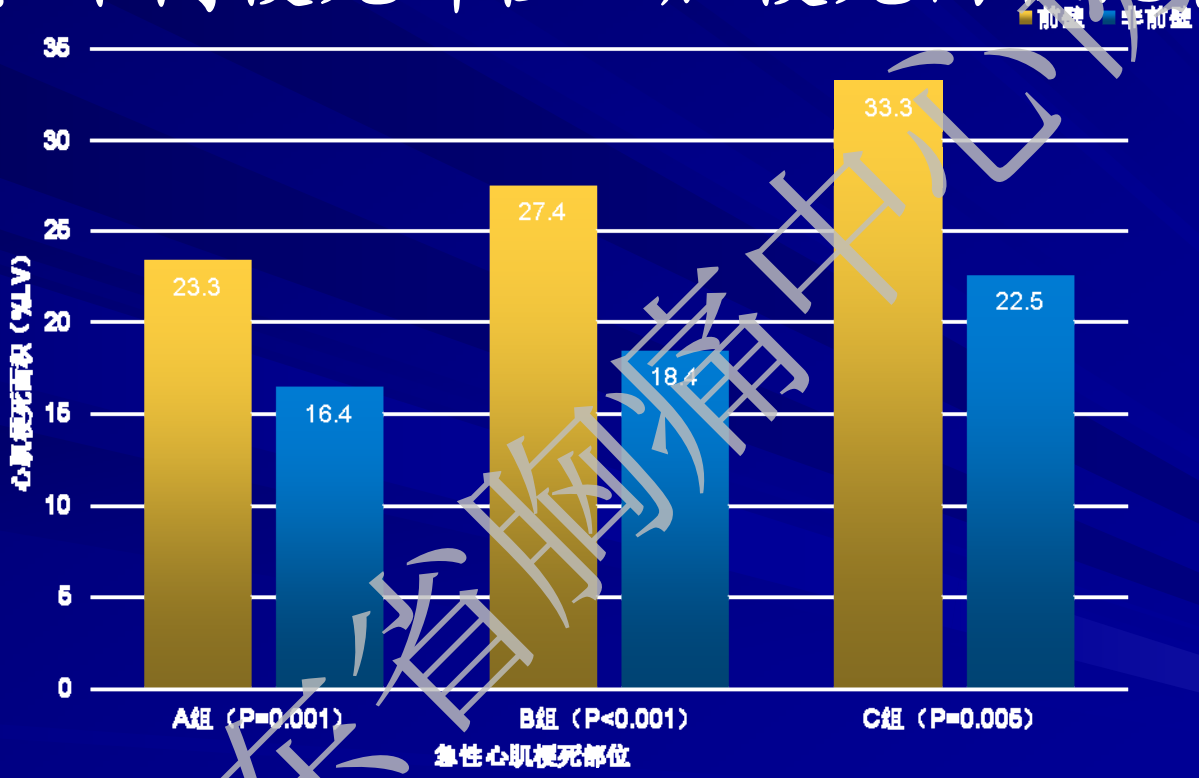


S2B时间延长，心肌梗死面积增加，差异有统计学意义，

STEMI患者MIS与S2B具有相关性（ r=0.48，P<0.001）

第一部分 ECG法

四、不同梗死部位心肌梗死面积比较



前壁较非前壁STEMI患者心肌梗死面积大

急性 STEMI 患者心肌梗死面积具有时间性关系，相关系数 r=0.566，P<0.001（图 3）。在发病 3-6 小时内，前壁心肌梗死患者较非前壁心肌梗死患者心肌坏死数量多：B 组（34±9.6）%vs（10±9.2）%，P=0.03。

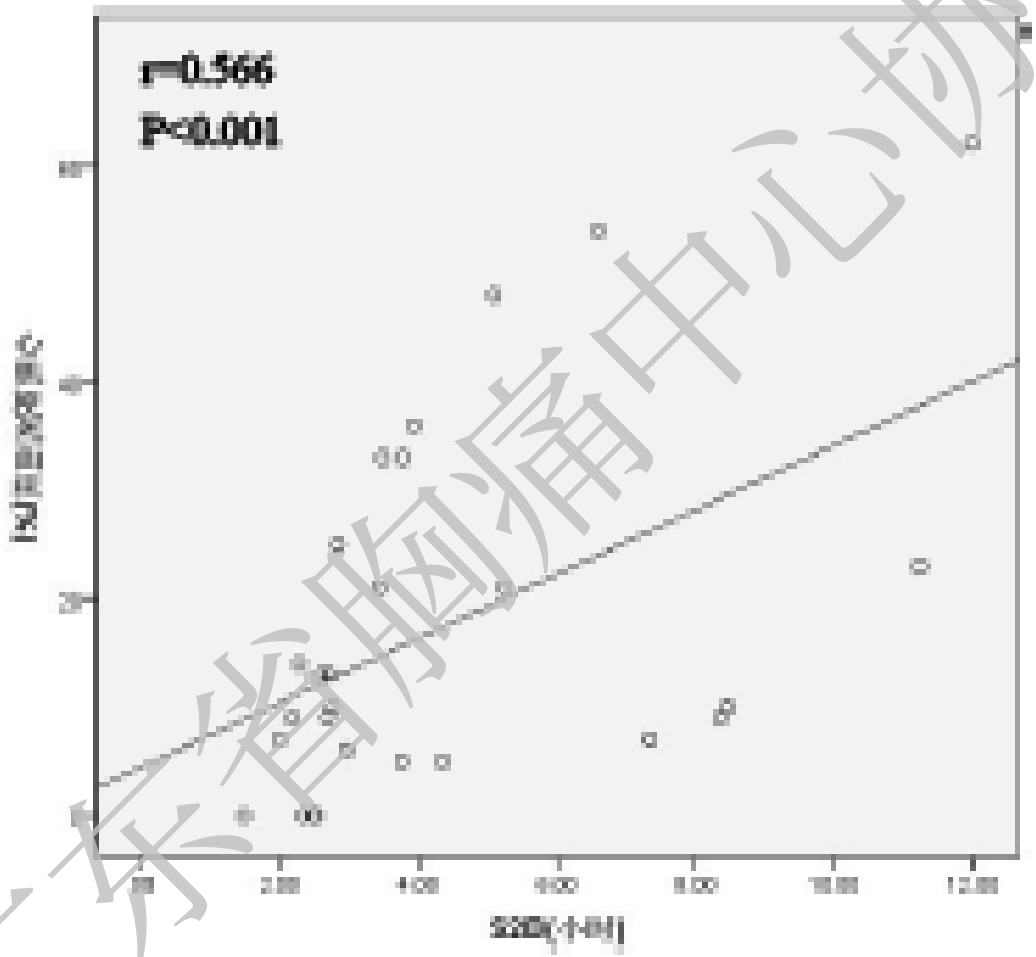


图 3：急性 STEMI 再灌注时间与心肌梗死面积线性相关

梗死范围和预后

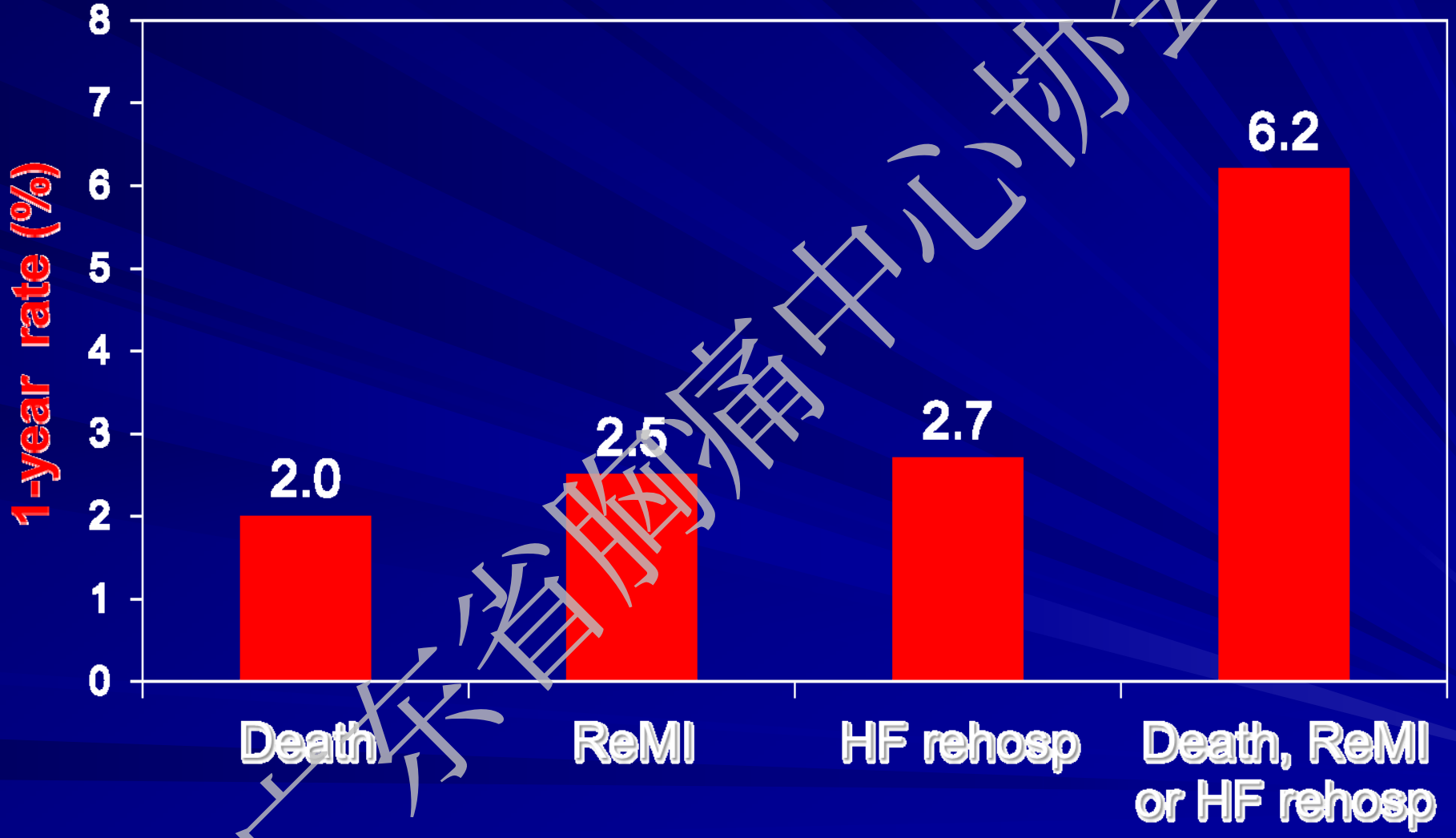
Included Trials

Trials	Years enrolled	N	Test	Days to test	FU duration
EMERALD	2002-2003	415	SPECT	10 [7, 13]	183 [179, 188]
AMIHOT-II	2005-2007	287	SPECT	16 [14, 18]	366 [353, 374]
IMMEDIATE	2006-2011	42	SPECT	33.5 [32, 35]	365 [365, 365]
APEX-AMI	2004-2006	94	MRI	4 [3, 5]	365 [184, 367]
LIPSIA-ABCIX	2006	132	MRI	2 [2, 3]	188 [184, 194]
LIPSIA-N-ACC	2006-2008	212	MRI	3 [2, 4]	190 [185, 245.5]
LIPSIA-STEMI	2006-2009	135	MRI	3 [2, 4]	192 [172, 257]
CRISP AMI	2009-2011	234	MRI	14 [10, 21]	183 [181, 189]
AIDA STEMI	2008-2011	522	MRI	3 [2, 4]	380 [368, 400]
INFUSE-AMI	2009-2011	303	MRI	6 [4, 30]	365 [351, 377]
Total		2,376	SPECT: 744 (31.3%) MRI: 1,632 (68.7%)	5 [3, 14]	340 [185, 370.5]

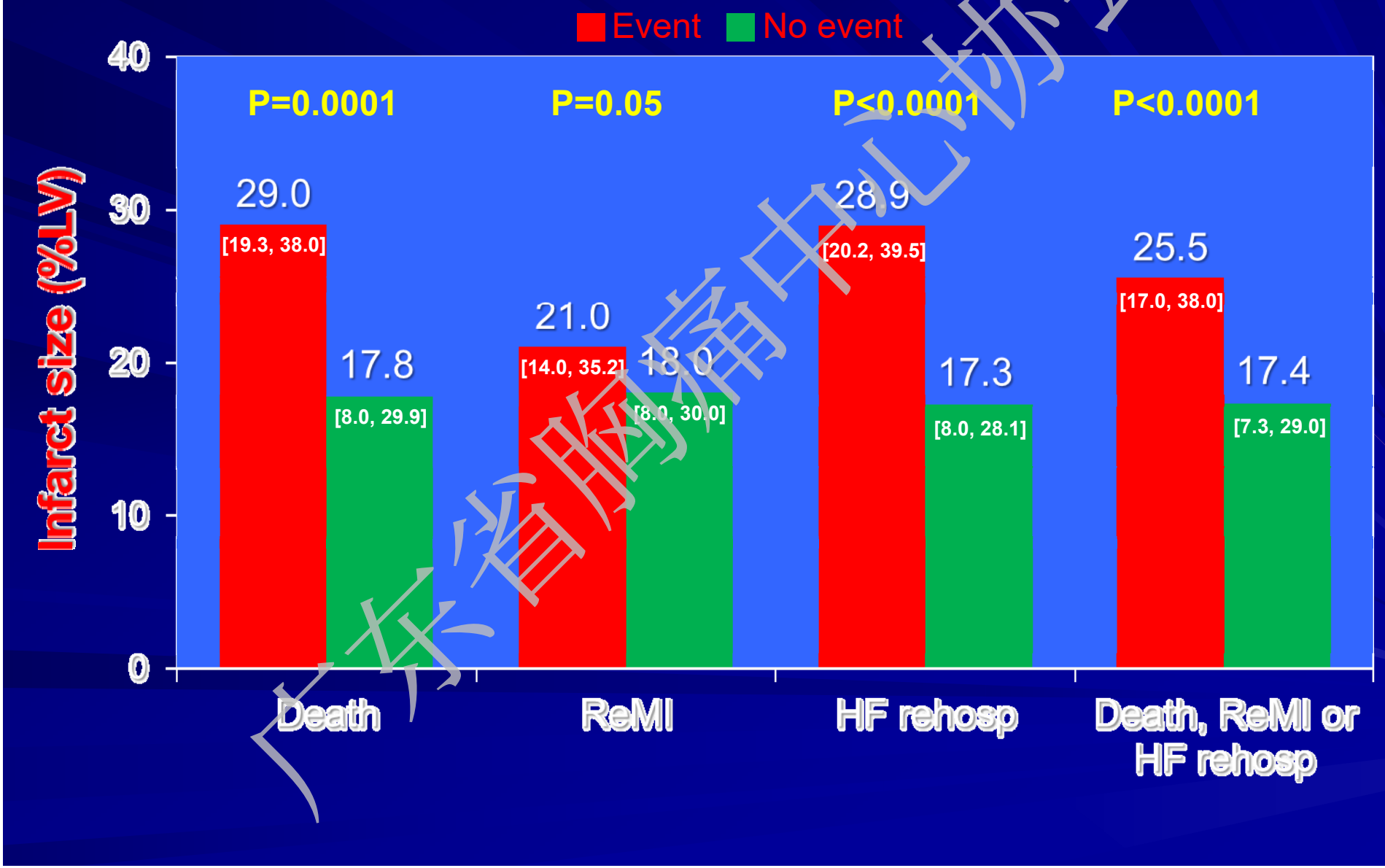
Median (IQR) Infarct Size (%LV mass)

Test type	N	Days to test	Infarct size
All	2,376	5.0 [3.0, 14.0]	18.0 [8.0, 30.0]
- SPECT	744	13.0 [8.5, 17.0]	14.0 [3.0, 30.0]
- MRI	1,632	4.0 [2.0, 6.0]	19.1 [10.2, 29.9]

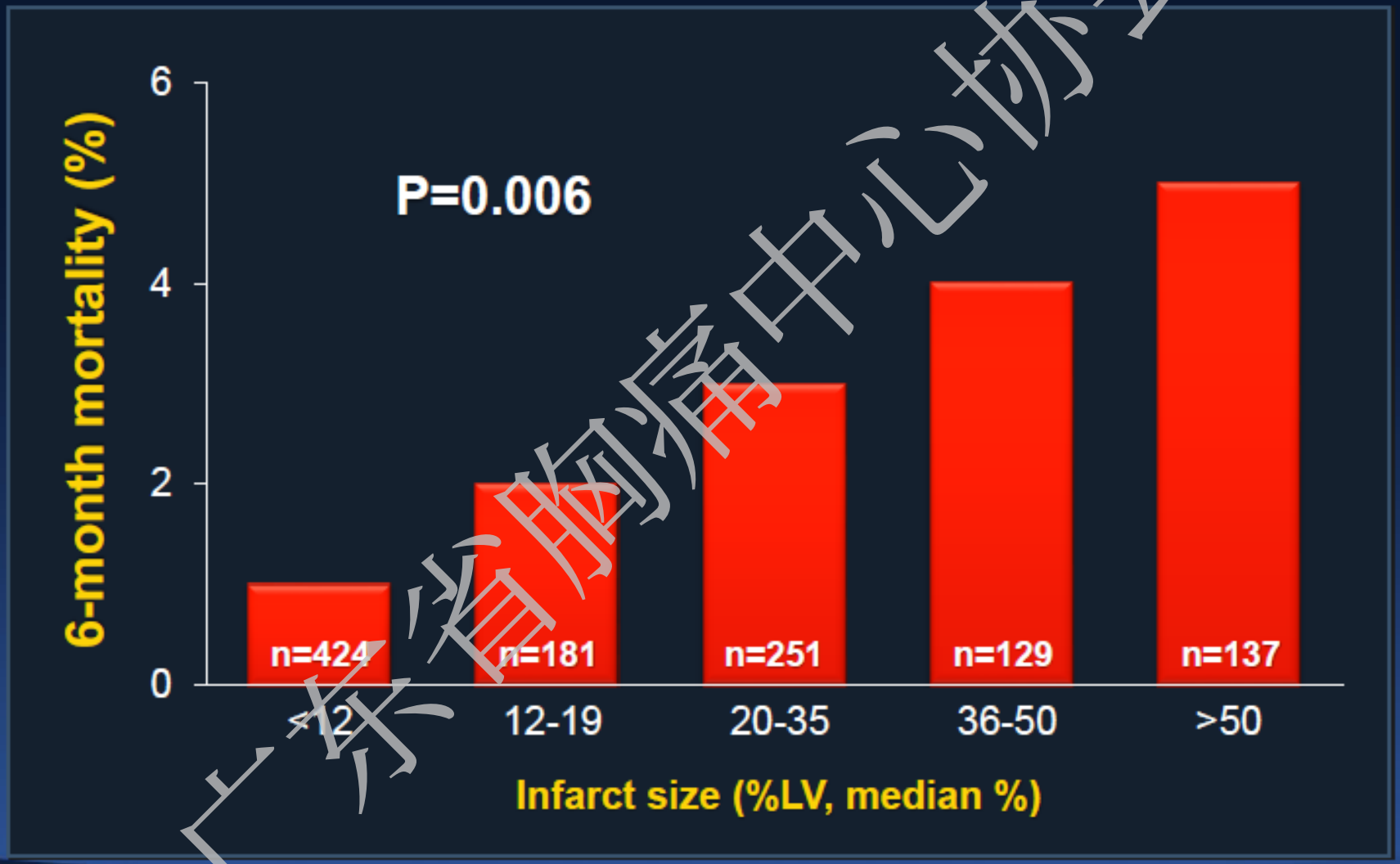
1-year Event Rates (N=2,376)



Relationship Between Infarct Size and Outcomes (from time of randomization)



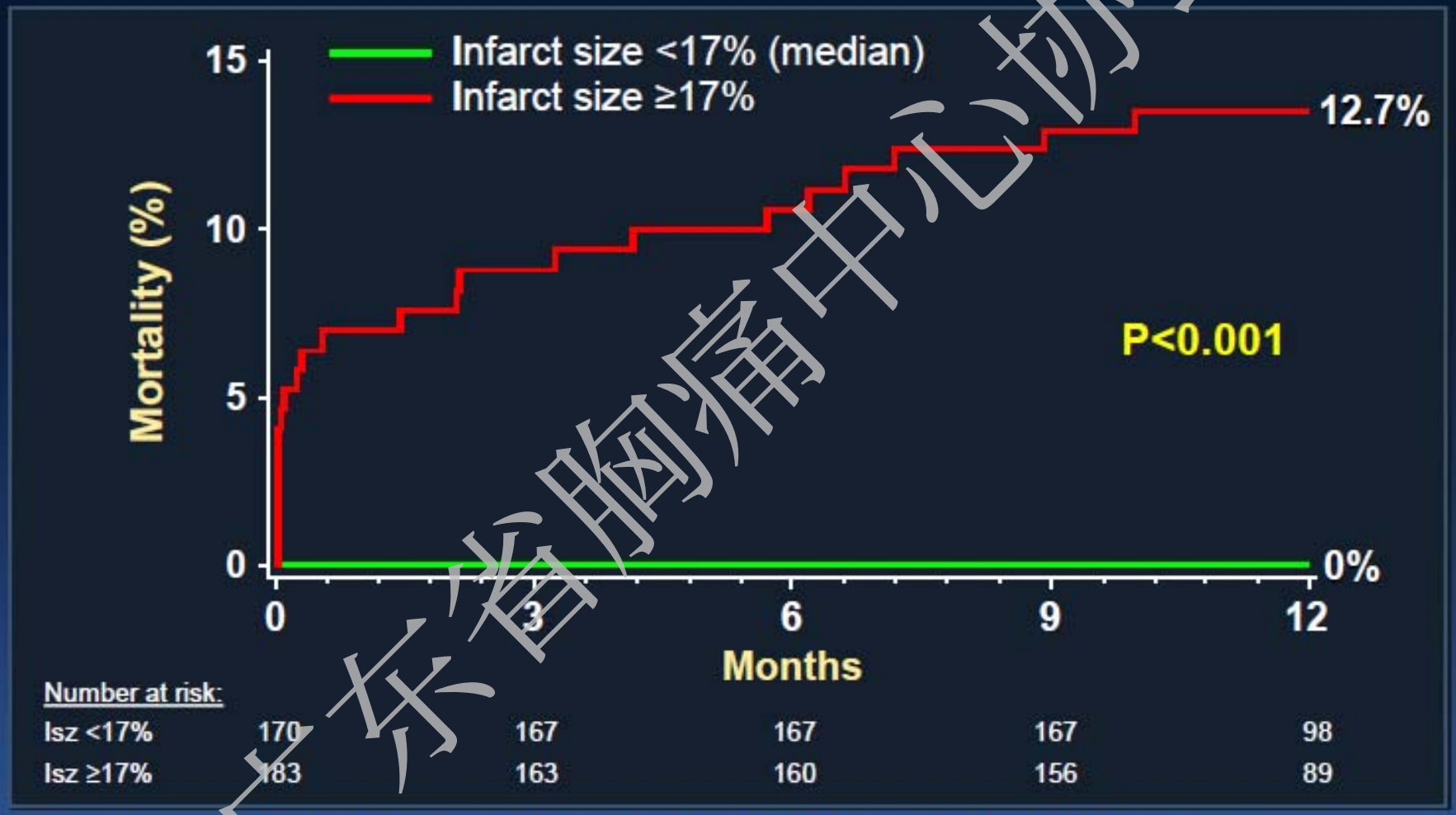
CORE: Relationship between infarct size and 6 month mortality (n=1122)



Burns RJ et al. J Am Coll Cardiol 2002;39:30-6

INFUSE-AMI: Impact of infarct size

Death or severe heart failure events* at 1 year

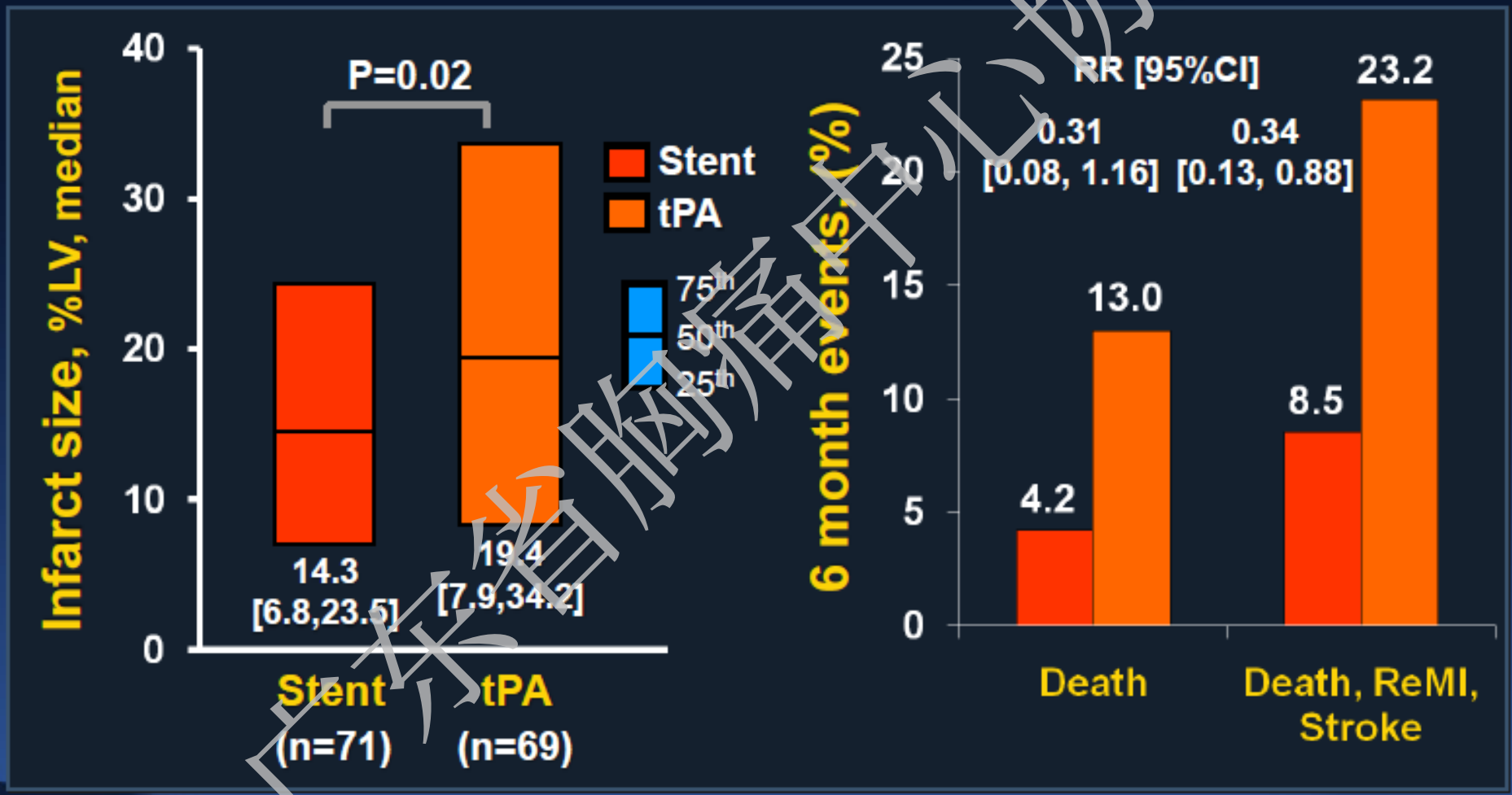


*New onset severe heart failure or rehospitalization for heart failure

Stone GW. TCT 2013

Reduction in Infarct Size Correlates with Improved Survival

RCT of PCI vs. tPA (n=140)



Schomig A et al. NEJM 2000;343:385-91

时间

如何争分夺秒

广东省胸痛中心协会

2014年ESC的推荐

- 对于12小时以内的STEMI患者或新发左束支传导阻滞的患者均应再灌注治疗（Ⅰ/A）
- STEMI引起心源性休克或急性左心衰发作，无论发病时间长短，均应急诊PCI治疗（Ⅰ/B）
- 即使发病大于12小时，疼痛消失或心电图ST段回落，如果存在持续性缺血的证据或出现恶性心律失常时仍应急诊PCI治疗（Ⅰ/C）
- 发病12~48小时内的患者应考虑急诊PCI再灌注治疗（Ⅱa/B）

2014年ESC的推荐

- 所有溶栓患者均应在24小时内转到能行PCI的中心（Ⅰ/A）
- 溶栓成功后24小时行冠脉造影，以便行血运重建（Ⅰ/A）
- 溶栓失败后应紧急补救性PCI（Ⅰ/A）
- 溶栓成功稳定患者的最佳造影时机为3~24小时（Ⅱa/A）

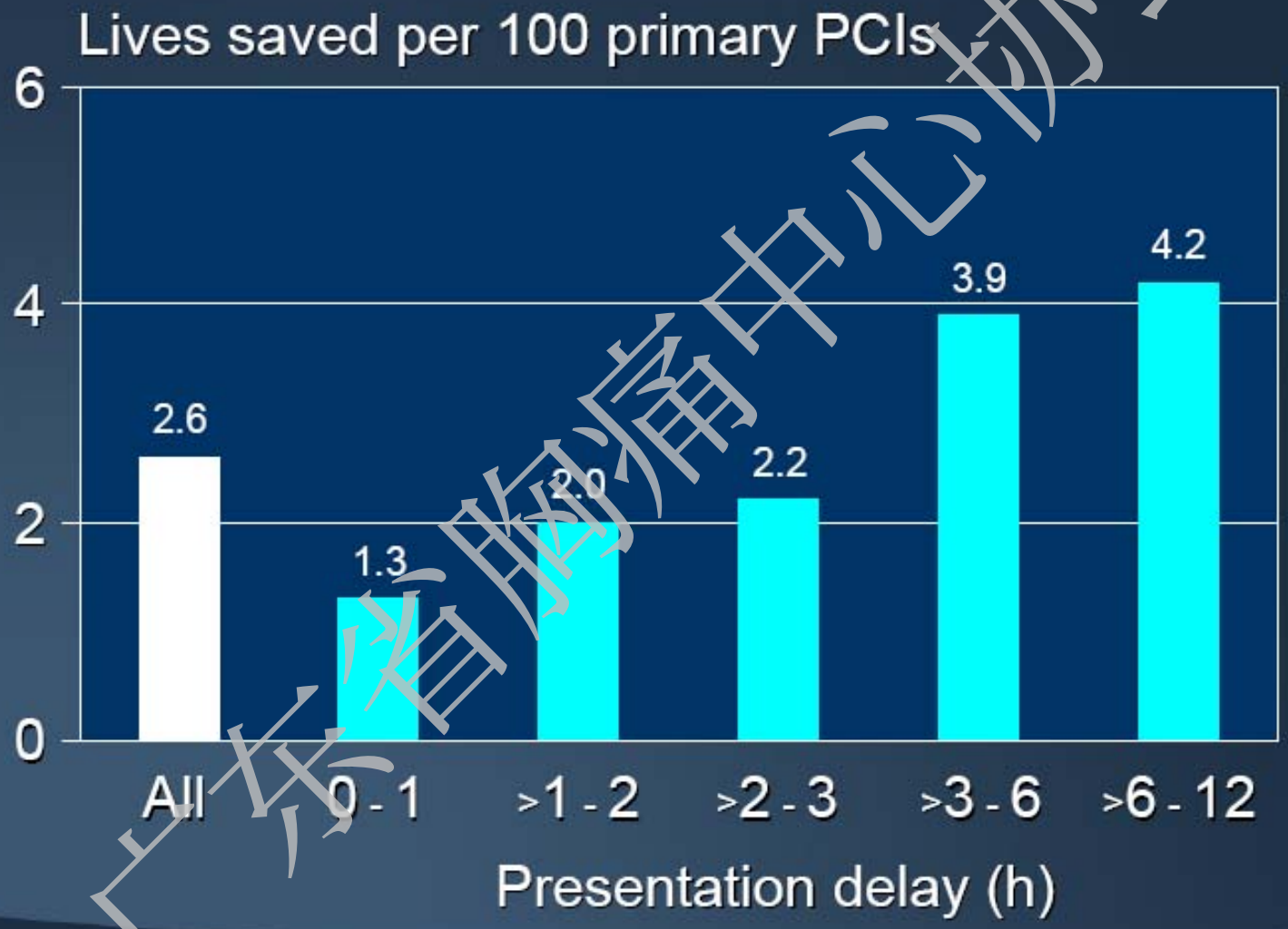
D 2 B 时间和一年死亡率的关系

- ≤2小时就诊： D to B时间＜1.5h 1.9%
  D to B时间≥1.5h 3.9%
- ≥2小时就诊： D to B时间＜1.5h 5.1%
  D toB时间≥ 1.5h 4.8%

Brodie JACC 2003

20 YEARS OF INNOVATION TCT 2008

Meta-analysis (N=7,000)

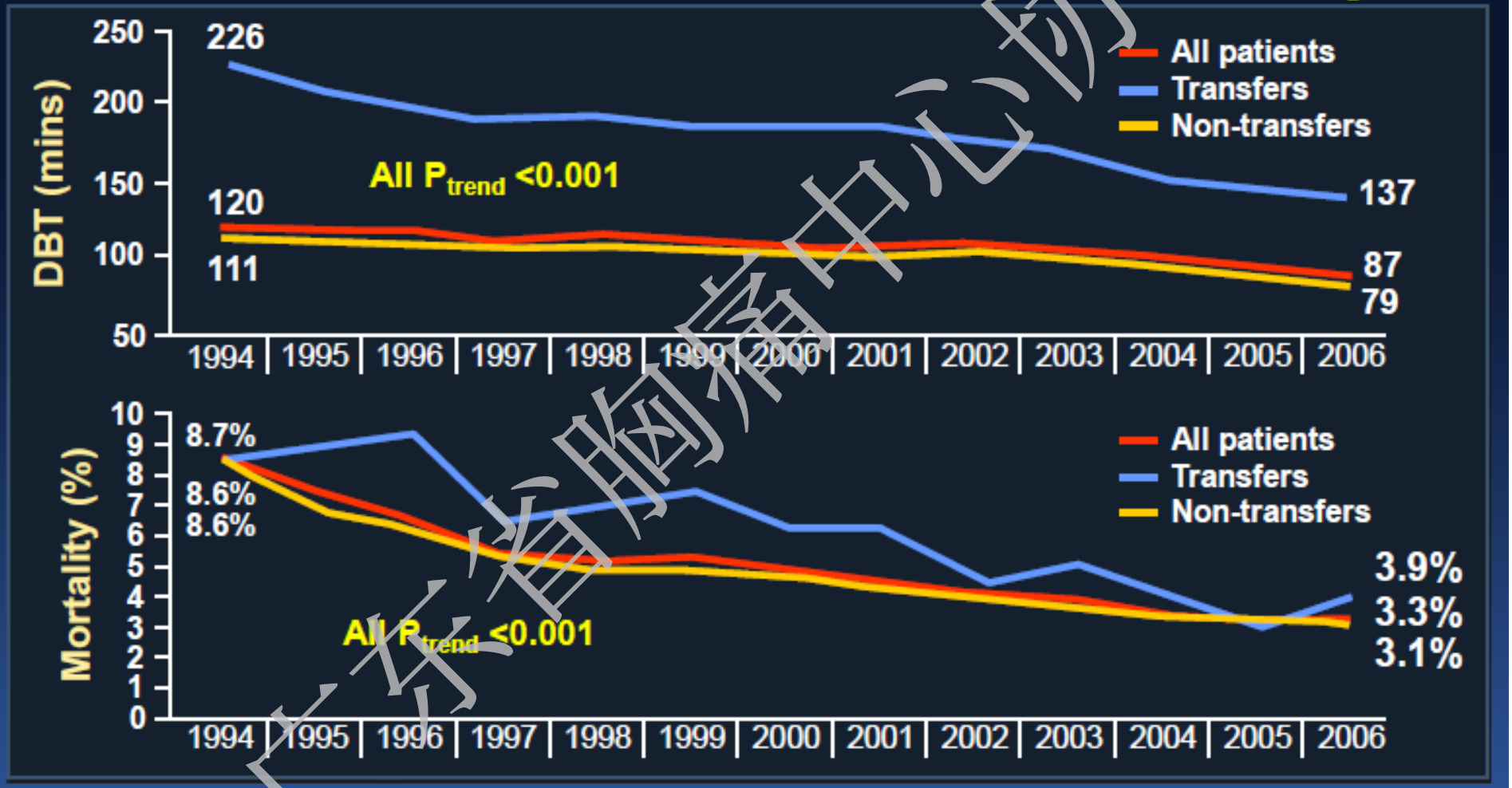


CARDIOVASCULAR RESEARCH FOUNDATION

NRMI: Evolution in Reperfusion

774,279 reperfusion eligible STEMI pts at 2,157 hospitals from 1990-2006

Reductions in DBT and In-hospital Mortality

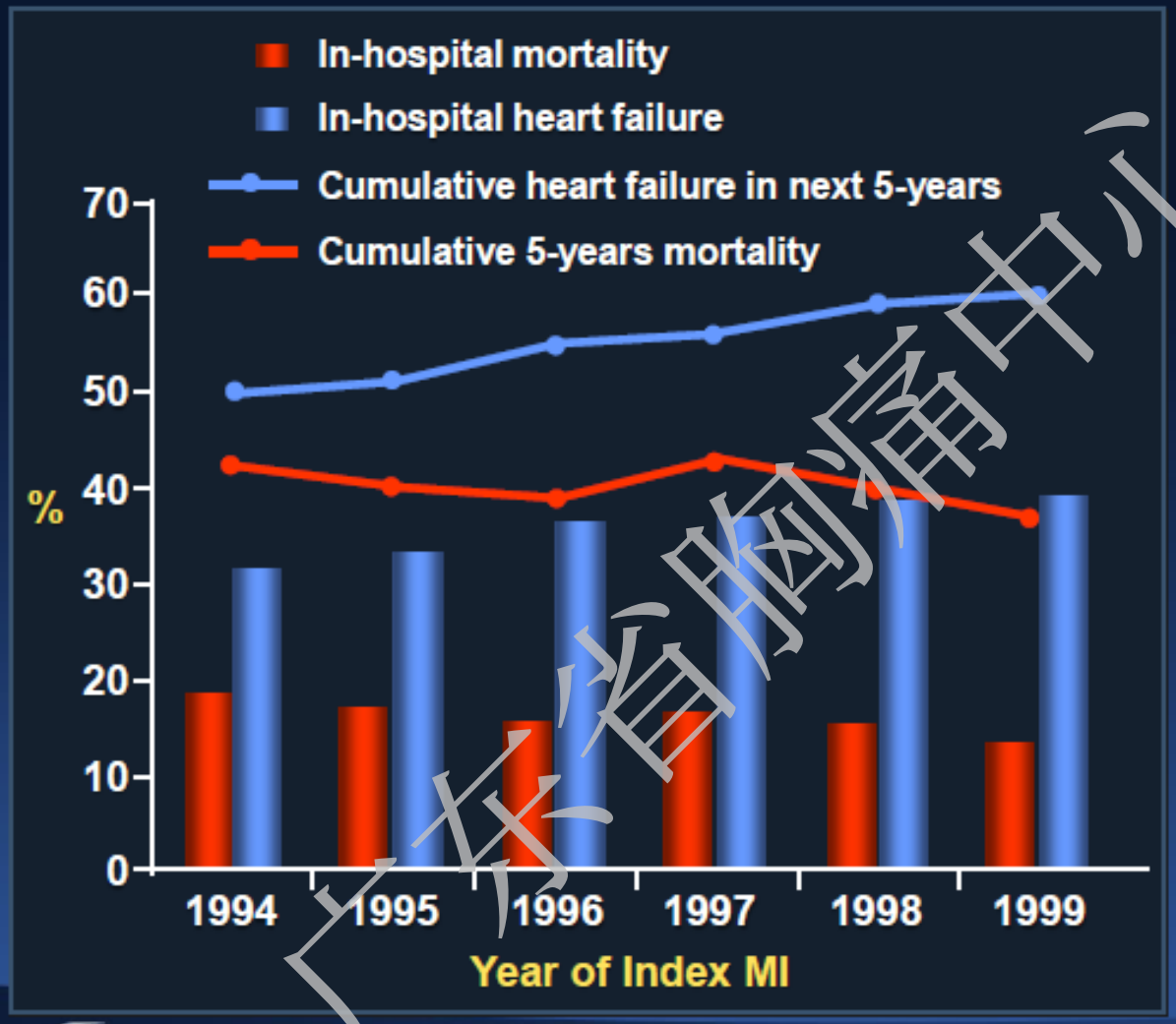


MV analysis: 5.8% of the reduction in mortality was explained by ↓DBT

Gibson CM et al. *Am Heart J* 2008;156:1035-44

Evolving Clinical Outcomes

7739 pts ≥65 yo w/o prior heart failure hospitalized for a 1st MI between 1994 and 2000 in Alberta, Canada, followed for 5 years



5-year trends

In-hosp death: ↓28%

In-hosp HF: ↑25%

5-year survival in hospital survivors

With in-hosp HF: 39.1%

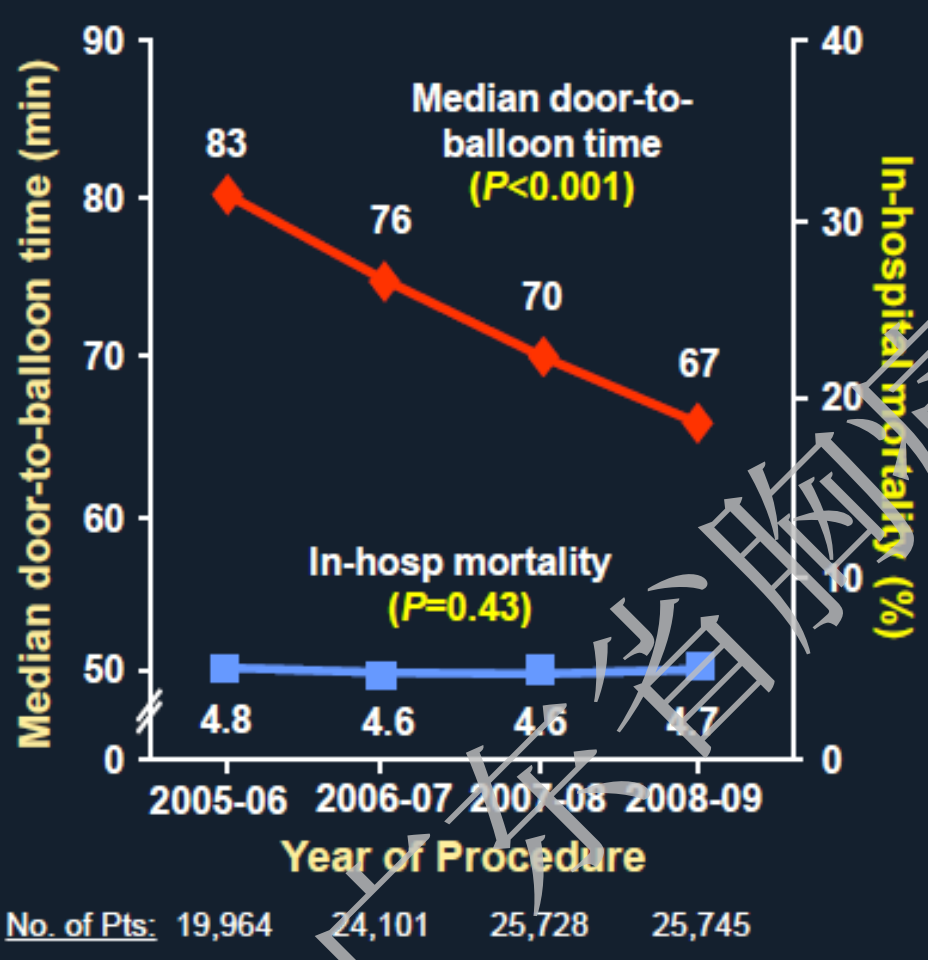
Without in-hosp HF: 26.7%

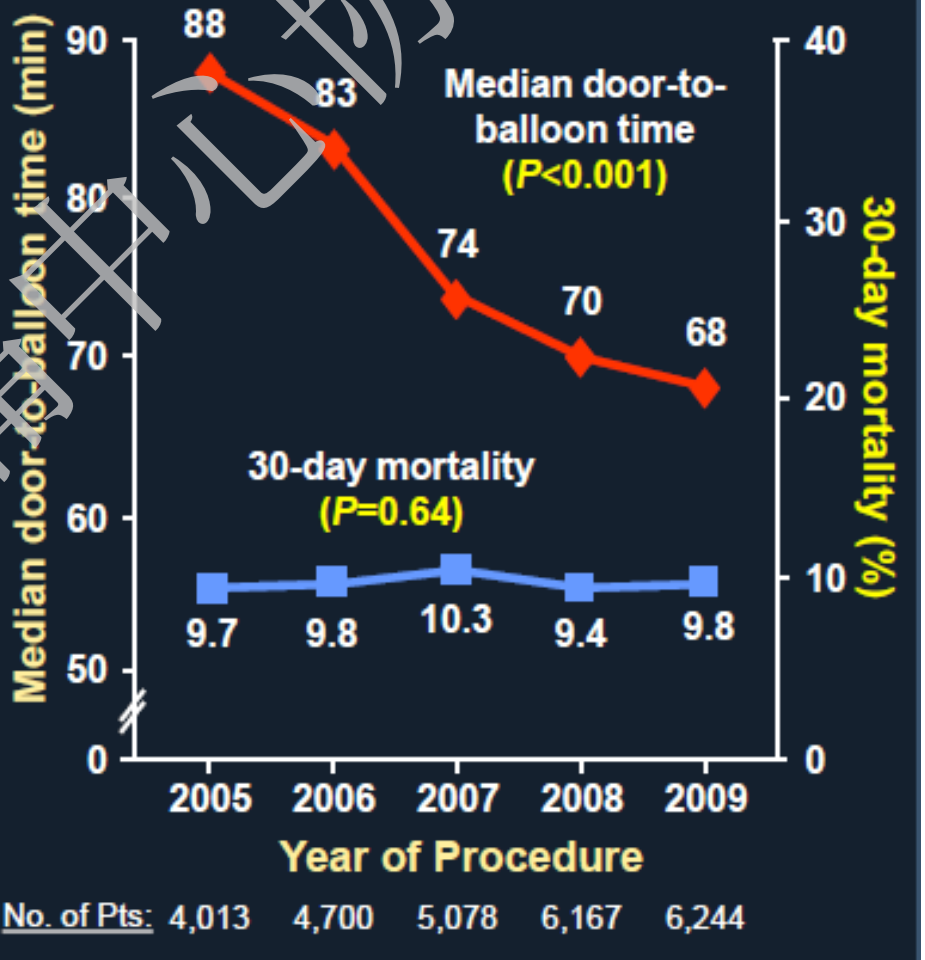
P<0.0001

Ezekowitz JA et al. *JACC* 2009;53:13-20

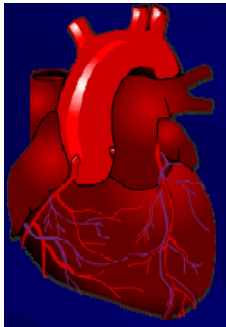
Reductions in National DBT and Mortality

96,738 primary PCIs 7/05 – 6/09 at 515 hospitals in the CathPCI Registry; 30d mortality data from CMS claims database

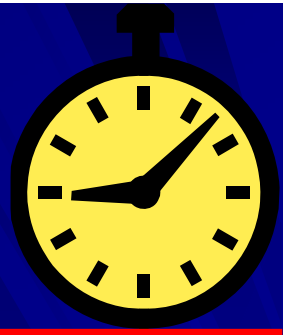


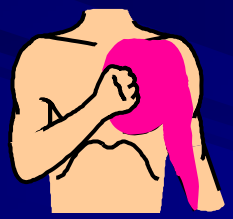


Menees DS al. *N Engl J Med* 2013;369:901-9



延迟治疗就是否定治疗





症状识别

呼叫急救系统

院前处理

急诊科

心导管室

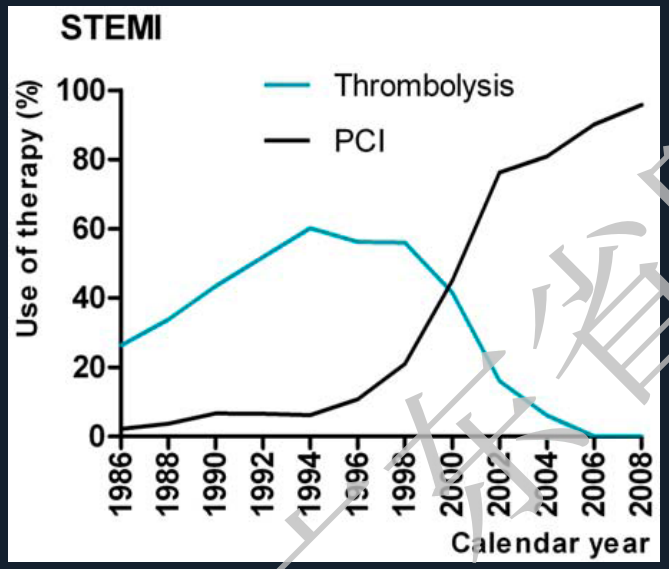
心肌细胞丢失增加

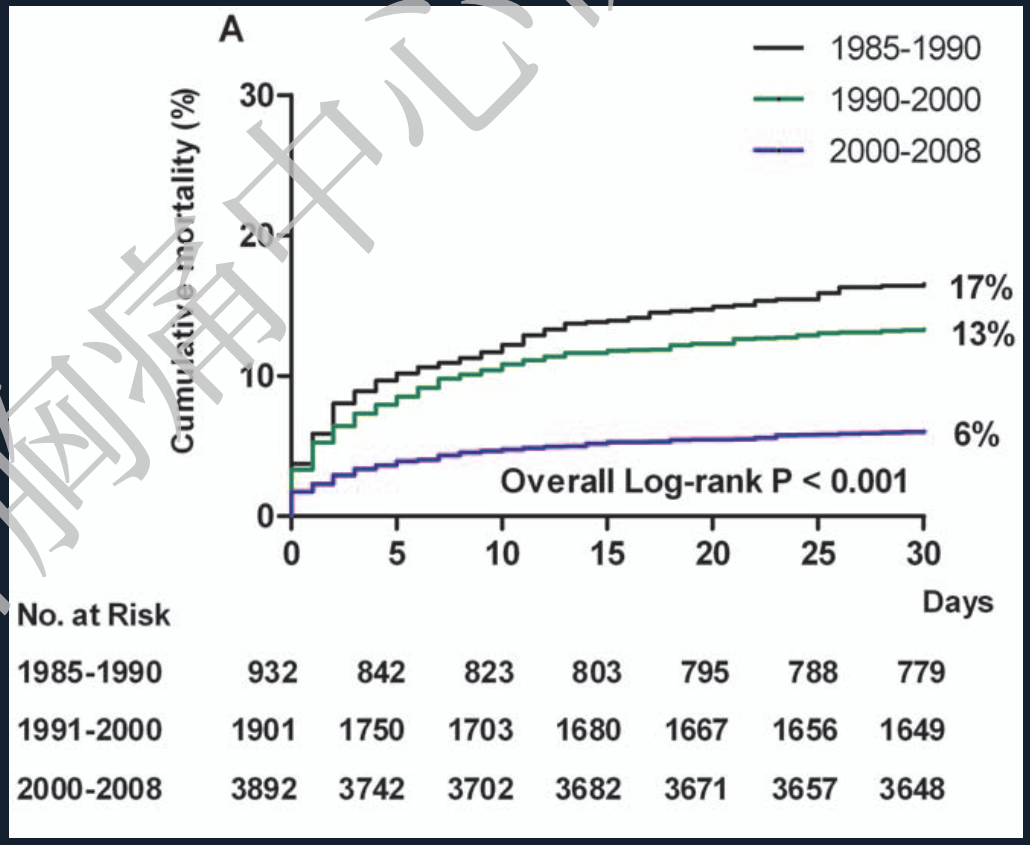
再灌注治疗时间延迟

STEMI Treatment

Impacting outcomes

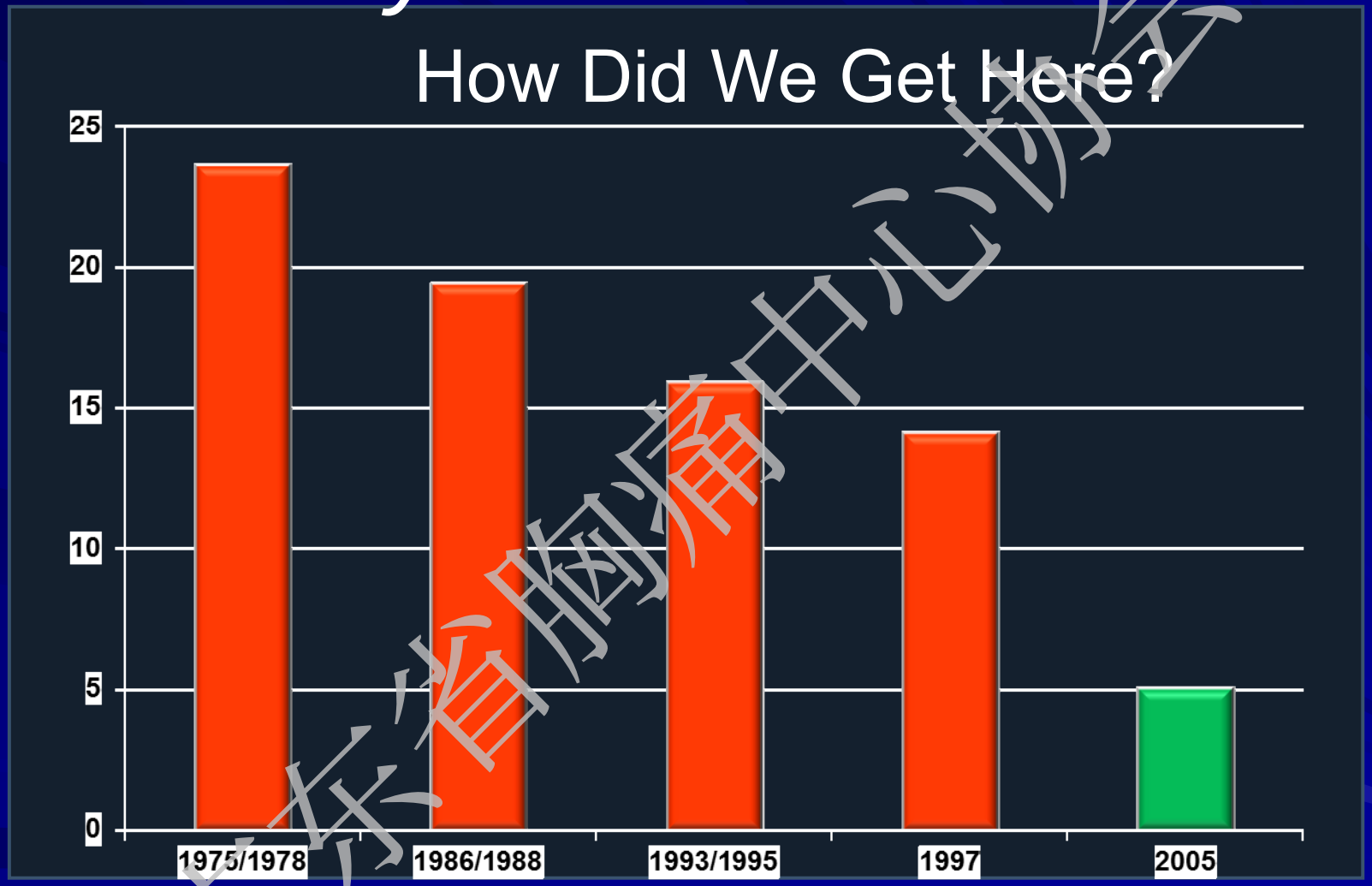
Introduction primary PCI





Nauta, S. et al, available at http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0026917

Mortality From a Heart Attack



Dauerman et al. Am J Cardiol 2002: The Worcester Heart Attack Study

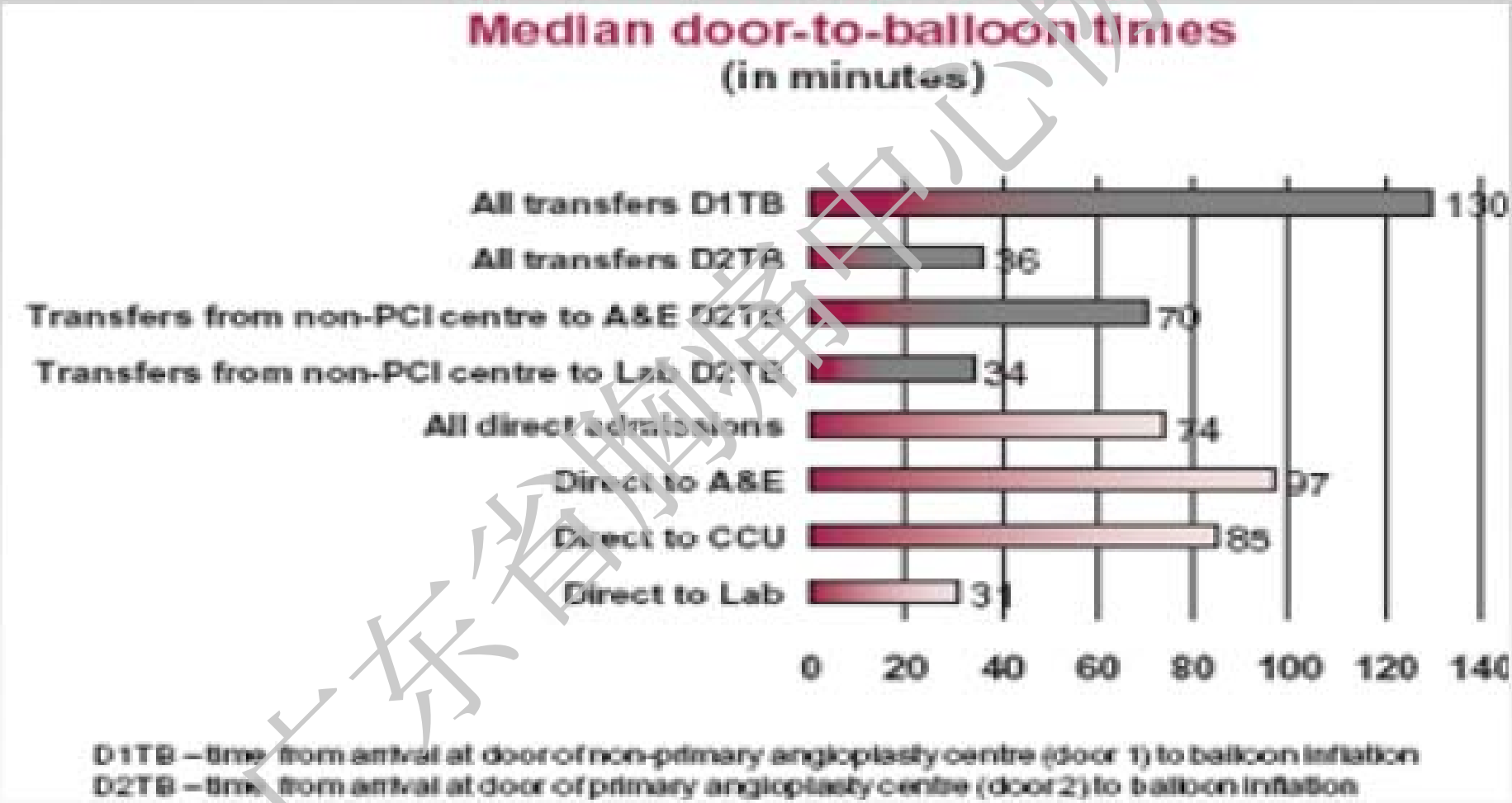
In-Hospital Outcomes - STEMI

Variable	STEMI (n=20,681)
Death*	5.7%
Re-infarction	1.0%
CHF	6.2%
Cardiogenic Shock	5.8%
Stroke	0.8%
RBC Transfusion#	6.6%

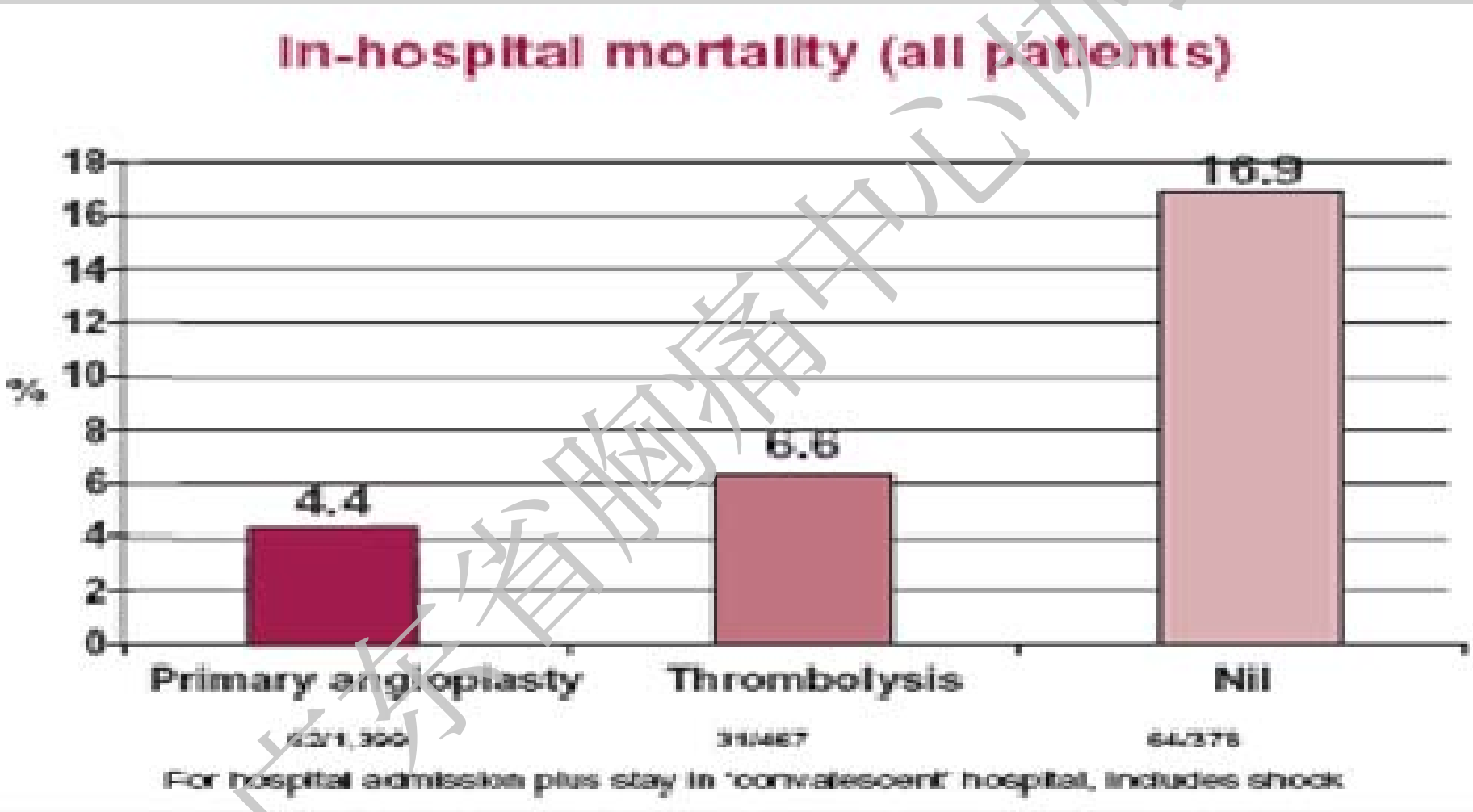
ACTION Registry-GWTG DATA: July 1, 2007 – June 30, 2008

* Unadjusted mortality
# Transfusion among non-CABG patients

NIAP Findings

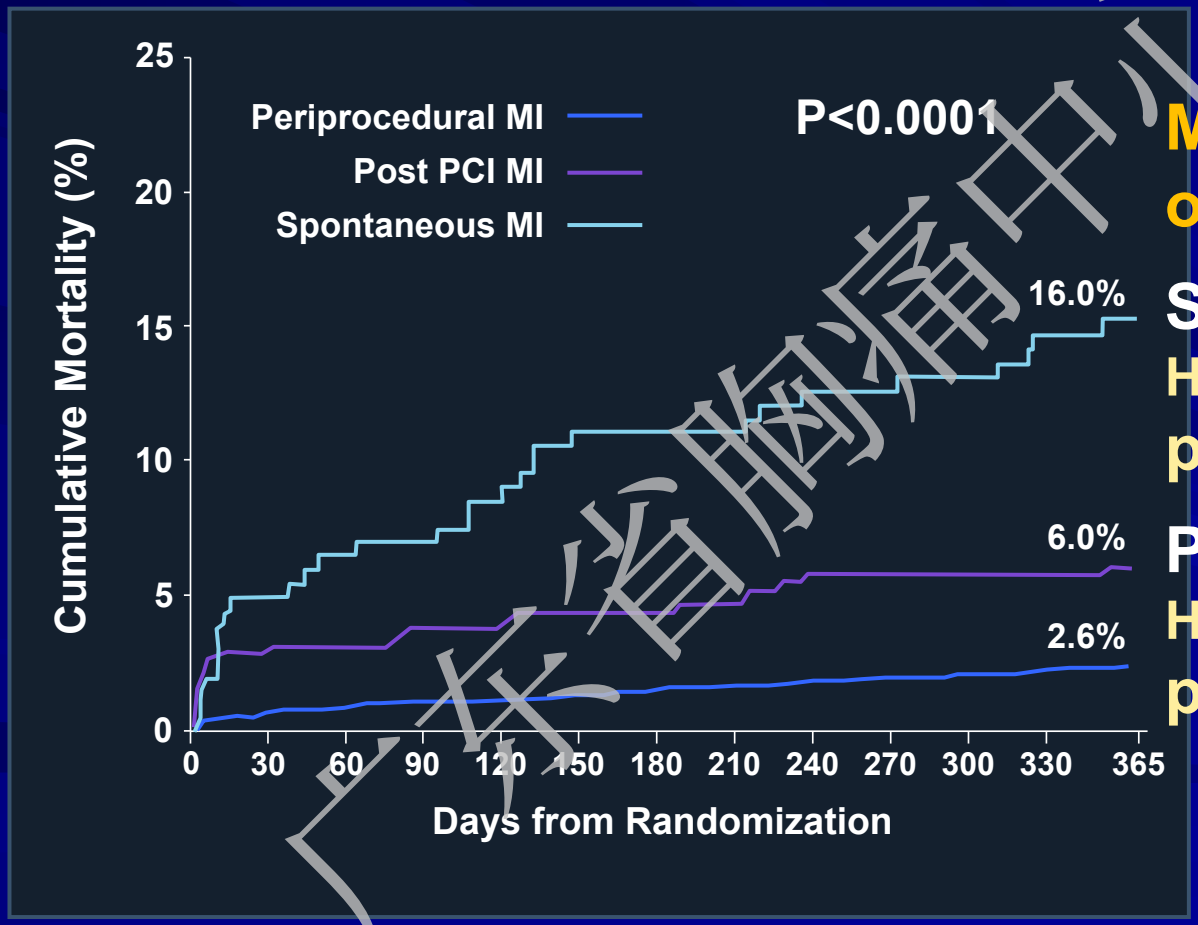


NIAP Findings



Prognostic Significance of Periprocedural vs. Spontaneously Occurring MI After PCI

7773 pts with ACS underwent PCI in ACUITY; peri-procedural MI (CK-MB >3x nl) developed in 466 pts (6.0%), and a spontaneous MI unrelated to PCI (troponin >nl) subsequently developed in 200 pts (2.6%)



Multivariate model of 1-yr mortality

Spontaneous MI
HR = 7.49 [4.95, 11.33], p<0.0001

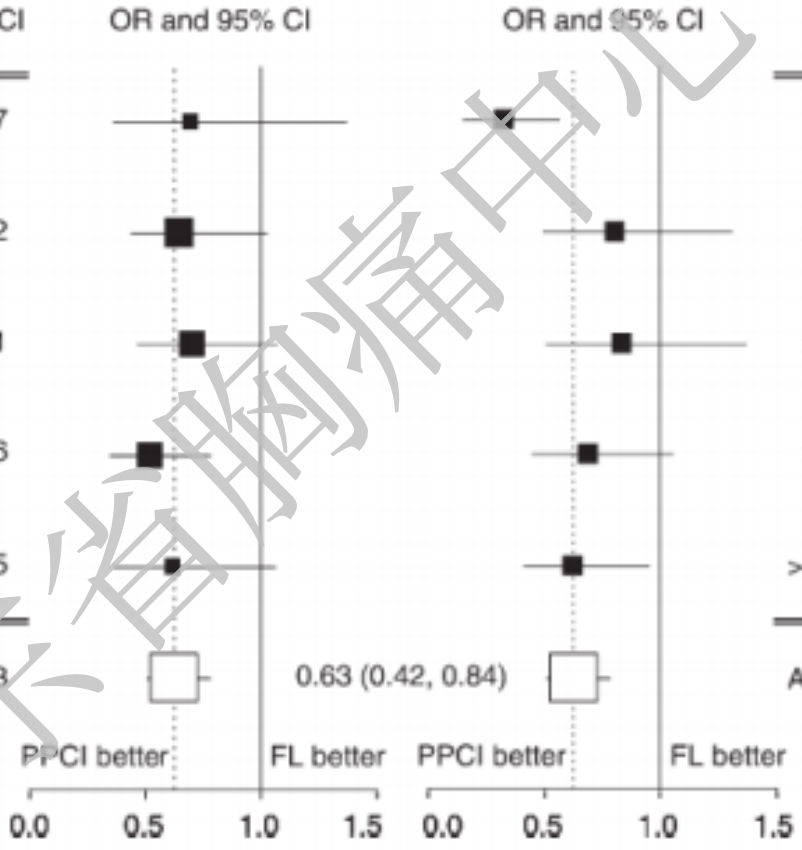
Periprocedural MI
HR = 1.30 [0.85, 1.98], p=0.22

Prasad A et al. Submitted

PCI-related delay

Boersma et al. European Heart Journal 2006

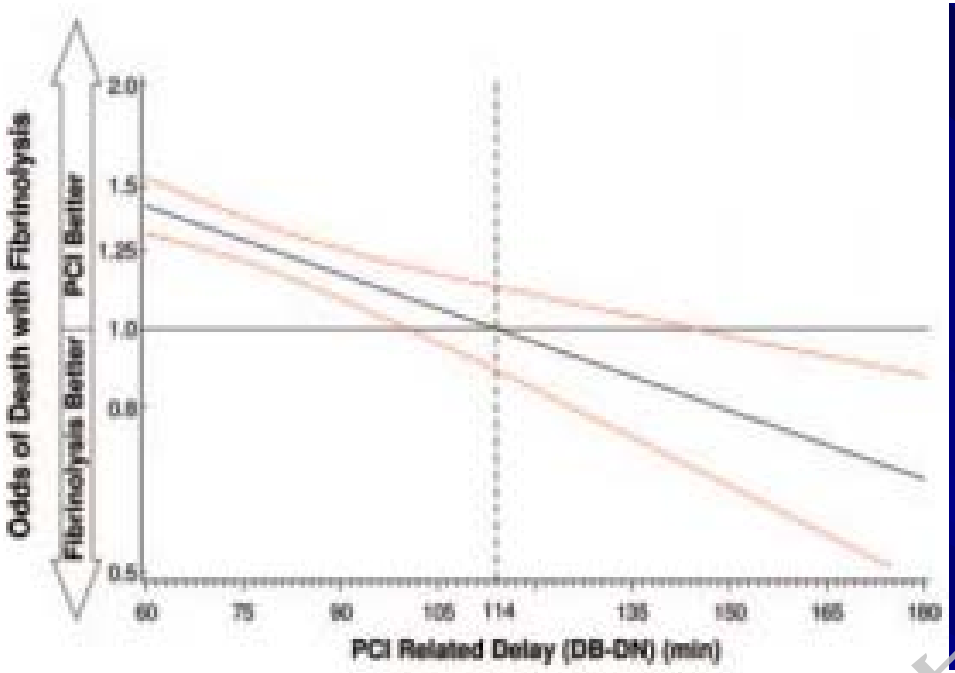
Presentation delay (h)	Number of patients	30-day death (%) FL	30-day death (%) PPCI
0 – 1	747	6.0	4.7
>1 – 2	2000	6.2	4.2
>2 – 3	1712	7.3	5.1
>3 – 6	1640	9.5	5.6
>6 – 12	664	12.7	8.5
All patients	6763	7.9	5.3

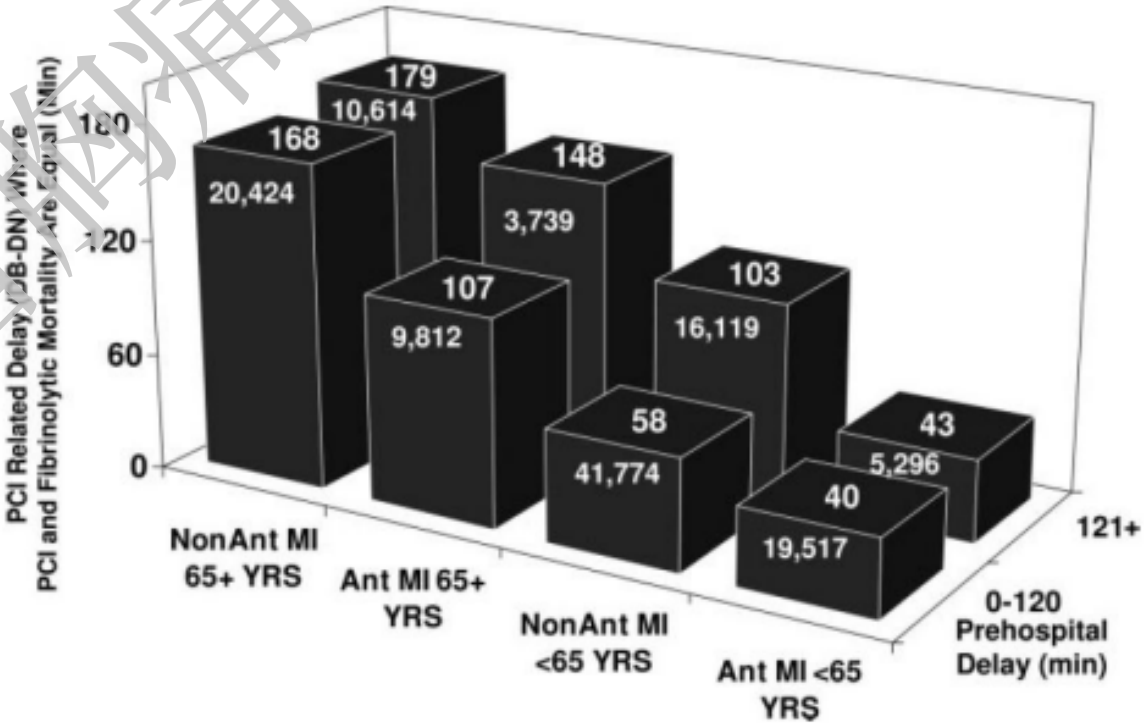


PCI-related delay (min)	Number of patients	30-day death (%) FL	30-day death (%) PPCI
0 – 35	1417	8.2	2.8
>35 – 50	1292	6.8	5.4
>50 – 62	1425	5.4	4.8
>62 – 79	1280	9.5	6.9
>79 – 120	1349	9.6	6.6
All patients	6763	7.9	5.3

PCI-related Delay

Pinto et al Circulation 2006





远程无线诊断启动急诊PCI缩短D-B时间

STAT-MI (ST-Segment Analysis Using Wireless Technology in Acute Myocardial Infarction) Trial

EMS transmitted ECGs to on-call cardiologists for triage to cath lab. Controls presented at hospital as walk-ins or by regular ambulance.

Median Outcomes	Control Group (n = 43)	STAT-MI Group (n = 72)	*P* Value
D2B, min*	119	63	< 0.00004
LVEF	35%	50%	0.004
Peak Troponin, ng/mL	87.6	39.5	0.005

* Primary endpoint.

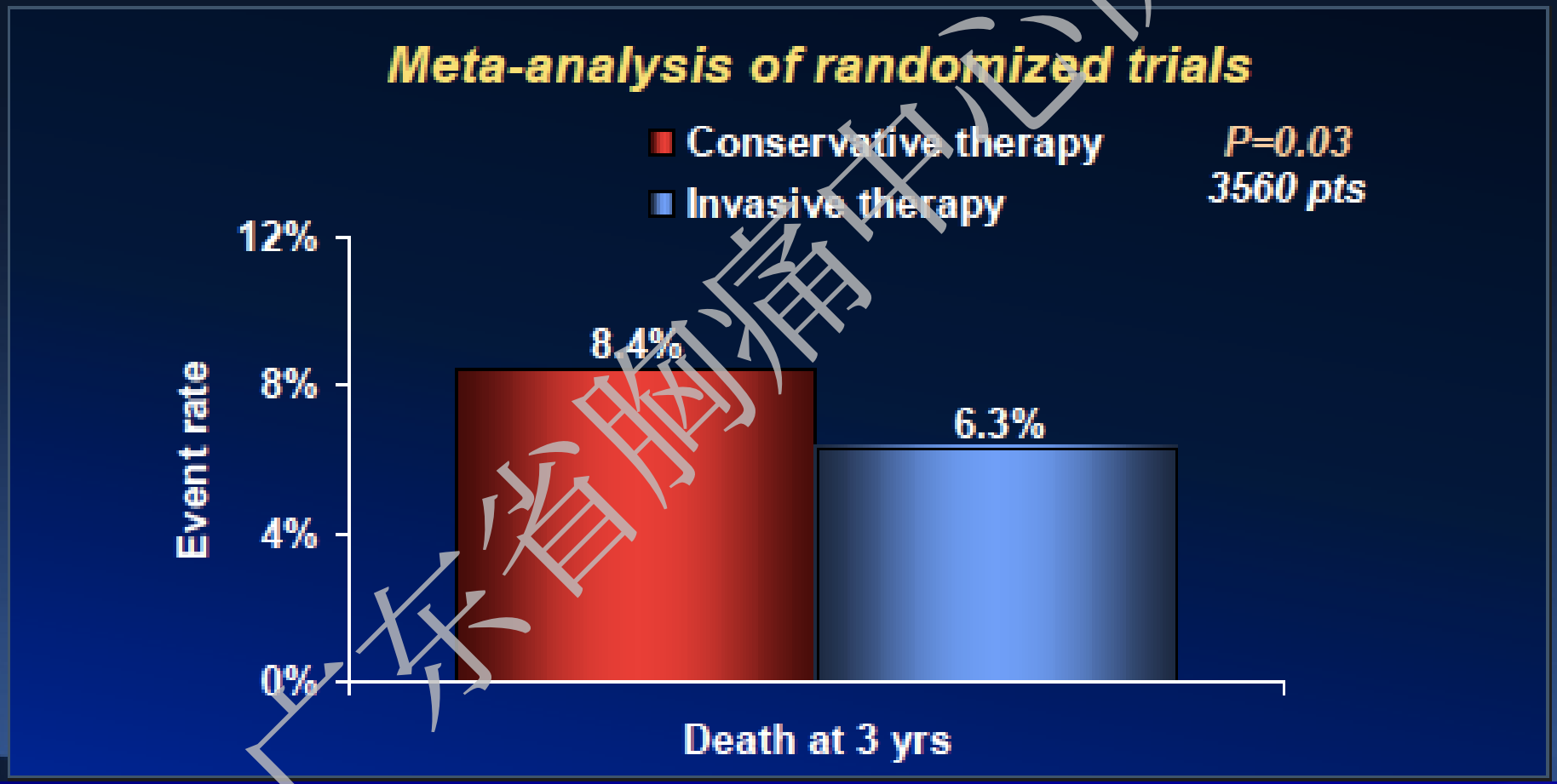
Conclusion: A fully automated wireless network that allows emergency medical personnel to transmit ECGs to cardiologists via handheld phones substantially shortens D2B times for patients with suspected STEMI.

Sanchez-Ross M, et al. *J Am Coll Cardiol Intv*. 2011;4:222-227.

Table 1. Outcomes According to Transport Method

	Direct (n = 454)	Interhospital (n = 127)	*P* Value
First-Medical-Contact-to-Balloon Time < 90 Minutes	82%	23%	< 0.01
Median Symptom-to-Balloon Time, min	149	219	< 0.01
TIMI Flow Grade 3	92%	84%	0.03
One-Year Mortality	7%	13%	0.03

Survival Benefits in Patients Undergoing Late Percutaneous Coronary Intervention of the Infarct-Related Artery



Abbate et al. J Am Coll Cardiol, 2008; 51:956-964

2014年与北京市平均数字的比较

	朝阳医院数字 n/N（%）	北京市平均数字 n/N（%）	比较
急诊PCI	6/430（**1.4%**）	118/5891（2.0%）	⬇
择期PCI	6/1523（0.39%）	32/42418（0.08%）	↑
总PCI	12/1953（0.61%）	150/48309（0.31%）	↑

我院急诊PCI死亡者均为心源性休克或心脏破裂者；
择期PCI死亡者多为泵功能严重衰竭合并多脏衰者，
反映我科PCI患者大多危重，临床情况较复杂，
期待新型介入诊治器材的引入与应用，改善结果。

死亡例数：12例（0.61%）

- 急诊PCI：6（1.4%）
- 择期PCI：6（0.39%）

心脏破裂：1

脑出血：1

亚急性支架内血栓：1

泵衰竭、多脏衰：9

2014年死亡病例汇总

序号	姓名	性别	年龄	诊断	急诊	日期	术者
1	高京生	男	49	急性广泛前壁心肌梗死 心源性休克	是	1.3	徐立
2	王树明	男	49	急性下壁心肌梗死 心源性休克	是	2.28	迟永辉
3	赵雪兰	女	75	急性广泛前壁心肌梗死 心源性休克	是	3.11	徐立
4	李松春	男	61	急性下壁、前壁心肌梗死 心源性休克 室颤	急诊 PTCA	3.28	张大鹏
5	索尚修	男	84	急性下壁心肌梗死 心源性休克	是	4.10	刘宇
6	刘玉文	女	68	急性广泛前壁心肌梗死 心脏破裂 心包填塞	是	12.31	王红石
7	左本初	男	84	NSTEMI	否	4.25	王乐丰
8	张连山	男	78	急性前壁心肌梗死 支架内血栓形成	否	8.21	王乐丰
9	张乃仁	男	61	急性下后壁心肌梗死 心肺复苏后 多脏器功能衰竭 猝死	否	8.27	徐立
10	白淑云	女	74	NSTEMI 心源性休克	否	9.12	王乐丰
11	唐耀平	女	77	UAP OMI	否	9.23	倪祝华
12	关莉华	女	69	UAP 脑出血	否	10.30	刘宇

基线资料—Endeavor组 *vs.* Cypher组

- 发病至入院时间：215±140 *vs.* 235±167 分钟，*P*=0.13。
- 入院至签字时间：53±61 *vs.* 59±73 分钟， *P*=0.28。
- 签字至穿刺时间：39±21 *vs.* 43±33 分钟， *P*=0.05。
- 穿刺至球囊时间：21±10 *vs.* 24±24 分钟， ***P*=0.04**。
- Door 2 Balloon 时间： 113±64 *vs.* 127±91 分钟，***P*=0.04**。

北京朝阳医院单中心急诊PCI结果分析

- 对上表数据需要说明：
  - 参与绿色通道的医护人员基本能保证在30分钟内全部到位
  - 时间耽误环节
    - 在患者家中：胸痛不及时求助医生，平均花费时间在3小时左右
    - 在急诊科：患者及家属商量及做出决定耗费很多时间，平均在60分钟左右

2017年1月-9月

心源性休克

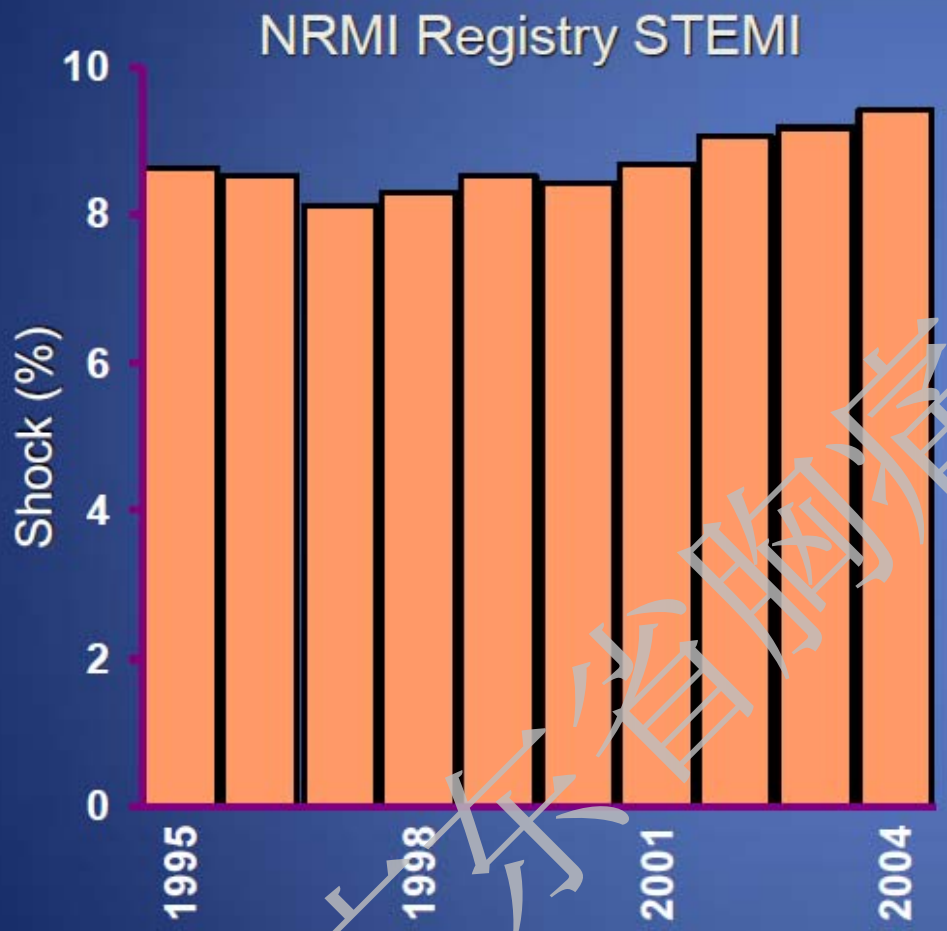
Temporal Trends in Cardiogenic Shock Complicating Acute MI

N= 9076	Cardiogenic Shock	In-Hospital Mortality (OR)	95% CI
1975-1978	7.2%	1.0	
1981-1984	7.2%	1.02	(0.56-1.85)
1986-1988	8.3%	1.30	(0.70-2.42)
1990-1991	5.9%	0.85	(0.45-1.60)
1993-1995	7.0%	0.49	(0.28-0.86)
1997	7.1%	0.46	(0.26-0.86)

Goldberg RJ, et al. NEJM 1999; 340:1162-1168

Cardiogenic Shock

Incidence



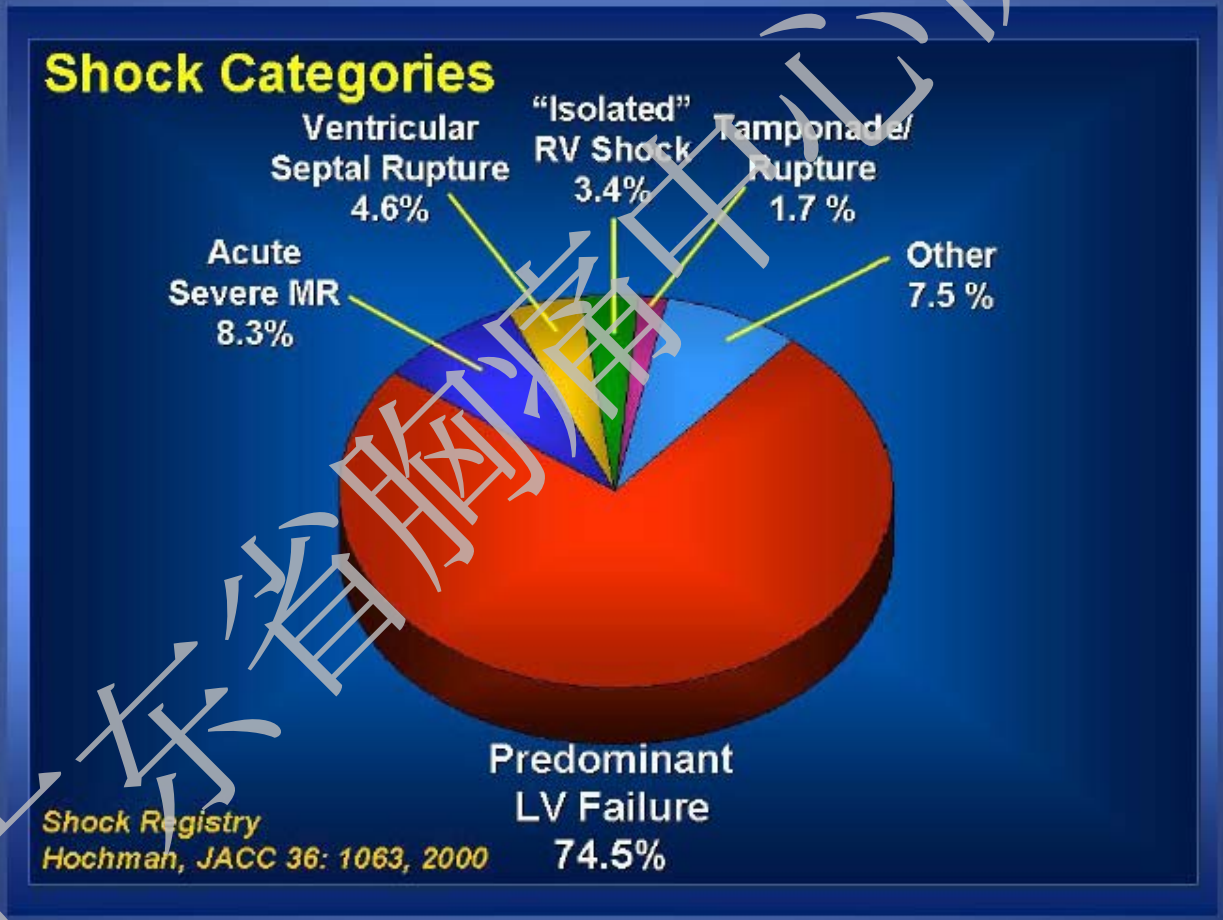
- ~8% of STEMI in NRMI
- 2% of NSTEMI
- ~50,000 patients per year

Babaev et al: *JAMA* 294:448, 2005

Cardiogenic Shock

Etiology

Shock Trial and Registry



Hochman et al. JACC 2000; 36: 1063

SHOCK Registry: Mortality by Shock Categories

p=0.001 6 Group; VSR vs each p<0.01

Hochman, JACC 36: 1063, 2000

PCI in Cardiogenic Shock: Importance of Time to Reperfusion

ALKK Registry
(80 centers in Germany 1992-2003)

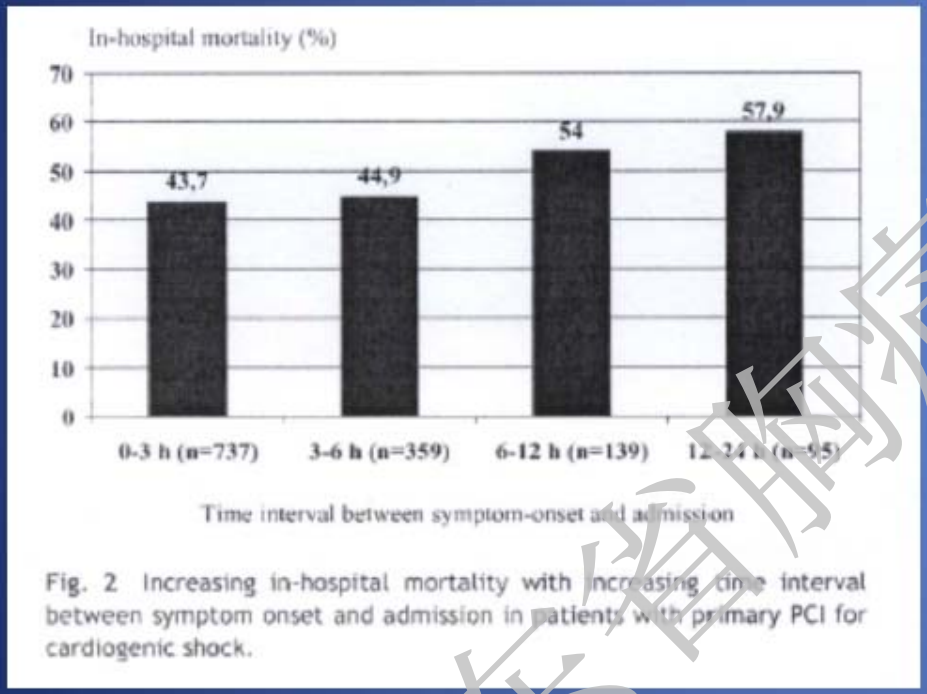
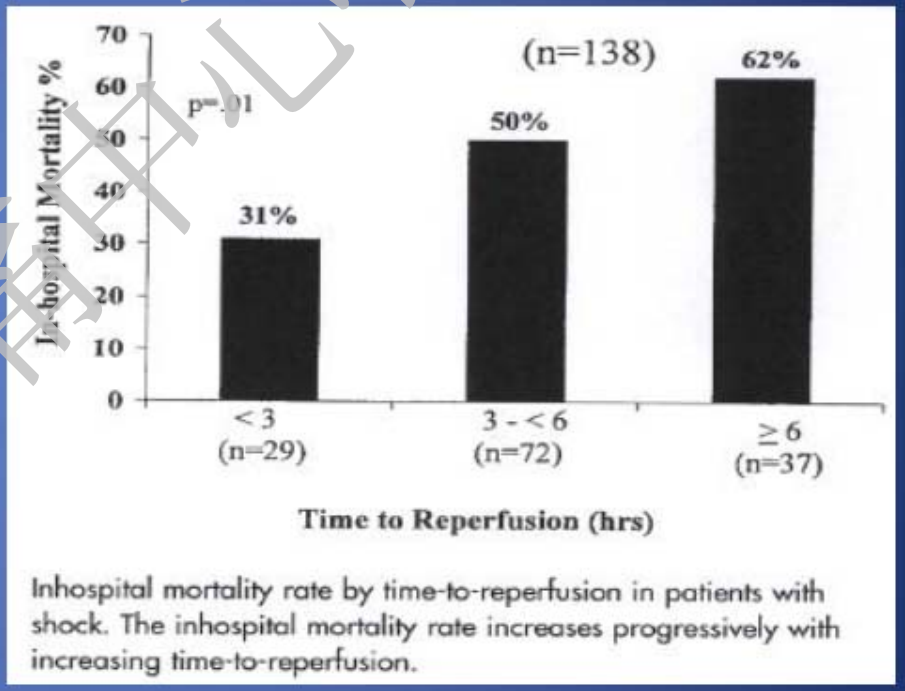


Fig. 2 Increasing in-hospital mortality with increasing time interval between symptom onset and admission in patients with primary PCI for cardiogenic shock.

Zeymer, EHJ 2004; 25:322-8.

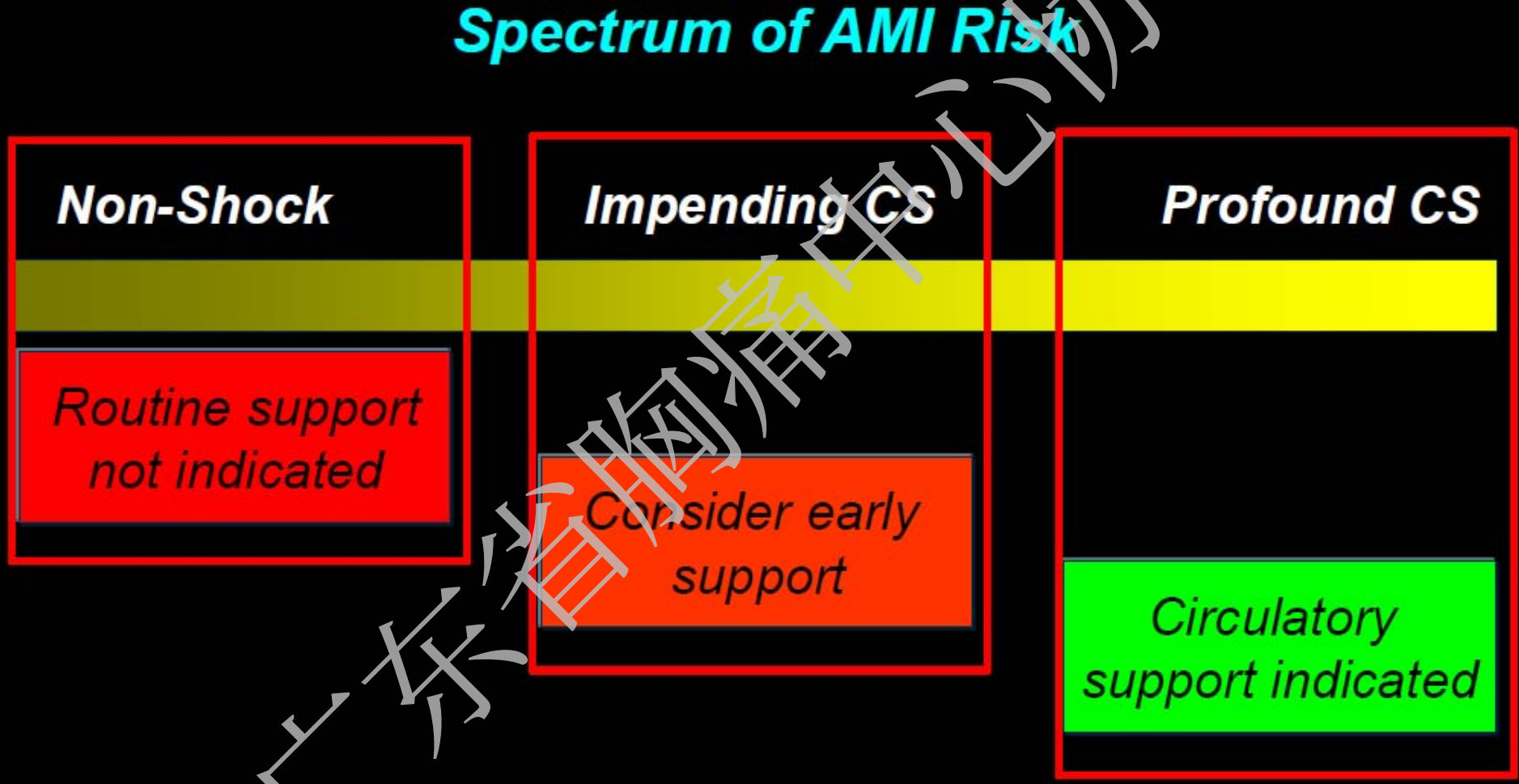
Moses Cone (1984-2000)



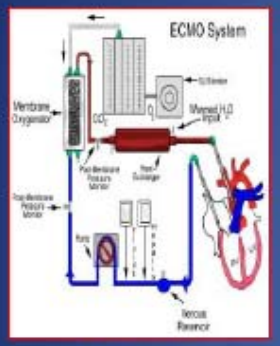
Inhospital mortality rate by time-to-reperfusion in patients with shock. The inhospital mortality rate increases progressively with increasing time-to-reperfusion.

Brodie, AHJ 2003; 145:708-15.

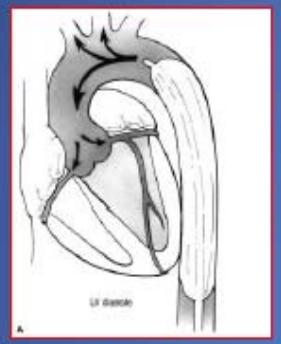
Hemodynamic Status in AMI



History of Ventricular Support

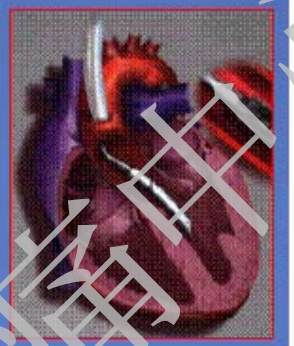


ECMO

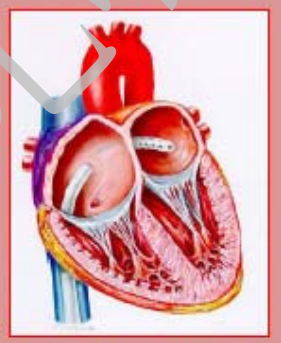


IABP

CPS



Hemopump

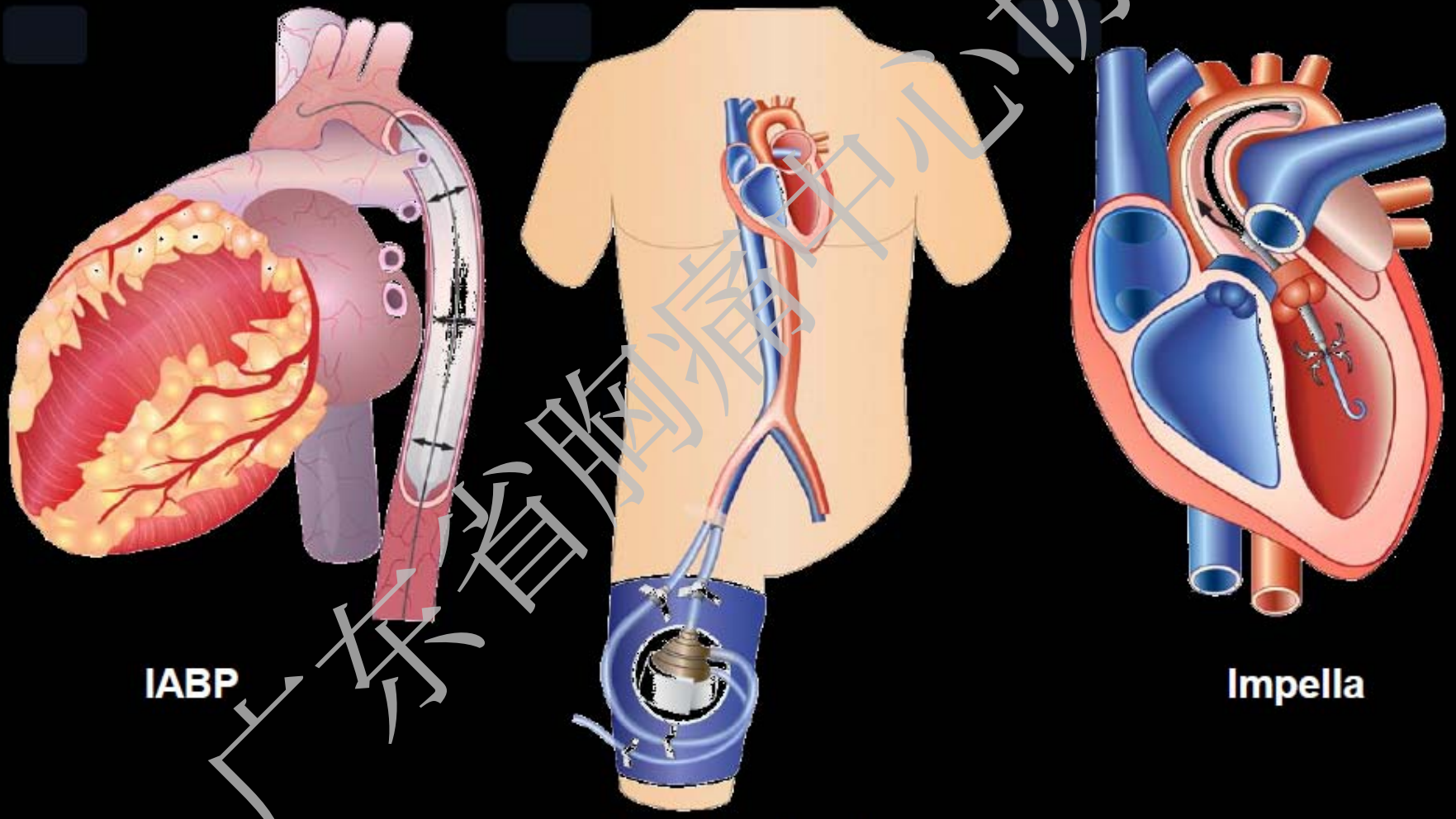


TandemHeart

Impella

70's 80's 90's 00's

Most Commonly Used Mechanical Devices in the CathLab



IABP

TandemHeart

Impella

Intra-aortic Balloon Counterpulsation and Infarct Size in Patients with Acute Anterior MI Without Shock

CRISP AMI: 337 pts randomized to primary PCI with or without intra-aortic balloon pump (IABP) pre-intervention.

	IABP Plus PCI (n = 161)	PCI Alone (n = 176)	*P* Value
Mean Infarct Size[a]	42.1%	37.5%	0.06
Mean LVEF	46.1%	48.2%	0.17
6-Month Mortality	1.9%	5.2%	0.12

[a] Primary endpoint.

Conclusion: IABP therapy fails to reduce infarct size or improve clinical outcomes when added prior to primary PCI in patients with high-risk STEMI but no cardiogenic shock.

Patel MR, et al. *JAMA*.
2011;Epub ahead of print.

Intraaortic Balloon Counterpulsation Reduces Mortality in Large Anterior MI Complicated by Persistent Ischemia

CRISP-AMI substudy: 36 patients with large STEMI and poor ST-segment resolution (n = 15 IABP and 21 control), representing 11% of overall trial.

- At 6 months, none of the patients in the IABP group had died, compared with 5 in the control group (0 vs 24%; *P* = .046)
- Trend favoring IABP therapy also seen for the composite endpoint of death, cardiogenic shock, or new/worsening heart failure (7% vs 33%; log-rank *P* = .06).

Implications: IABP therapy seems most beneficial in patients with large anterior STEMI complicated by persistent ischemia.

van Nunen LX, et al. *EuroIntervention.* 2014;Epub ahead of print.

2014年ESC的推荐

- AMI引起的心源性休克，如果冠状动脉病变适合PCI，则建议急诊PCI治疗（Ⅰ/B）
- AMI引起的心源性休克，如果冠状动脉病变不适合PCI，则建议急诊CABG治疗（Ⅰ/B）
- ACS患者出现心源性休克可考虑短期机械辅助循环（Ⅱb/C）
- 不建议常规对心源性休克患者使用IABP（Ⅲ/A）

The Evolution of MI Care

>80% Mortality Reduction:

Robust Drug/Device Development, Clinical Investigation (evidence-based medicine), and a Dynamic Regulatory Process

1955

2010

Courtesy of Aaron Kaplan, MD

POST: Ischemic Postconditioning During Primary Percutaneous Coronary Intervention

700 STEMI patients undergoing primary PCI within 12 hours of symptom onset were randomized to direct postconditioning or conventional care.

	Postconditioning (n = 350)	Conventional PCI (n = 350)	*P* Value
Complete ST-Segment Resolution at 30 min	40.5%	41.5%	0.79
MACE at 30 Days	4.3%	3.7%	0.70

Conclusion: Ischemic postconditioning during primary PCI improves neither myocardial perfusion nor clinical outcomes in STEMI patients.

Hahn J-Y, et al. *Circulation*. 2013;Epub ahead of print.

STEMI Success has Plateaued!

Remaining challenges in STEMI reperfusion therapy

- Further reductions in DBT (apparently) not beneficial
  - Symptom time to first medical contact unchanged
- Suboptimal salvage of myocardium
  - Reperfusion success only ~65%
    - In part due to distal embolization
  - Reperfusion injury
- Mortality remains high in cardiogenic shock and out-of-hospital cardiac arrest
- Ongoing inflammation → high rates of non-culprit lesion-related events

Therapies to Enhance Myocardial Recovery

Epicardial Reperfusion/ Systems of care

Regionalization of STEMI care
Pre-hospital ECGs
Pre-hospital cath lab activation
Bypass non-PCI hospital
Bypass PCI-hospital ED
Onsite primary PCI team

Microvascular integrity/ function

Thrombus aspiration
Intracoronary abciximab
MGuard stent
Adenosine
Sodium nitroprusside
Ca^{+2} channel blockers

Myocardial Reperfusion/ Recovery

Cell Therapy

Autologous endothelial/bone marrow progenitor cells
Cardiac stem cells

Cardioprotection

Pre- and post-ischemic conditioning
Non-infarct related artery reperfusion
Mechanical LV unloading
Cyclosporine
Mitochondrial targeting peptides
Losmapimod
Exenatide
Nitric oxide
Supersaturated oxygen
Hypothermia

Treatment of STEMI
Conclusions

- STEMI comprises ~22% of all ACS admissions; the incidence is falling, and the case fatality rate is also markedly decreasing, explaining much of the survival in pts with coronary heart disease
- Rapid reperfusion with primary PCI saves lives and prevents recurrent ischemia and reinfarction with STEMI – the faster the better! But there may be diminishing gains…
- The evolution from PTCA to BMS to DES has reduced recurrent ischemia and restenosis, but not death or MI
- Myocardial salvage is suboptimal in STEMI, and new strategies are required to reduce infarct size!

Cannon CP, et al. N Engl J Med 2001;344:1879–87.

Improving the STEMI Process (3)

Team Work!
Training & In Situ Simulation

谢谢!

广东省胸痛中心协会