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Gender Differences in Outcome of Acute Coronary Syndrome

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여자가 남자보다 오래 사는 이유 - 1

8·24 수

오늘의 만남

왜 여자는 남자보다 오래 살까?

상식

선천적으로 남성이 여성보다 우월한 신체 조건을 갖고 태어나지만, 인생을 장거리 경주로 본다면 마지막까지 남는 주자는 여성이다. 세계적으로 여성이 남성보다 5~8년쯤 더 오래 사는데, 과거에는 그 원인을 주로 남성의 음주와 흡연, 과도한 스트레스에서 찾았다. 하지만 여성의 사회진출이 활발해지면서 다양한 분석이 이루어지고 있다.

여성의 성호르몬인 에스트로겐은 장수의 결정적 원인으로 꼽힌다. 에스트로겐은 느리지만 꾸준히 활동해 노화를 촉진시키는 유해 산소의 발생량을 줄이고, 항체를 활발히 생산하여 튼튼한 면역체계를 만든다. 반면 남성은 신진대사를 활발하게 하는 성호르몬 테스토스테론의 작용으로 유해 산소가 많이 발생하며, 각종 감염 질환 가능성이 상대적으로 높다.

체질 또한 수명과 관련이 깊다. 여성은 남성보다 체지방이 많아 생명활동을 유지하는 데 에너지를 덜 소비한다. 기온 변화에도 유연하게 체온을 조절하여 에너지를 절약하지만 남성은 급격한 신진대사를 일으켜 에너지 소비가 많다.

Positive Thinking (좋은 생각), 2005 년 8월호, p98

여자가 남자보다 오래 사는 이유 - 2

영국의 일간지 〈더 타임즈〉에 따르면 여성의 장수 비결은 심장에 있다. 남성은 70세가 되면 심장 기능의 75%가 제 기능을 잃지만, 여성은 20세 때 심장을 그대로 유지한다. 하지만 남성도 규칙적인 운동으로 심장의 퇴화를 예방할 수 있다.

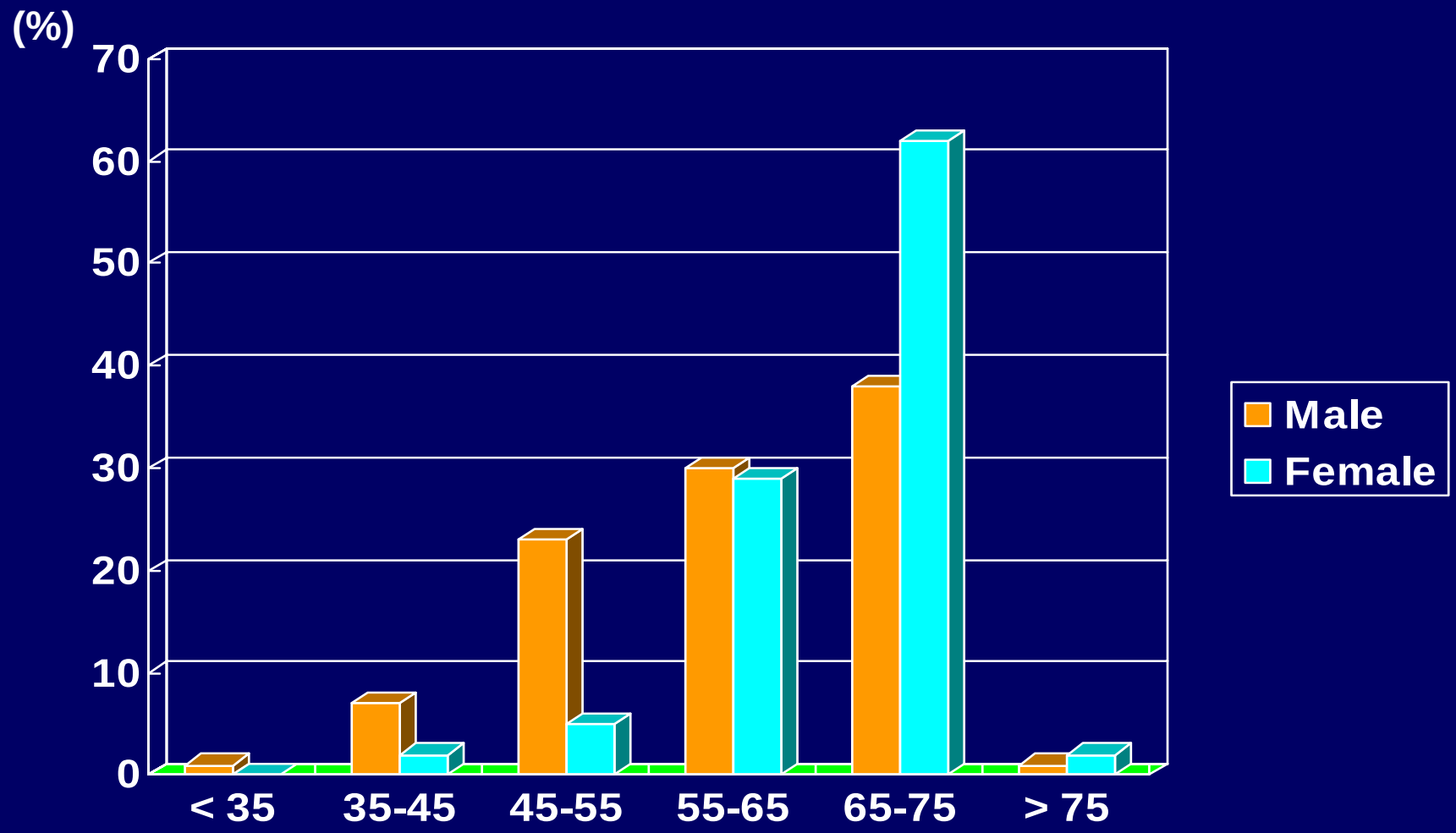
여성이 남성에 비해 감정 조절을 관장하는 우뇌가 발달한 것도 유리한 점이다. 여성은 일반적으로 잘 웃으며, 스트레스 상황에서는 눈물이나 대화 등 감정적인 대응을 함으로써 이를 극복하지만, 남성은 어려운 문제에 부딪히면 폭음·폭식으로 해결하는 경향이 높고 뇌손상의 충격이 커 심근경색이나 뇌출혈로 쓰러지는 비율이 높다. 또한 의학의 발달로 임신과 출산에서 감수하던 위험이 줄어든 반면, 남성은 공격적인 성향이나 경쟁 욕구로 갖가지 범죄와 사고에 노출되면서 수명 차이가 꾸준히 벌어져 왔다.

그러나 하버드대학에서는 수명의 차이가 성별에 따른 선천적 요인과 더불어 그 사람이 속해 있는 사회적 계층, 즉 환경적 요인에도 좌우된다고 발표했다. 장수 노인들을 보면 남녀 구분 없이 규칙적인 운동과 부지런한 삶을 비결로 꼽는다. 결국 장수는 여성에게 주어진 특혜가 아닌 개인의 생활 습관에 따른 선물인 셈이다.

Positive Thinking (좋은 생각), 2005 년 8월호, p98

Sex-Age Distribution of Patients with ACS

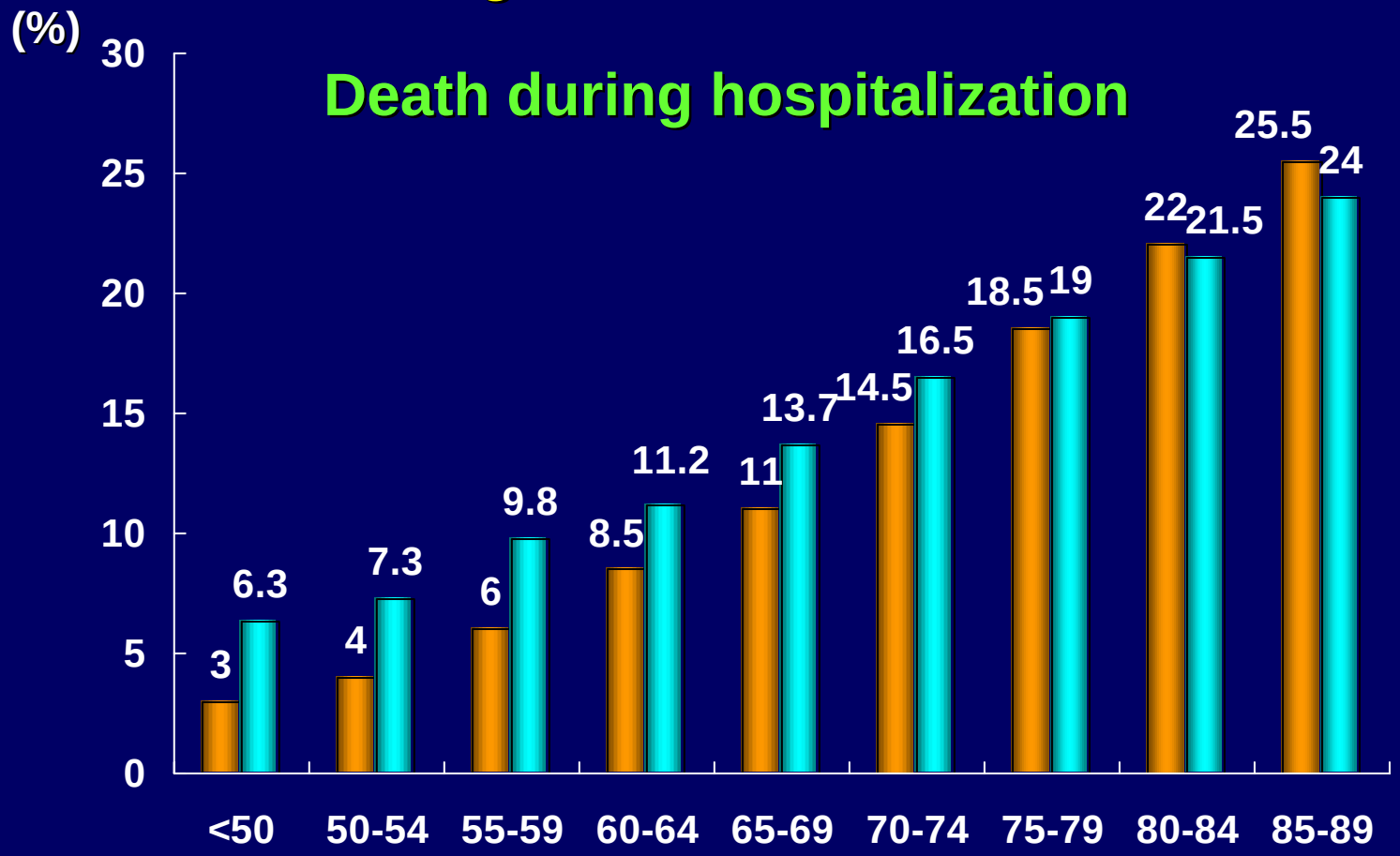
The CARDIO 2000 Study



Chrysohoou C et al., Prev Cardiol 2003;6:71-77

CV Risk in Young Women: NRMI 2 (N=384,878)

The younger the age of the patients, the higher the risk of death among women relative to men



Vaccarino et al. NEJM 1999;341:217

Risk Factors for CAD in Women

- Diabetes mellitus
- Hypertension>140/90 mmHg
- Age>55 or postmenopausal state
- Obesity (3.5X greater risk)
- Tobacco use
- Family history of premature CAD
- High LDL worse for women than men
- Low HDL (< 50 mg/dL) worse for women than men

. Gordon et al. Ann Intern Med 1977;87:393-7

. Gordon et al. JAMA 1977;238:497-9

Emerging Risk Factors for CAD

- Elevated CRP
- Elevated homocysteine
- Elevated lipoprotein (a)
- Elevated plasma insulin
- Elevated small, dense lipoprotein molecules
- Elevated B-type natriuretic peptide

Kannel et al. J Atheroscler Thromb 2000;6:60-6

Lee EM et al. Korean Circ J 1998;28:1307-13

Shin GJ et al. Korean Circ J 1996;26:35-43

Koh KK et al. Korean Circ J 2000;30:251-9

Jeong MH et al. Korean Circ J 2003;33:891-900

Risk Factors of Korean Women

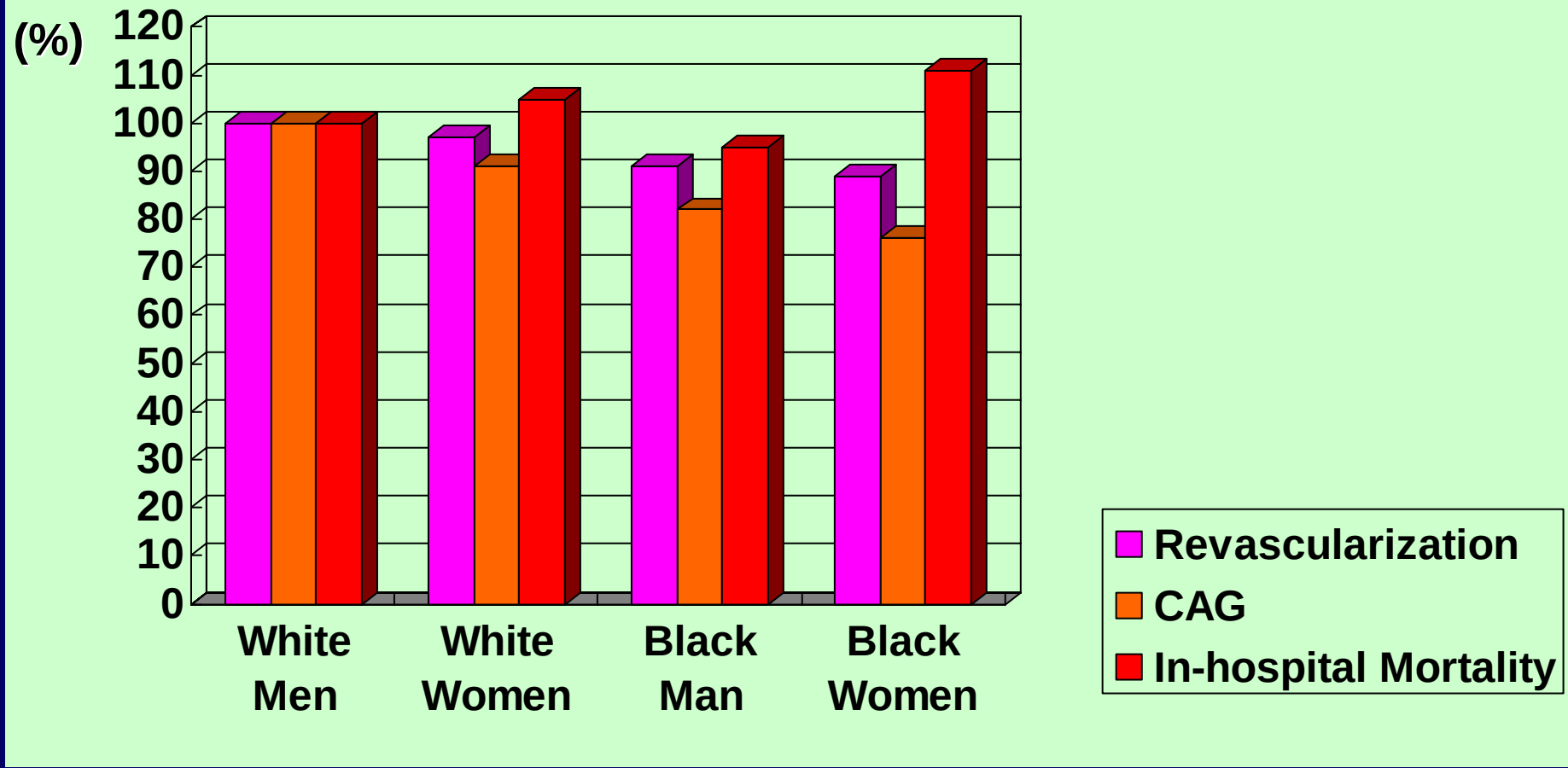
- **Pre-menopause**
  - DM
  - HT
  - hs CRP
  - Hi TG
  - Homocysteine
- **Post-menopause**
  - DM
  - Hi LDL-C

CNUH Data. 2005 Korean Circulation Society
2005 Korean Society of Internal Medicine

Controversies in the Management of Women with ACS

Does Gender Make a Difference ?

National Registry of Myocardial Infarction (1994-2002, n=598,911)



Vaccarino V. New Engl J Med 2005;353:671-82

ACS: TACTICS TIMI-18 (1997-1999) Supports Early Invasive Rx in Women

2,220 pts (757 women, 1,463 men) treated with ASA, Tirofiban randomized to early cath / PCI (4-48 hours) vs. only if needed

	Women	Men	p value
Age	64.3	60.5	< 0.001
HT	70%	62%	< 0.001
Non-obstructive CAD	17%	9%	< 0.001
Cath. performed	75%	76%	0.56
Invasive arm	97%	98%	0.20
Conservative arm	50%	54%	0.28

Glaser R et al. JAMA 2002

ACS: TACTICS TIMI-18 (1997-1999) Supports Early Invasive Rx in Women

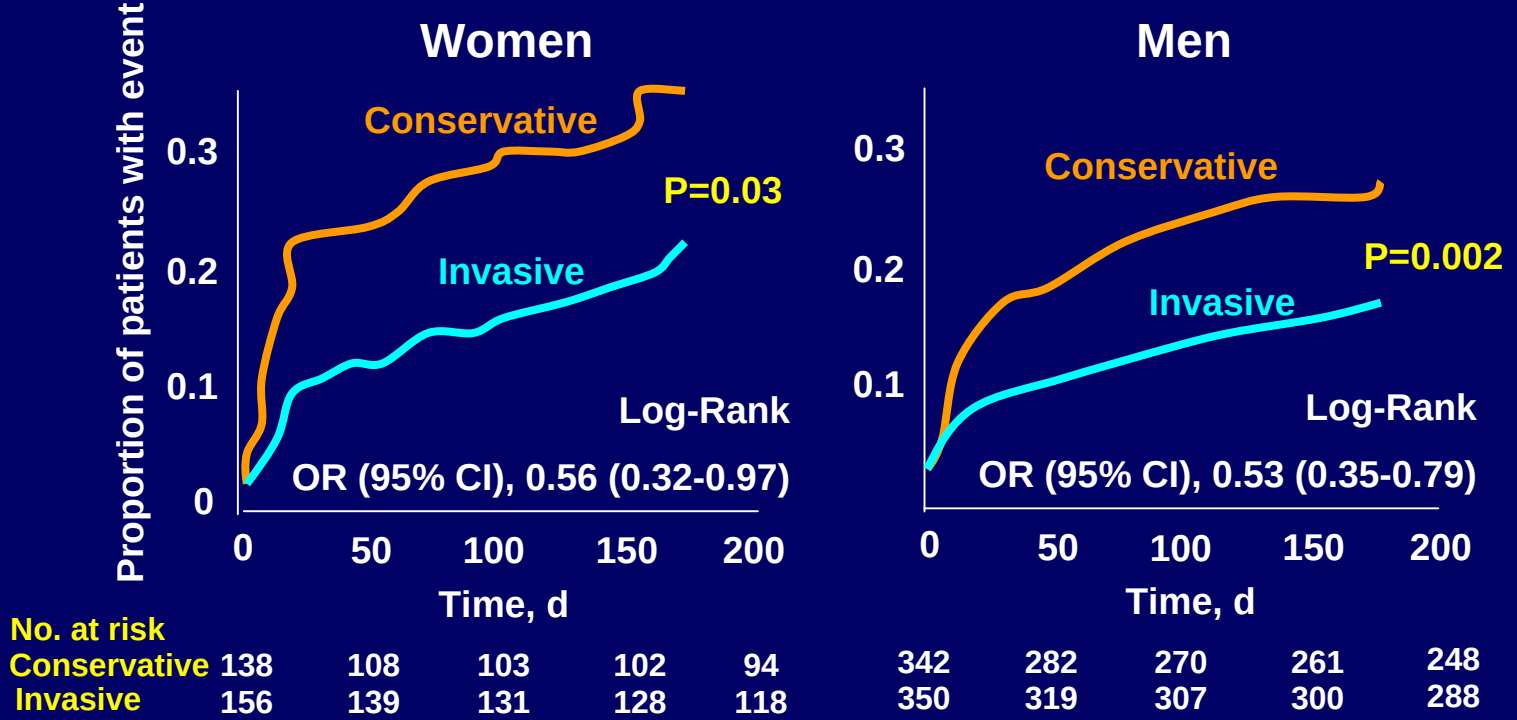
Adjusted OR (95% CI) for Invasive vs. Conservative Rx.

Outcome @ 6 Mo	Women	Men
Death	0.94 (0.37-2.44)	0.75 (0.36-1.56)
Death / MI	0.45 (0.24-0.88)	0.68 (0.43-1.05)
Death / MI / Rehospitalization		
All patients	0.72 (0.47-1.11)	0.64 (0.47-0.88)
High troponin pts	0.56 (0.32-0.97)	0.53 (0.35-0.79)
Normal troponin pts	1.46 (0.78-2.72)	1.02 (0.64-1.62)

Glaser R et al. JAMA 2002

ACS: TACTICS TIMI-18 (1997-1999) Supprots Early Invasive Rx in Women

Death, MI, rehospitalization for ACS in women and men with elevated troponin T levels, by strategy

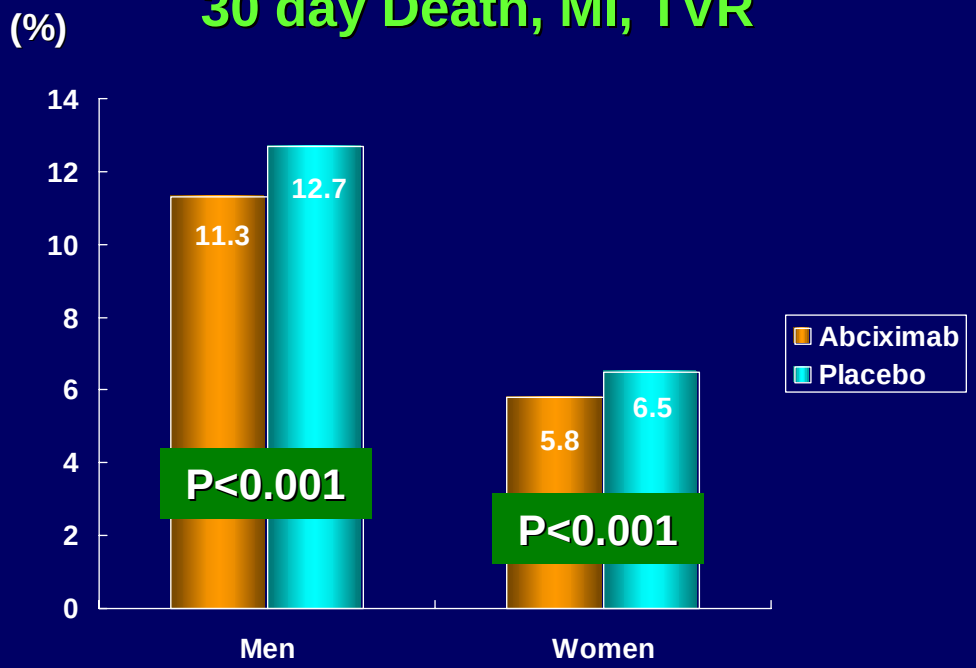


Muller C et al. JACC 2002

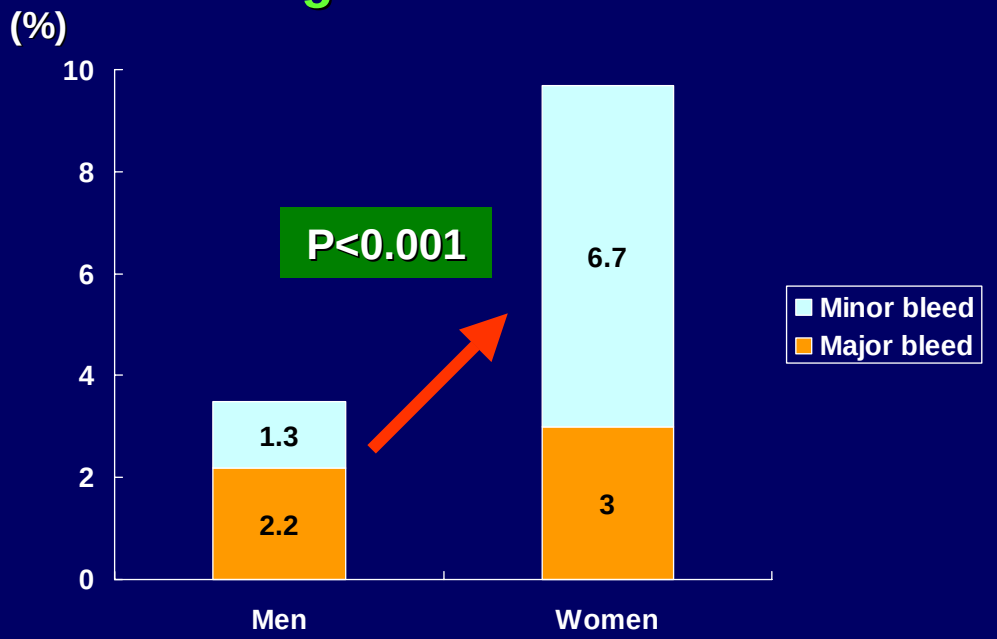
Clinical Benefits of GPIIb/IIIa Blocker with Abciximab is Independent of Gender

6,595 PCI pts (27% women, 73% men) enrolled in the EPIC, EPILOG, and EPISTENT trials were assessed in a meta analysis

30 day Death, MI, TVR



Bleeding with Abciximab

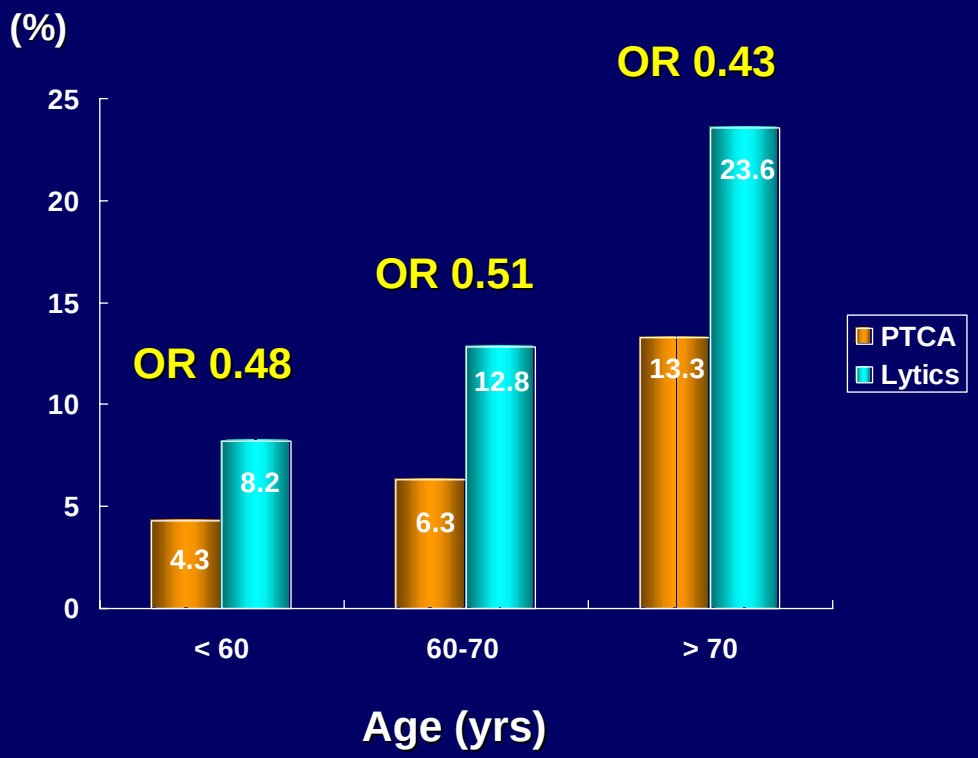


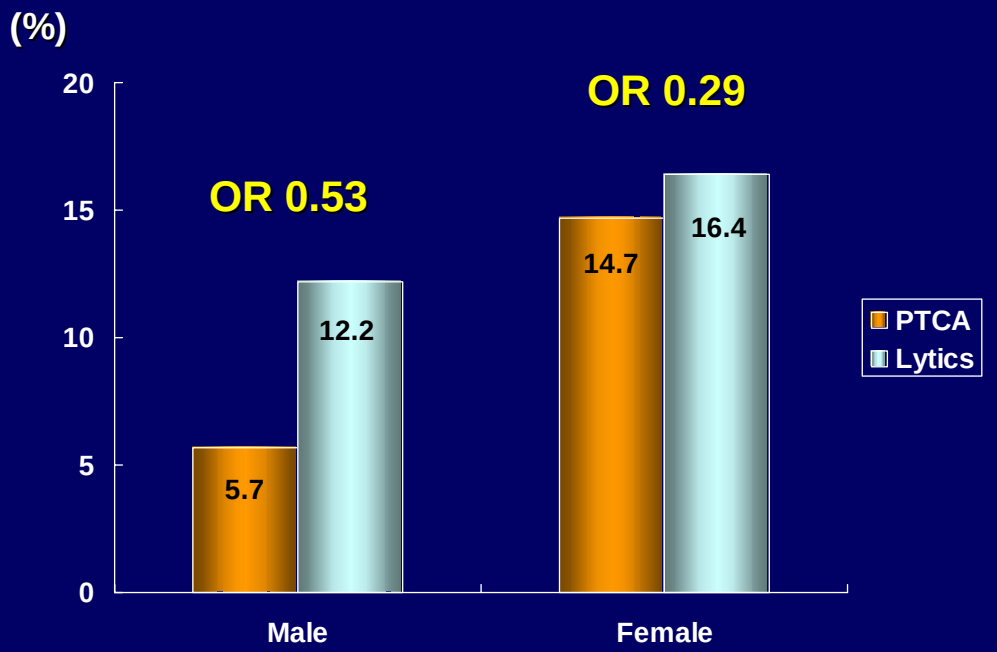
Cho L et al. JACC 2000:36;381-6

Primary PCI Superior to Lytics in Women

Meta-analysis of 10 randomized trials of primary PTCA vs. thrombolytic Rx

30-day Death or MI (%)





Weaber et al. JAMA 1997

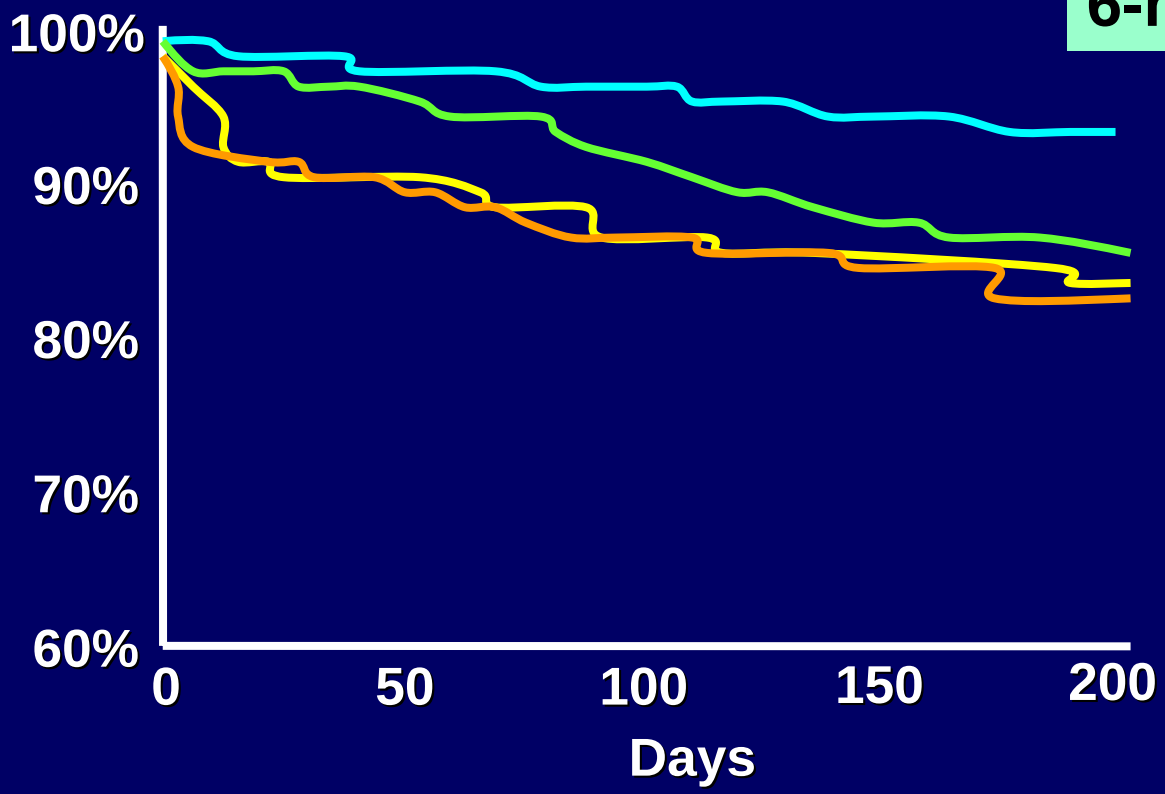
The PAMI Trials: Gender Specific Outcomes

- Multivariate predictors of mortality -

	Odds ratio	95% CI	P value
Women			
t-PA (vs. PTCA)	2.7	1.1-5.4	0.034
Advanced age	2.4	1.1-5.1	0.035
Men			
Advanced age	1.9	1.2-3.2	0.02

Stent PAMI: Event-Free Survival

N=900, Heparin-coated stent vs. PTCA



6-month cumulative events

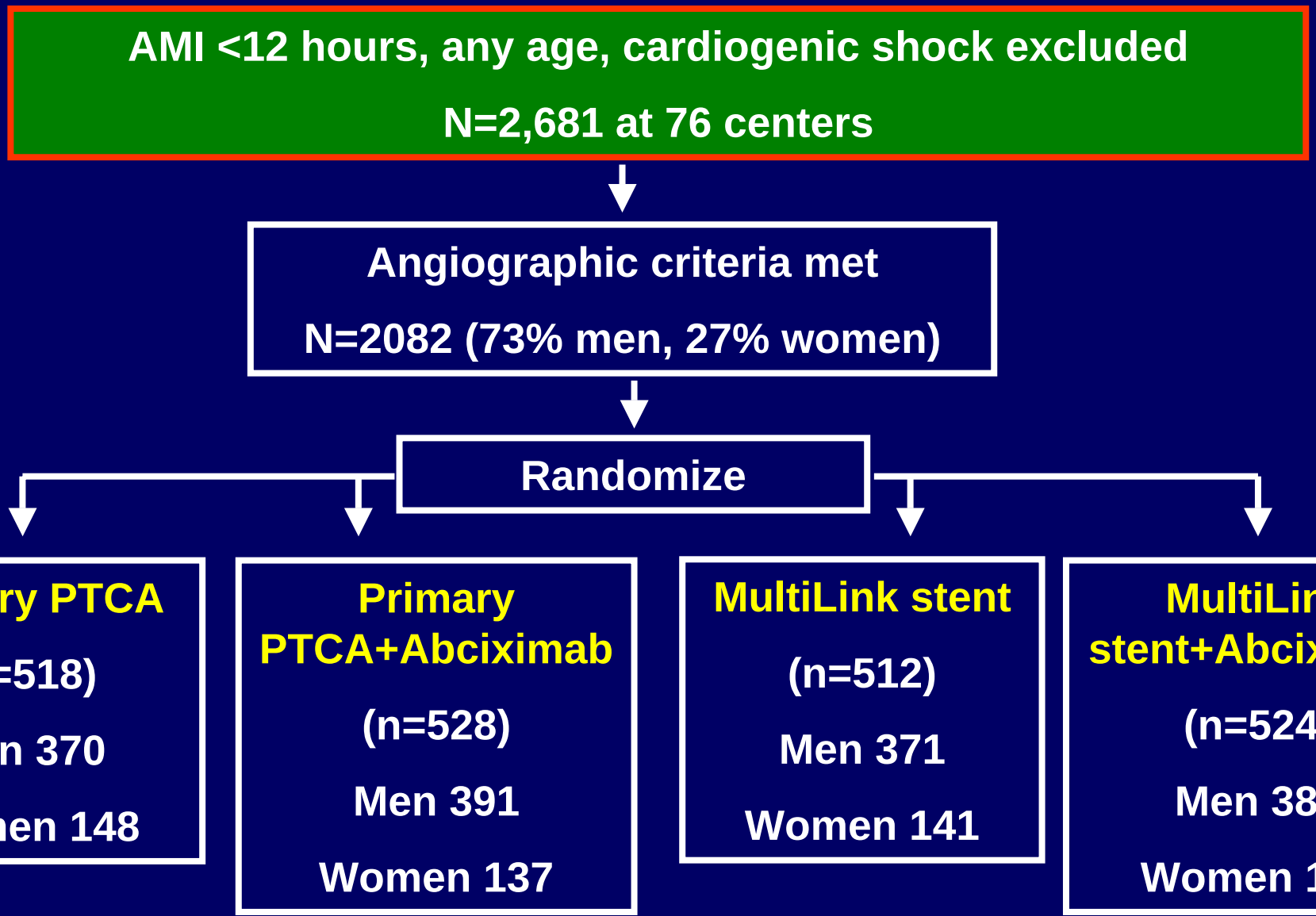
Men (Stent)	7.7%	P=0.001
Men (PTCA)	16%	
Women (Stent)	18%	P=0.52
Women (PTCA)	18.9%	

Stent PAMI: Predictors of 1-Year Mortality

-Multivariate logistic regression analysis-

	OR	95% CI	P value
Female	2.243	1.07-4.69	0.032
Age > 70 yrs	3.491	1.70-7.18	<0.001
Stent arm	2.360	1.11-5.03	0.026
Final TIMI < 3	2.995	1.27-7.06	0.012
EF %	0.946	0.92-0.98	<0.001

CADILLAC: Gender Based Outcomes



Lansky et al. Circulation 2005;111:1611-8

CADILLAC: Gender Based Outcomes

-Determinates of 1-year Mortality-

Multivariate predictors	OR	95% CI	P value
Female gender	1.77	1.03-3.04	0.037
Age	1.06	1.03-1.09	<0.0001
Killip class 2/3	2.24	1.19-4.20	0.0003
Final TIMI 3	0.54	0.31-0.93	0.007
Pre-TIMI 3	0.68	0.53-0.87	0.012
Insulin treated DM	2.70	1.03-7.11	0.012
Sx to procedure start	1.07	1.01-1.11	0.031
LAD vessel (vs. other)	2.38	1.39-4.07	0.035
# Diseased vessels	1.54	1.10-2.16	0.019

Lansky et al. Circulation 2005;111:1611-8

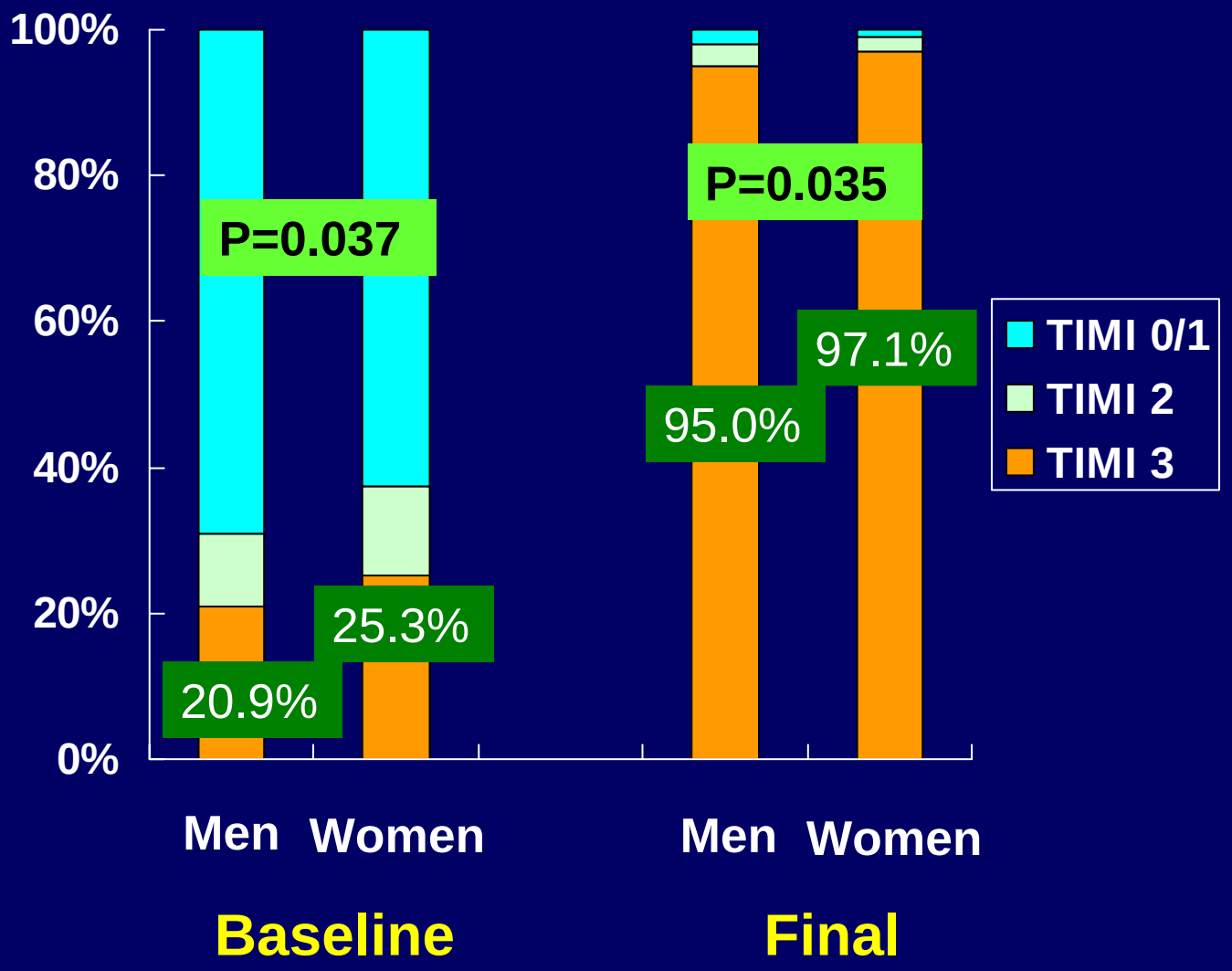
CADILLAC: Gender Based Outcomes

Baseline data

	Men	Women	P value
N	1520	562	-
Chest pain to ER (hrs)	2.6±2.5	3.0±2.6	<0.001
ER to procedure (hrs)	1.9±2.2	2.1±2.3	<0.001
Stent use	57%	57%	NS
Abciximab use	54%	54%	NS

Lansky et al. Circulation 2005;111:1611-8

CADILLAC: TIMI Flows

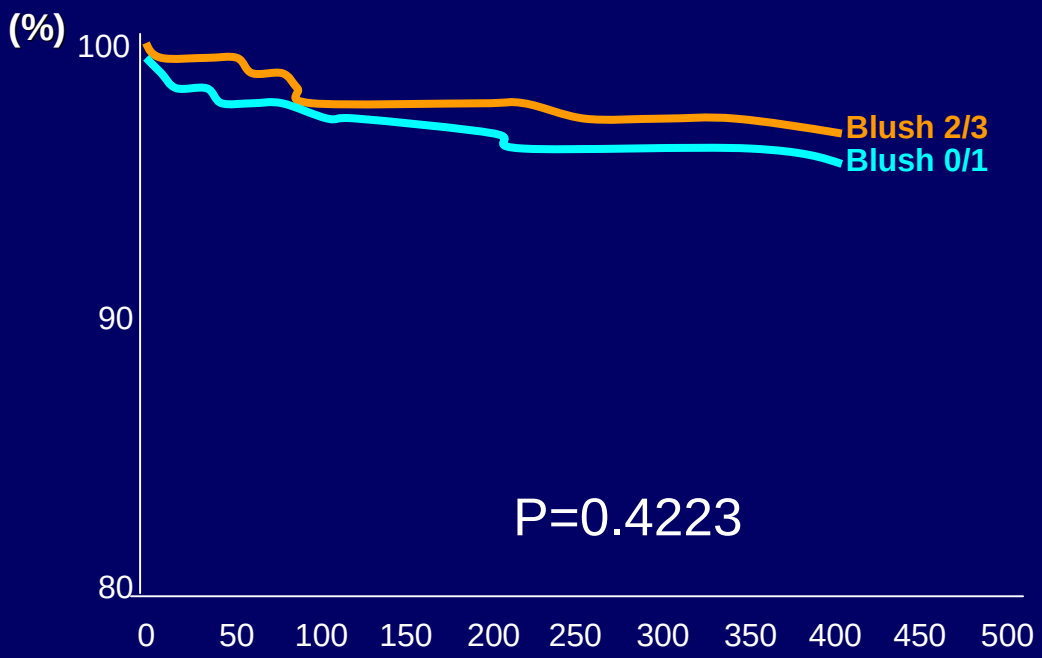


Lansky et al. Circulation 2005;111:1611-8

CADILLAC: Gender and Myocardial Blush

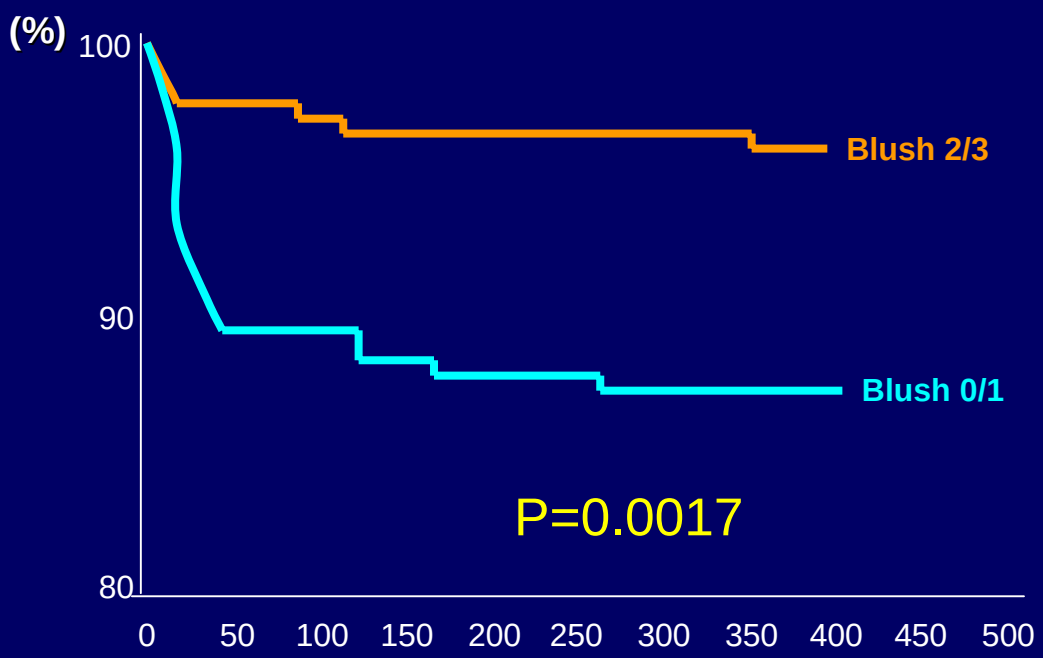
Survival curves

Male: one year freedom from death



Male (n=935)

Female: one year freedom from death



Female (n=366)

Lansky et al. Circulation 2005;111:1611-8

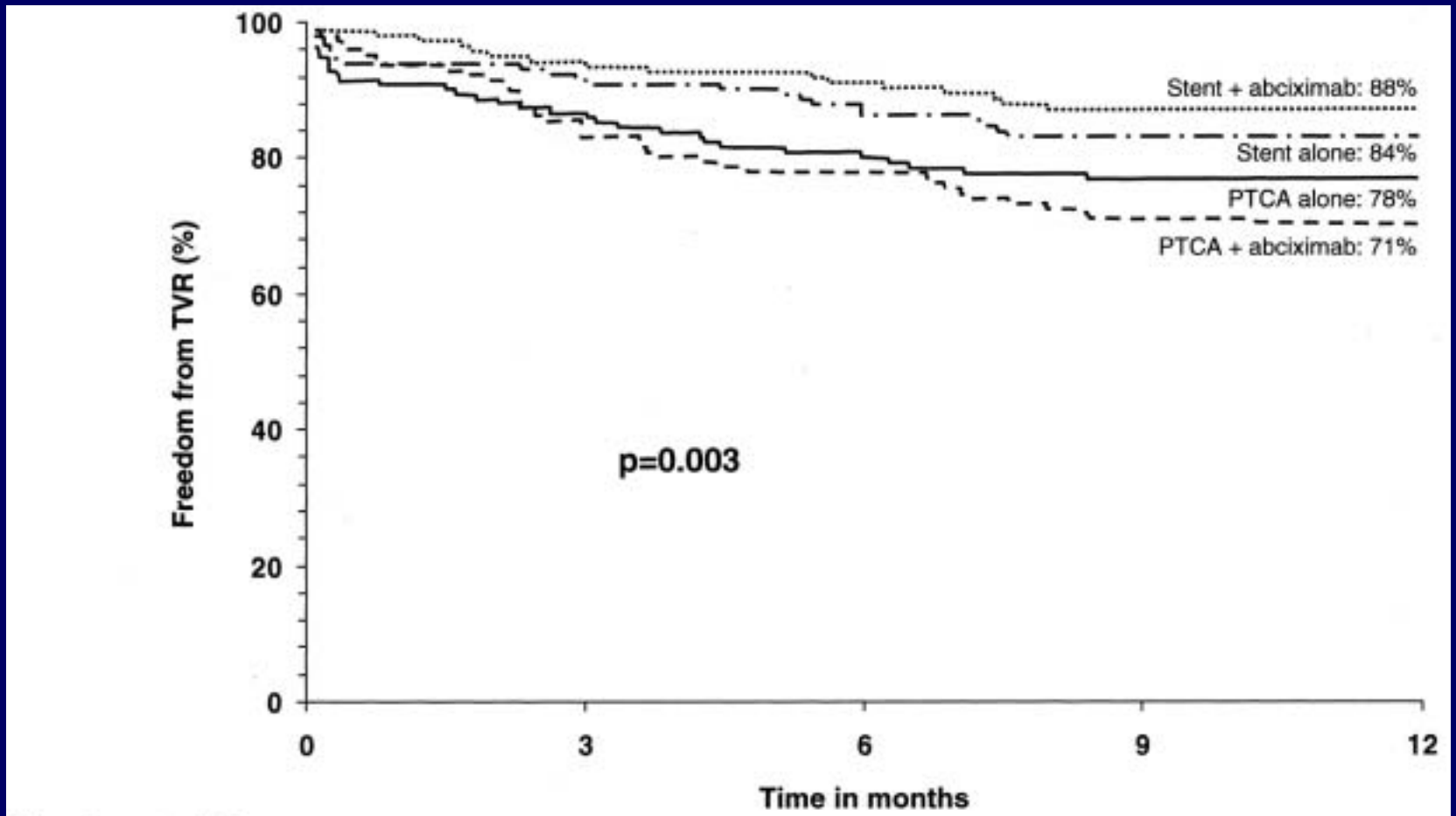
CADILLAC: Gender and Myocardial Blush

-One year multivariate predictors of death-

Multivariate predictors	OR	95% CI	P value
Male patients			
Final MBG 0/1	0.86	0.39-1.92	0.7139
Age (yrs)	1.08	1.05-1.12	<0.0001
LAD	4.84	2.04-11.52	0.0004
Triple vessel ds	3.52	1.61-7.70	0.0017
Female patients			
Final MBG 0/1	5.15	1.98-13.40	0.0008
Final TIMI 0/1	10.47	1.09-100.40	0.0042
Creatinine	3.87	1.86-8.02	0.0003
Age (yrs)	1.09	1.04-1.14	0.0006
Hypertension	4.31	1.24-14.95	0.0212

Lansky et al. Circulation 2005;111:1611-8

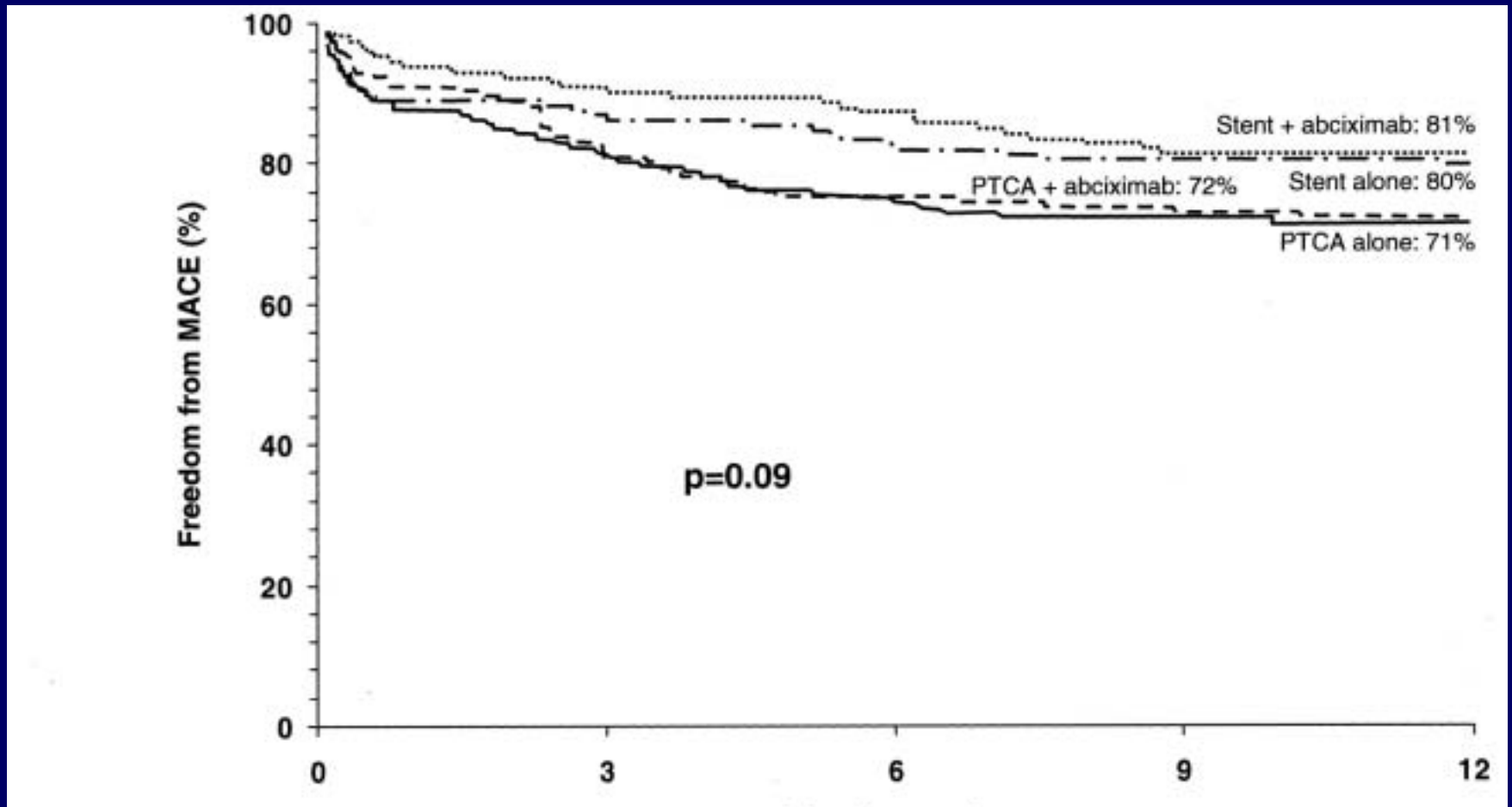
CADILLAC: Effect of Tx. on TVR in Women



Number at risk					
PTCA done	144	117	105	99	98
PTCA + abciximab	136	109	101	91	90
Stent alone	140	119	112	106	105
PTCA + abciximab	135	118	113	104	103

Lansky et al. Circulation 2005;111:1611-8

CADILLAC: Effect of Tx. on MACE in Women



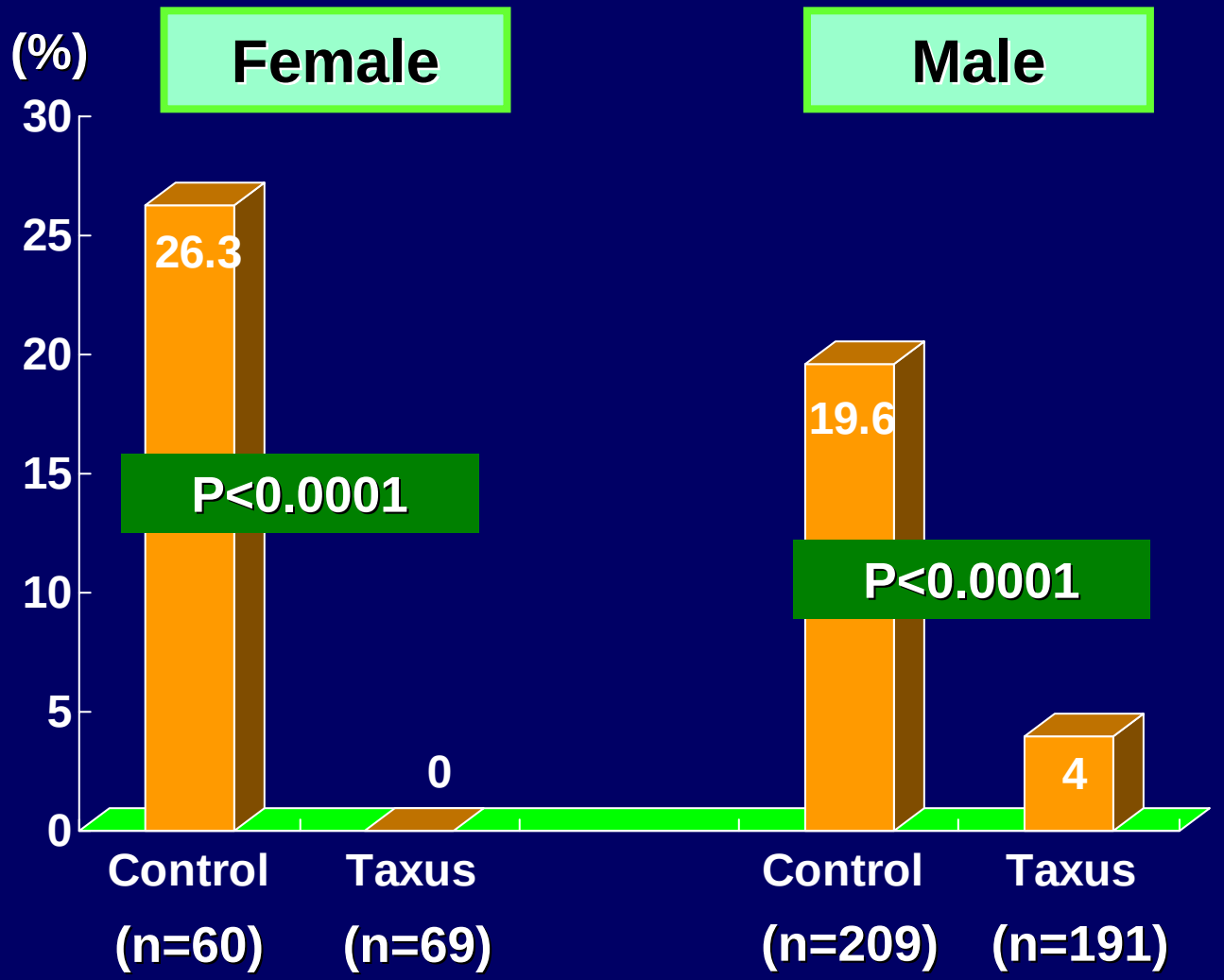
Number at risk					
PTCA done	144	117	105	100	99
PTCA + abciximab	135	110	102	99	98
Stent alone	140	118	111	108	107
PTCA + abciximab	135	120	115	105	105

Lansky et al. Circulation 2005;111:1611-8

TAXUS I & II: Gender Based Outcomes

The benefits of the Taxus stent are generalizable in women

ISR



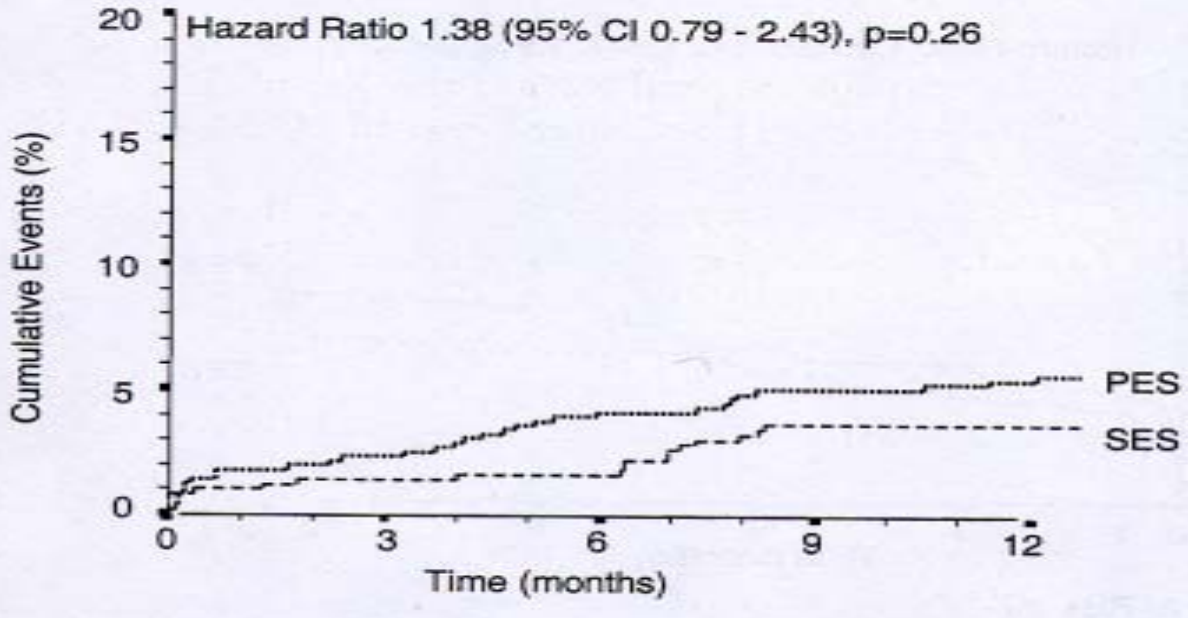
T-SEARCH Registry

(TAXUS-Stent Evaluated At Rotterdam Cardiology Hospital)

	SES Group (n=508)	PES Group (n=576)	p
Diabetes, %	18	18	0.8
Multi-vessel Ds	54	56	0.5
AMI with CS	10	13	<0.001
LM Stent	3	4	0.3
IIb/IIIa inhibitor	19	28	<0.002
Lesion types (B2, C)	76	87	<0.001
One month MACE	4.5	5.9	0.3
Stent thrombosis	0.4	1.0	0.3

JACC 2005;45:1135-41

T-SEARCH Registry
(TAXUS-Stent Evaluated At Rotterdam Cardiology Hospital)



Patients At Risk (n)					
PES	576	541	524	513	495
SES	508	486	481	470	430

Events (%, 95% CI)		
PES	4.1 (2.5-5.8)	5.4 (3.5-7.3)
SES	1.6 (0.5-2.7)	3.7 (2.0-5.3)

JACC 2005;45:1135-41

T-SEARCH Registry

(TAXUS-Stent Evaluated At Rotterdam Cardiology Hospital)

Multivariate Predictors of MACE at One Year

	HR	95% CI	p
Cardiogenic shock	4.54	2.44-8.48	<0.001
Female gender	1.72	1.22-2.43	0.002
Multi-vessel Ds	1.74	1.19-2.25	0.005
Diabetes mellitus	1.65	1.12-2.42	0.01
Left main stenting	1.96	1.10-3.48	0.02
Bifurcation stenting	1.59	1.06-2.38	0.03
Lesion types B2 or C	1.85	1.01-3.40	0.047

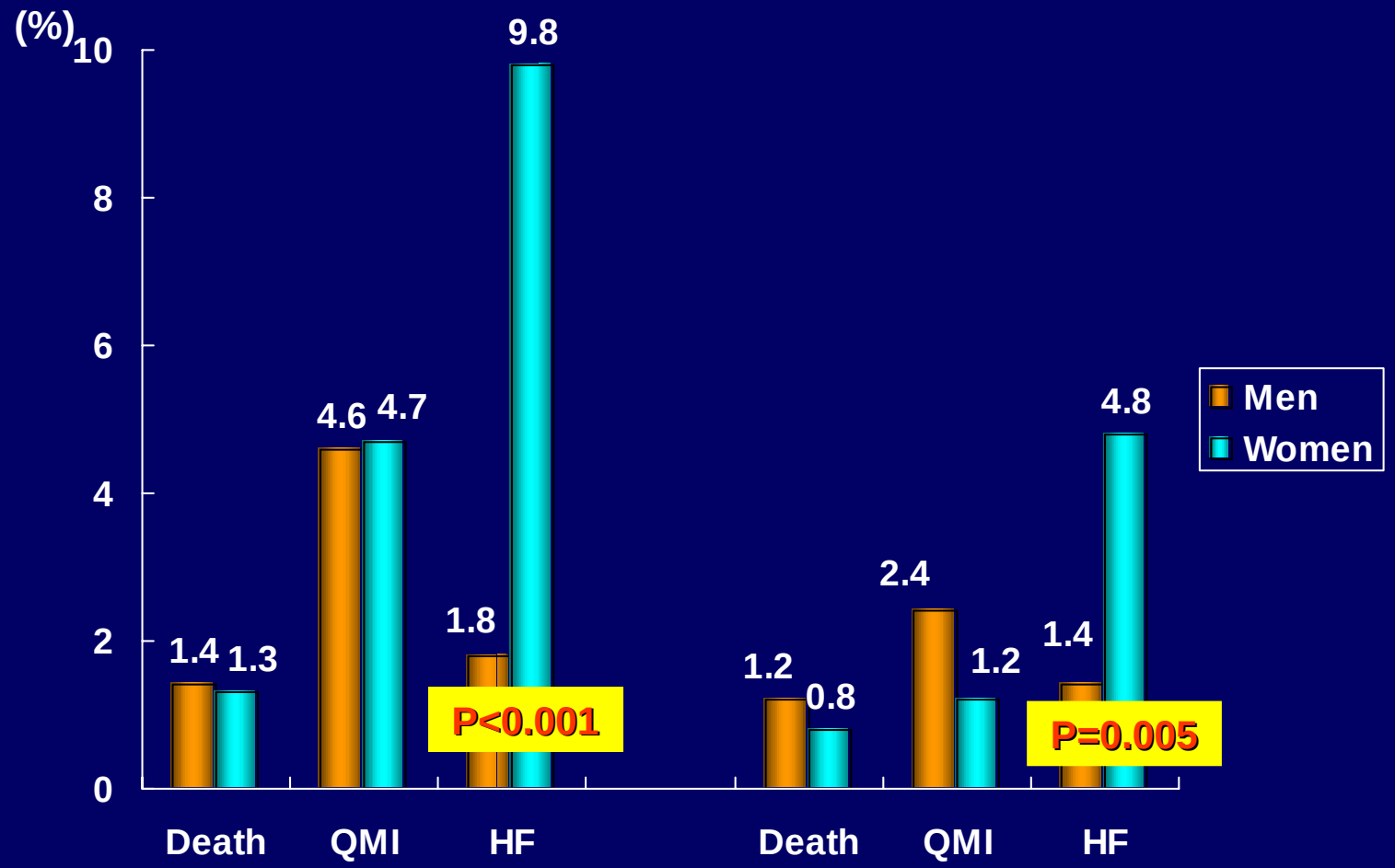
JACC 2005;45:1135-41

Cardiogenic Shock in Women

Background Issues

- Women have worse prognosis post-MI and a higher incidence of HF
- Women have higher incidence of cardiogenic shock complicating acute STEMI
- Women have a worse prognosis post PCI/CABG and a higher incidence of HF

Acute outcome in BARI



CABG

Men=670
Women=238

PTCA

Men=670
Women=251

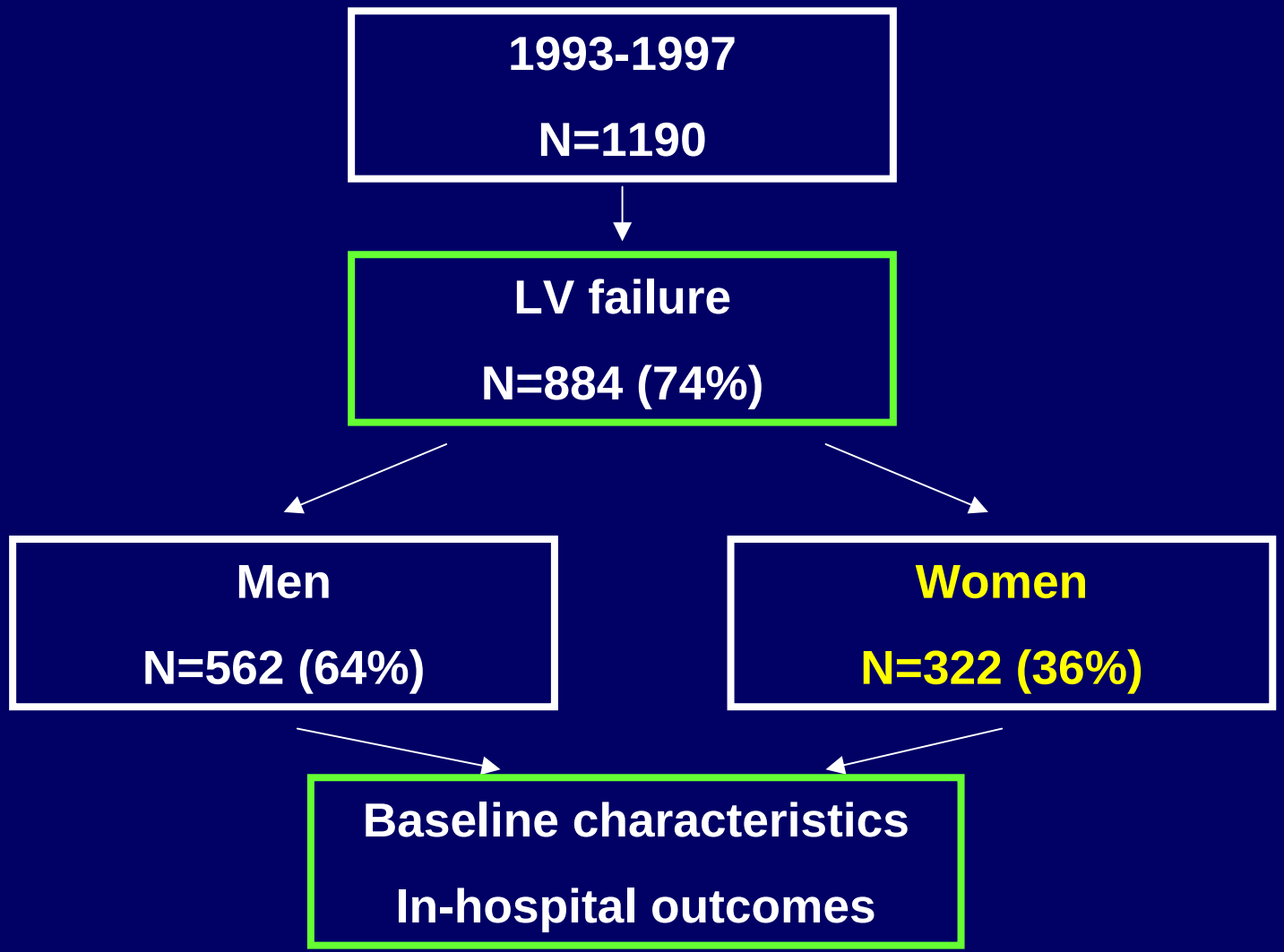
Jacobs et al. Circulation 1998;98:1279-85

Predictors of Mortality at One Year Following PCI

	Risk Ratio	95% CI
Female gender	1.32	0.88-1.96
Shock	13.22	7.51-23.28
Total occlusion	2.24	1.46-3.44
Total occlusion supplying collateral	2.03	1.20-3.44
Hx of CHF	1.97	1.26-3.07
Co-morbid disease	1.83	1.22-2.74
Hx of diabetes	1.79	1.21-2.65
Age	1.05	1.03-1.07

Jacobs et al. J Am Coll Cardiol 2002;39:1606-14

Should We Emergently Revascularize Occluded Coronaries in Cardiogenic Shock ? (SHOCK Trial Registry)



SHOCK Trial Registry

Etiologies of Cardiogenic Shock by Gender

	Men (n=709)	Women (n=482)	P Value
Predominant LV failure (%)	79.3	66.9	0.0001
Severe mitral regurgitation (%)	7.1	11.4	0.014
Ventricular septal rupture (%)	3.5	7.7	0.003
Isolated RV shock (%)	2.8	4.2	0.251
Others (%)	10.7	14.0	NS

Wong et al. J Am Coll Cardiol 2001;38:1395-1401

SHOCK Trial Registry

Baseline Characteristics

	Men (n=562)	Women (n=322)	P Value
Age (yrs)	66.8±12.3	71.4±11.1	<0.001
Hypertension (%)	45.8	62.1	<0.001
Diabetes mellitus (%)	28.3	40.8	<0.001
Prior MI (%)	44.7	32.0	<0.001
Smoking (%)	57.5	40.7	<0.001
Prior CABG (%)	12.1	6.7	<0.001
Prior PCI (%)	7.6	5.1	<0.200
Hx of CHF (%)	20.1	19.2	0.788

Wong et al. J Am Coll Cardiol 2001;38:1395-1401

SHOCK Trial Registry

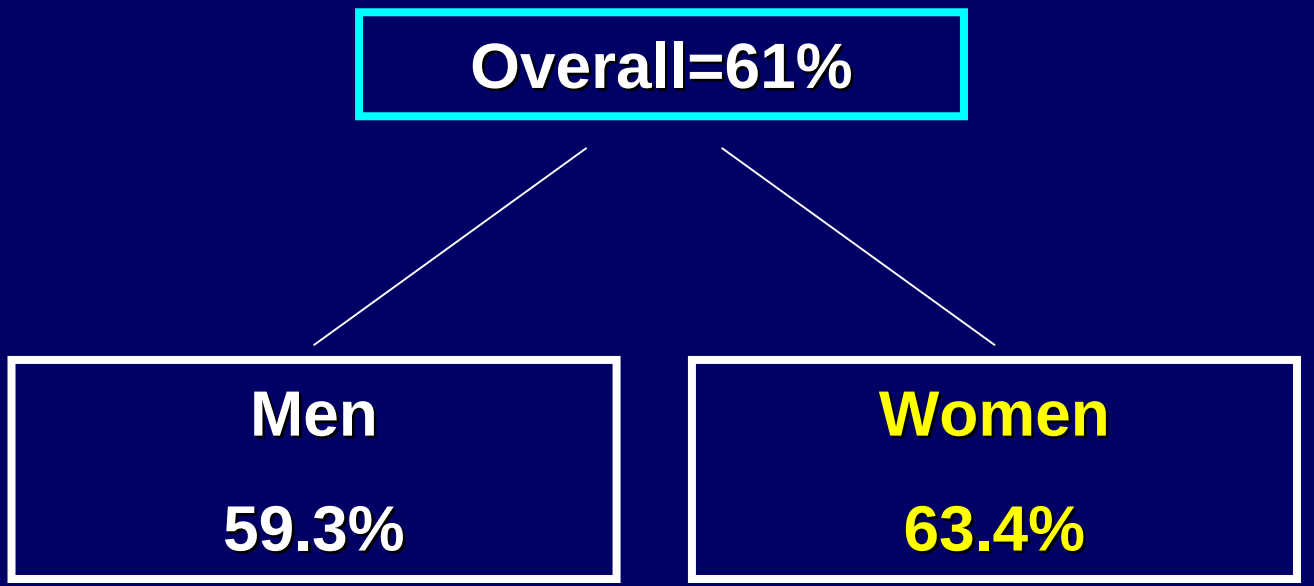
Treatment Approaches

	Men (n=292)	Women (n=172)	P Value
Treatment received (%)			
Thrombolysis	36.0	32.4	0.304
Vasopressors (n=633)	95.3	96.5	0.543
Ventilation	75.8	74.5	0.686
IABP	55.2	48.1	0.050
Transfusion	35.2	46.6	0.001
PCI	31.3	35.4	0.234
CABG	17.3	12.1	0.042

Wong et al. J Am Coll Cardiol 2001;38:1395-1401

SHOCK Trial Registry

In-hospital Mortality



P=0.252

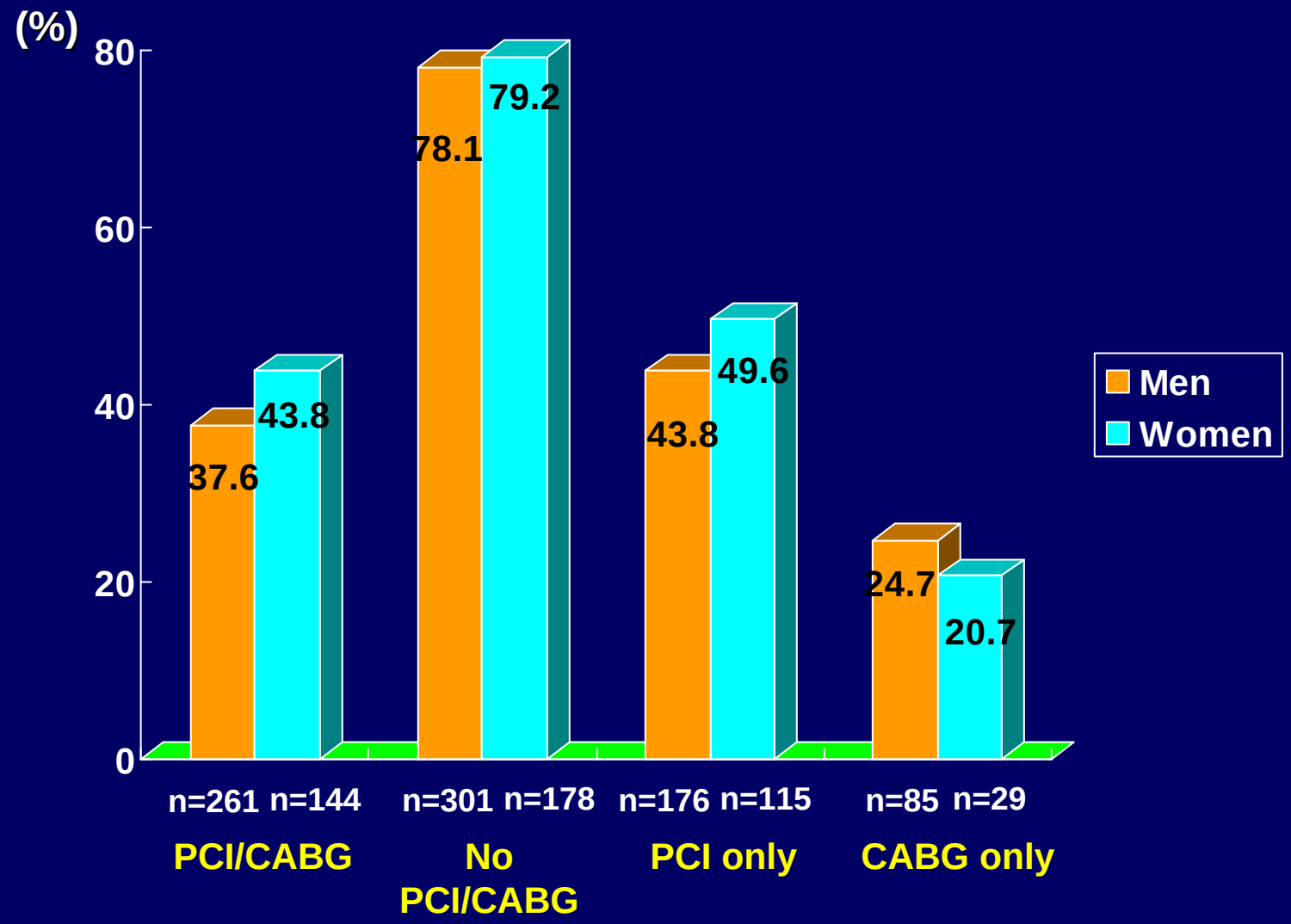
OR=1.16

95% CI 0.87-1.55

Wong et al. J Am Coll Cardiol 2001;38:1395-1401

SHOCK Trial Registry

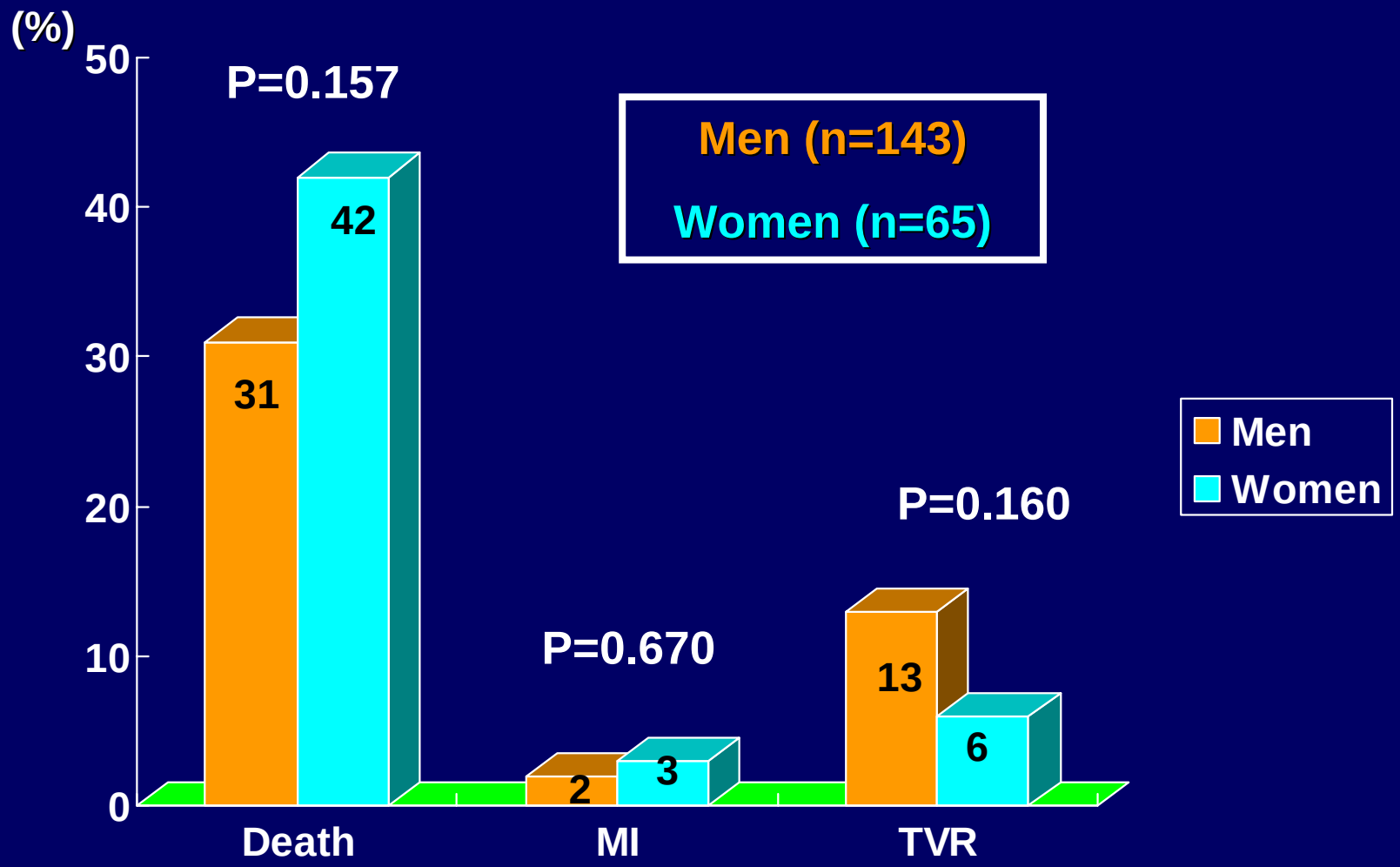
Impact of revascularization on mortality



Wong et al. J Am Coll Cardiol 2001;38:1395-1401

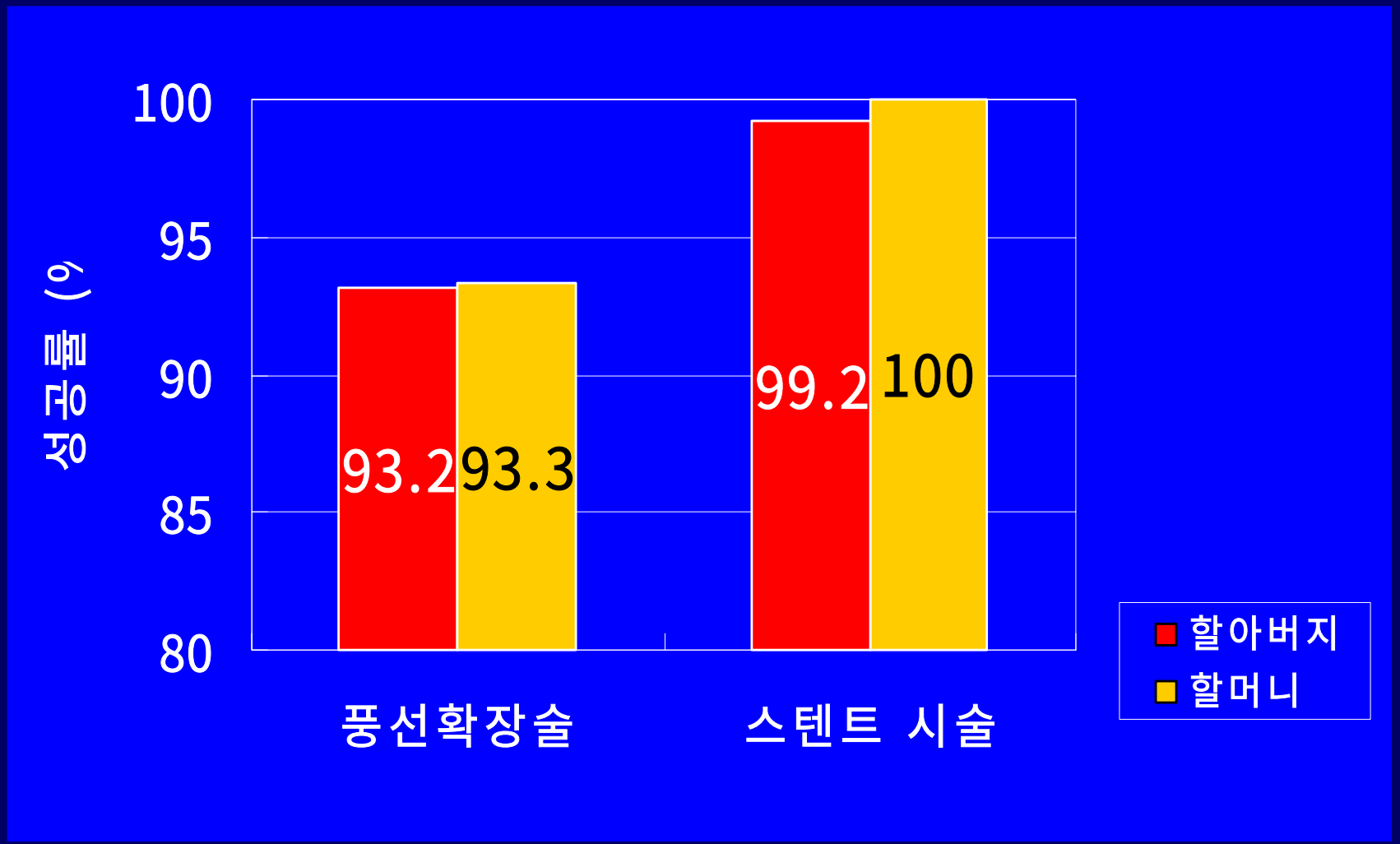
SHOCK Trial Registry

Outcomes at six months following PCI



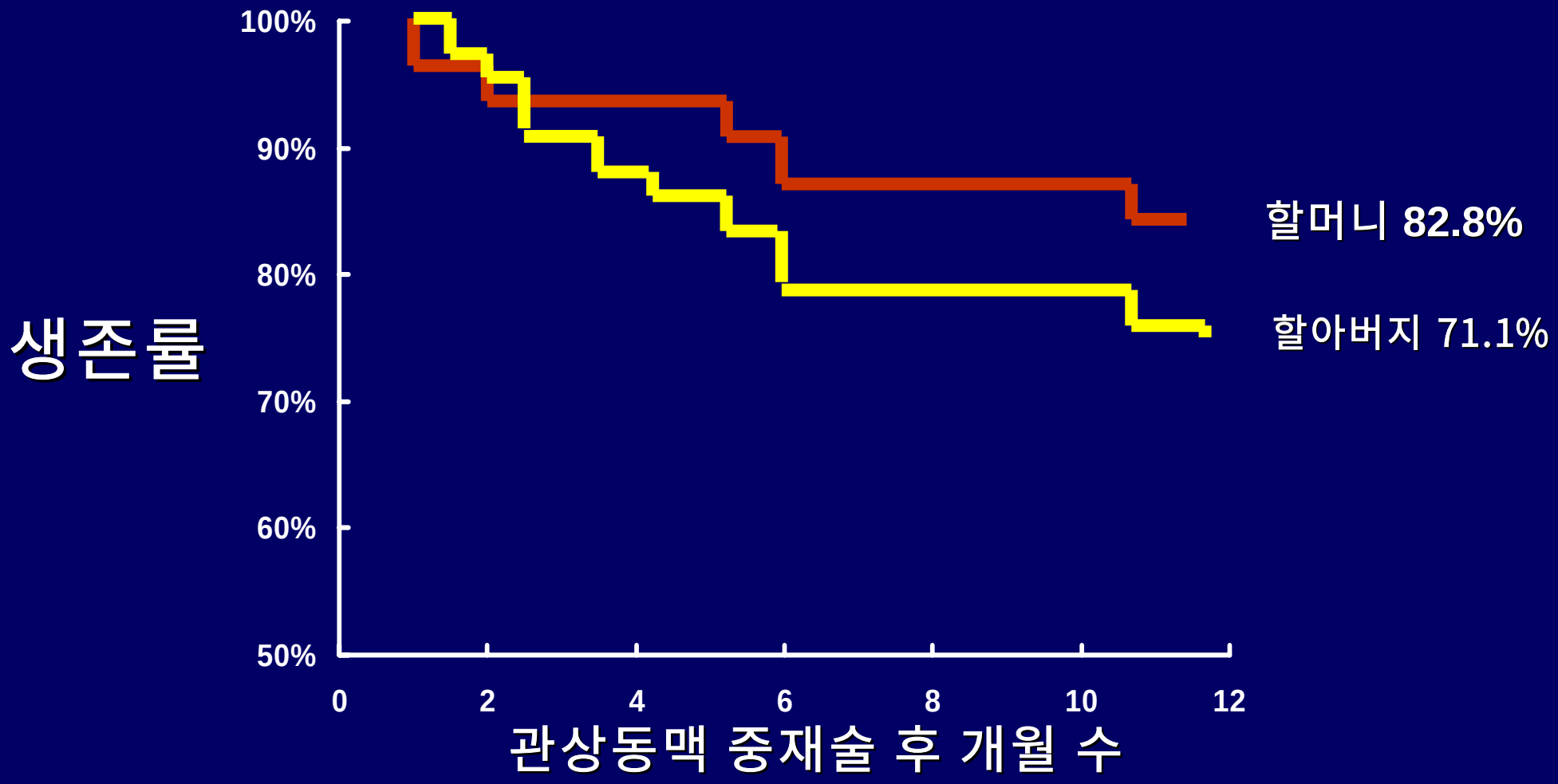
Wong et al. J Am Coll Cardiol 2001;38:1395-1401

Success Rate of Elderly Patients More Than 70 Years Between 1996 and 1998



CNUH Data. Korean J Med 2001;60:456-62

MACE Free Survival During One-Year Clinical Follow-Up after PCI in Octogenarian (1996-2001)



CNUH Data. Korean Circulation J 2002;32:864-71

One-Year Clinical Outcomes of Cardiogenic Shock after Primary PCI (147 out of 1,986 AMI Patients, 1999-2001)

	Group I (n=121) Survivor w/o MACE	Group II (n=26) MACE	*P* value
Age (years)	64.2 ± 10.6	68.1 ± 10.0	0.004
Female sex (%)	27 (22.3)	12 (46.2)	0.03
CRP (mg/dL)	3.6 ± 3.8	13.8 ± 10.0	< 0.001
Complex Lesion (>B1)	63 (52.0)	23 (88.4)	0.001
Total occlusion	53 (43.8)	20 (76.9)	0.001
IABP insertion (%)	30 (20.1)	7 (8.7)	0.012
TIMI III after PCI (%)	92 (76.0)	8 (30.8)	< 0.001
Complication after PCI	14 (11.5)	9 (34.6)	0.041
	95 % CI	OR	*P* value
Low TIMI flow after PCI	0-0.49	1.3	0.02

CNUH data. Circulation Journal 2005;69:154-8

Summary - 1

- The risk factor profile in women presenting with ACS and AMI is distinctive compared to men
- Women are older, have more HT and DM, but less extensive CAD and better preserved LVEF
- In ACS, women benefit from an early invasive approach with Cath/PCI within the first 48 hours

Summary - 2

- In AMI, women benefit from immediate primary PCI with stent implantation +/- IIb/IIIa inhibitor
- A high mortality is seen among women with impaired myocardial perfusion
- More expeditious time from symptom onset to balloon reperfusion and adjunctive pharmacology would likely improve these outcomes in female patients

Conclusion

Active treatment of women with ACS can improve event free survival after PCI or CABG