# THE ROLE OF BETA-BLOCKERS IN THE MANAGEMENT AFTER MYOCARDIAL INFARCTION

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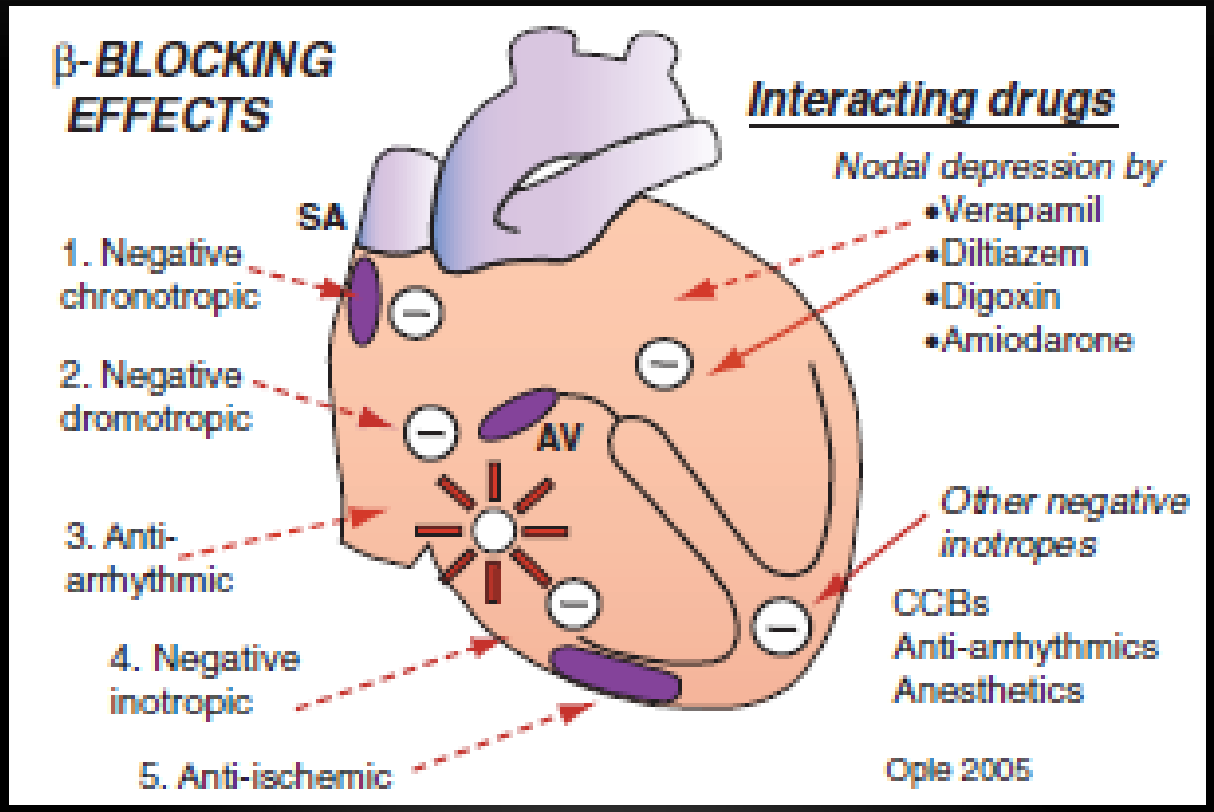
# BETA-BLOCKERS REPRESENT 2 OF 7 RX STEPS THAT SHOULD BE PROVIDED IN ALL ACUTE MYOCARDIAL INFARCTIONS

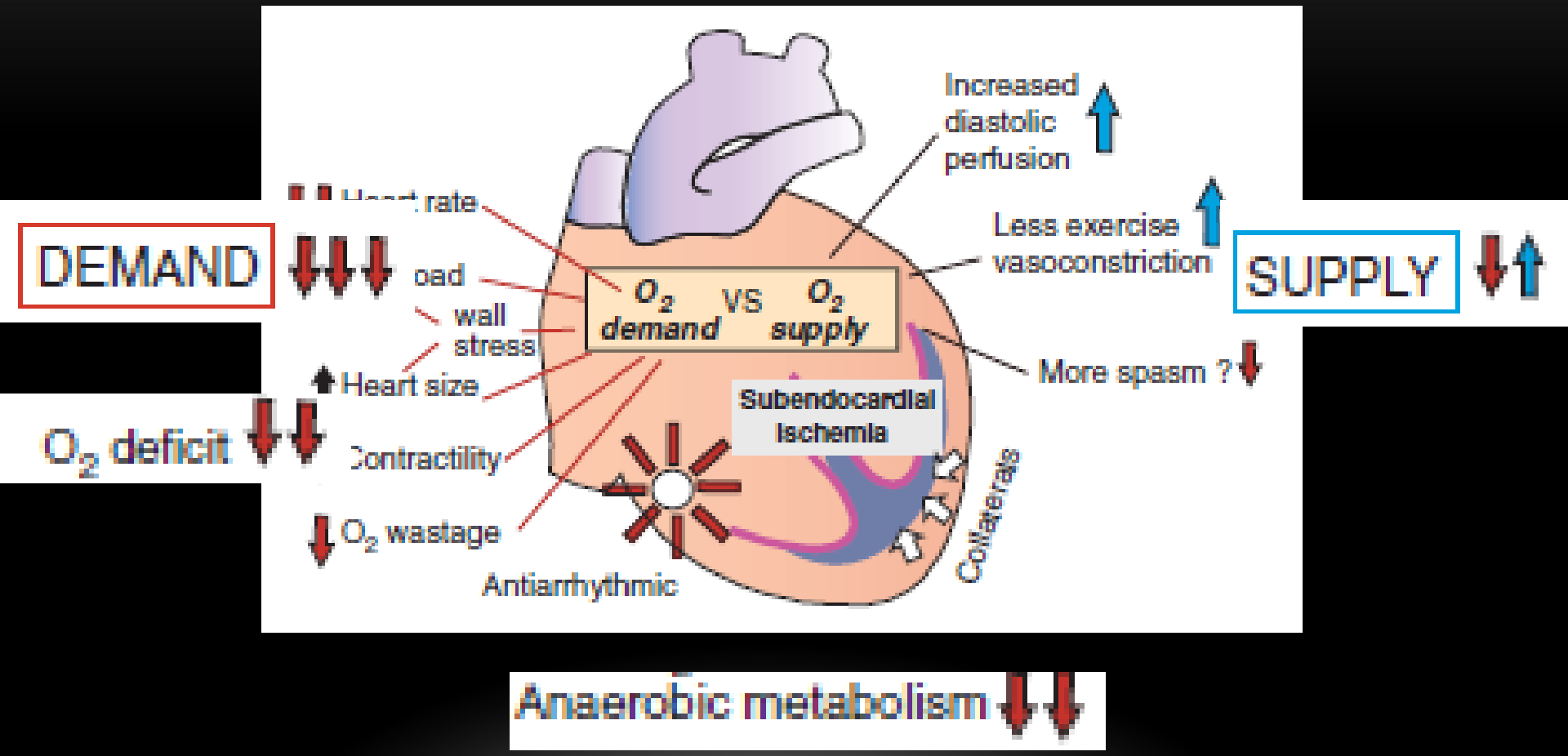
- Aspirin - Early Administration
- Aspirin at Discharge
- Beta-Blocker - Early Administration
- Beta-Blocker at Discharge
- ACE or ARB at Discharge if LV Systolic Dysfunction
- Statin – Early Administration
- Timely Initiation of Reperfusion
- Life-Style Modification

# CARDIAC EFFECTS OF BETA-ADRENERGIC BLOCKING DRUGS



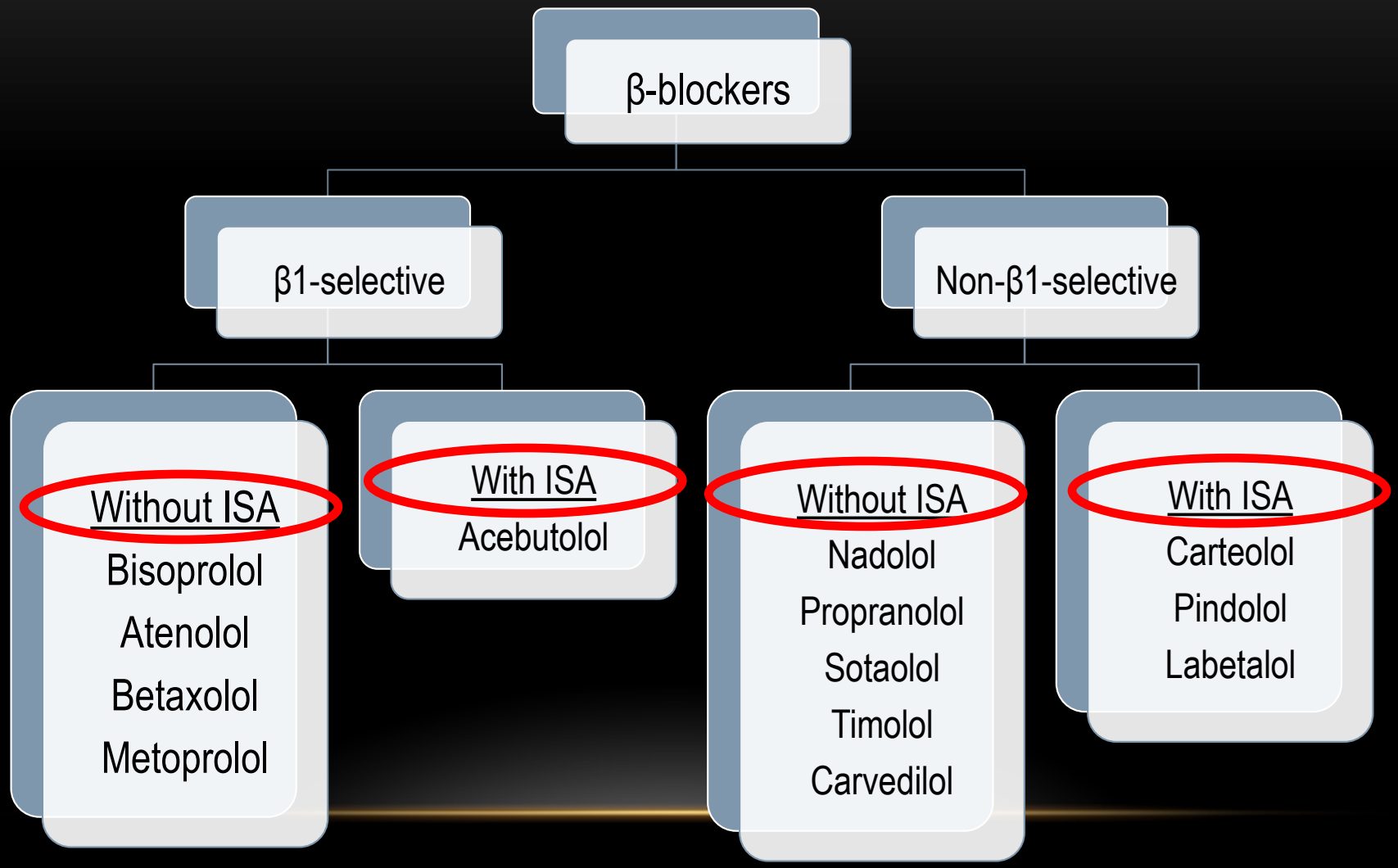

Opie LH, Gersh BJ, et al. Drugs for the Heart. 7th Ed, 2009

# EFFECTS OF BETA-BLOCKADE ON ISCHEMIC HEART




Opie LH, Gersh BJ, et al. Drugs for the Heart. 7th Ed, 2009

# CLASSIFICATION OF β-BLOCKERS



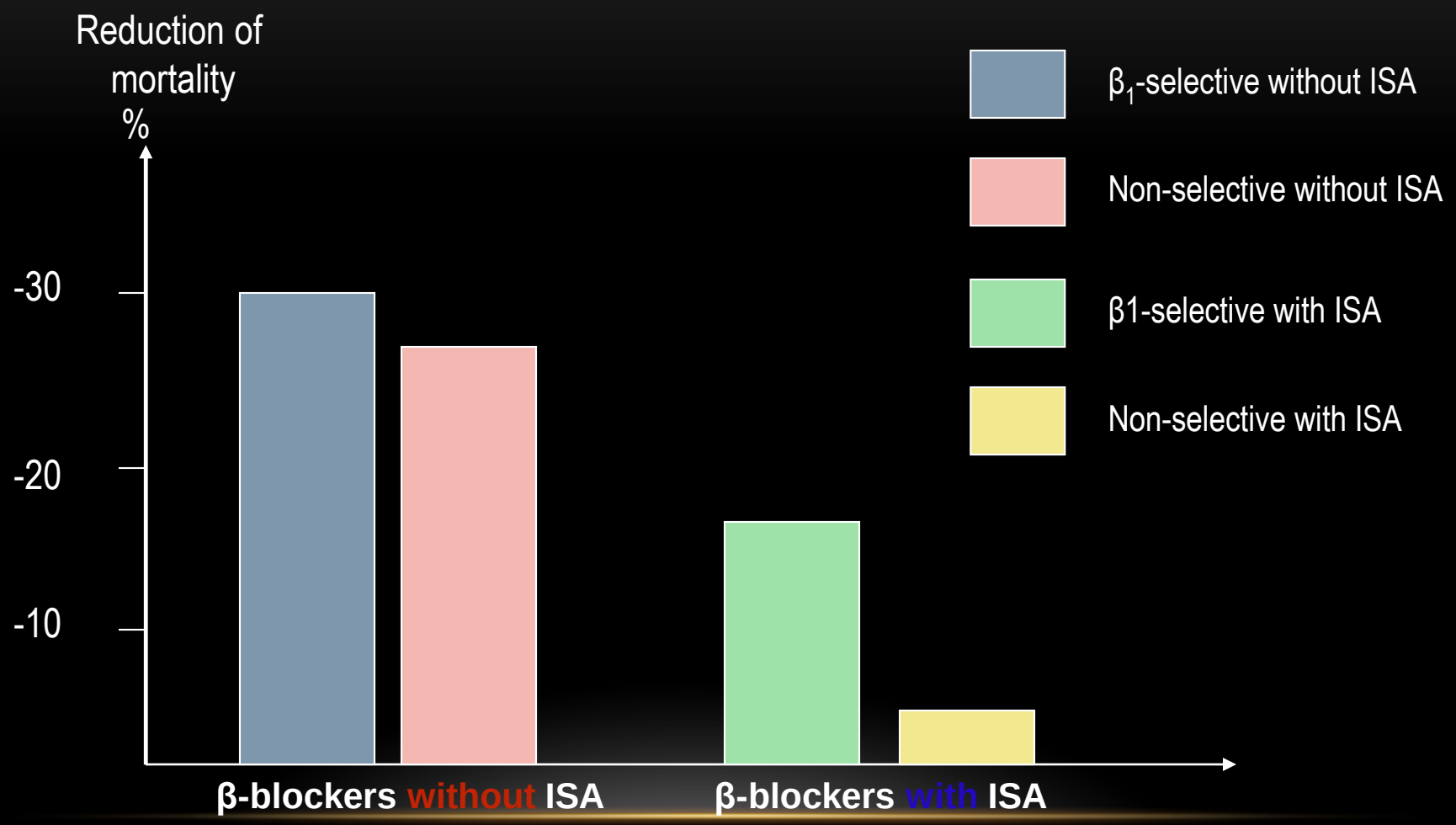

ISA: Intrinsic Sympathomimetic Activity

Adapted from: European Heart Journal (2004) 25, 1341-1362

# Intrinsic Sympathomimetic Activity (ISA) or Partial Agonist Effect

The most obvious pharmacological aspect of Beta-blockers with ISA is that they produce less of a decrease in resting heart rate than agents without ISA

# SECONDARY PREVENTION OF MYOCARDIAL INFARCTION WITH DIFFERENT TYPES OF BETA-BLOCKERS






Adapted form:***Progress*** *in* ***Cardiovascular Diseases****. 27(5):335-71, 1985 Mar-Apr*

# WHY IS DELIVERING RELIABLE AND EVIDENCE-BASED AMI CARE IMPORTANT?

- **This is a frequent and important clinical problem.**

  Every year, an estimated 1.1 million people in the United States are diagnosed with an acute myocardial infarction, and approximately 350,000 of these patients die during the acute phase.

- **Lives can be saved by good medical care.**

  Medicare estimates that by implementing all seven evidence-based care components, acute myocardial infarction inpatient mortality will be reduced by as much as 40%.

ACCF/AHA Guideline for The Management of ST-Elevation Myocardial Infarction, 2013
McGlynn et al. The Quality of Healthcare Delivery To Adults in the United States. N Engl J Med 2003

# NEED FOR THIS PRESENTATION
## MEDICARE QUALITY DATA DEMONSTRATED

- **Despite knowledge since the early 1980s** of the benefits of beta-adrenergic blockers, after acute myocardial infarction, only 45% received beta-blockers.

- **Subsequent studies have shown improvement,** but there is still a big treatment gap.

McGlynn et al. The Quality of Healthcare Delivery To Adults in the United States. N Engl J Med 2003

# LET'S REVIEW THE DATA THAT SUPPORTS THE BENEFIT OF BETA-BLOCKER THERAPY IN AMI

- Pre-Thrombolytic Era
- Reperfusion Era (Lytics, PCI, and CABG)

# PRE-TROMBOLYTIC ERA

# BETA BLOCKER HEART ATTACK TRIAL (BHAT) 1986

- 3,837 patients randomized
- Propranolol or placebo and followed for 25 months

  - Propranolol significantly reduced:
    - total mortality
    - cardiovascular mortality
    - sudden death
    - nonfatal infarction

A randomized trial of propanolol in patients with acute myocardial infarction. JAMA 1982;247

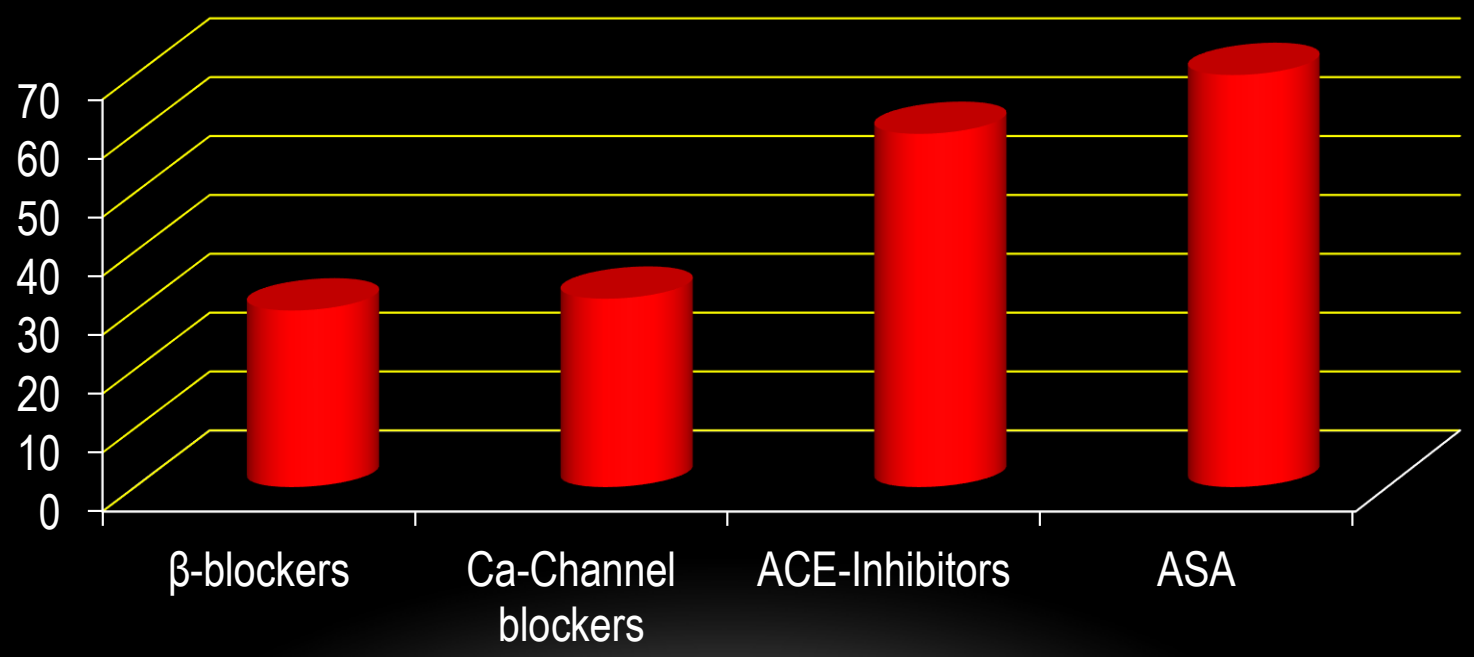
# CONCLUSION OF PRE-TROMBOLYTIC ERA

Multiple studies for over 20 years have demonstrated:

→ Beta-blockers in patients Pre-Thrombolytic Era have a mortality benefit ranging between 10 and 15%

# REPERFUSION ERA

# UNDER-USAGE OF BETA-BLOCKERS AFTER MYOCARDIAL INFARCTION




Ellerbeck et al. JAMA 1995; 273: 1509

# BETA BLOCKADE AFTER MYOCARDIAL INFARCTION - 1999

- Meta analysis of 31 long-term trials performed during the reperfusion era on almost 25,000 patients

- 10.1% reduction in overall mortality

Freemantle et al. Beta Blockade after Myocardial Infarction: Systematic Review and Meta Regression Analysis. BMJ 1999 318:1730

# INTERNATIONAL STUDY OF INFARCT SURVIVAL ISIS-1

- 16,027 patients randomized
- Atenolol or placebo followed for 1 year

- Atenolol significantly reduced :
  - Total mortality
  - Cardiovascular mortality

A randomized trial of intravenous atenolol among 16,027 cases of suspected acute myocardial infarction : ISIS-1. Lancet 1986;2

# CAPRICORN-2001

- 1.959 patients randomized
- Carvedilol or placebo followed for 1 year
- Demonstrate the benefit carvedilol following acute MI in patients with LV dysfunction
- Carvedilol significantly reduced :
  - All-cause mortality
  - All-cause mortality or hospital admission secondary to cardiovascular cause
  - Sudden death
  - Hospital admission for heart failure
  - Non-fatal MI

Effect of carvedilol on outcome after myocardial infarction in patients with left-ventricular dysfunction : the CAPRICORN randomized trial. Lancet 2001 May 5

# CONCLUSION OF TROMBOLYTIC ERA

- Large trials have demonstrated that beta-blockers benefit all these AMI patient groups
  - No reperfusion therapy
  - Thrombolytic therapy
  - Percutaneous coronary intervention
  - CABG

# CAUTION #1: DOCUMENTATION

- Failure to give a beta-blocker, with a good clinical reason, and to then not appropriately document this, is often analyzed and publicly interpreted as underuse, a gap in care or poor medical *care.*

- The further assumption is that these non- treated patients often suffered a higher unnecessary rate of death and complications.

# THE PRACTICE STANDARD FOR BETA BLOCKERS MAKES TWO MEASUREMENTS AND REQUIRES TWO CHART DOCUMENTATIONS :

- Was it given in the first 24 hours?
- Was the patient discharged on a BB?

# 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction

1. Oral beta blockers should be initiated in the first 24 hours in
3. Patients with initial contraindications to the use of beta blockers in the first 24 hours after STEMI should be reevaluated to determine their subsequent eligibility. (*Level of Evidence: C*)

third-degree heart block, active asthma, or reactive airways disease) (414–416). (*Level of Evidence: B*)

ization for all patients with STEMI and with no contraindications to their use (417,418). (*Level of Evidence: B*)

3. Patients with initial contraindications to the use of beta blockers in the first 24 hours after STEMI should be reevaluated to determine their subsequent eligibility. (*Level of Evidence: C*)

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http://dx.doi.org/10.1016/j.jacc.2012.11.019

# 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction

## 8.1. Beta Blockers: Recommendations

1. It is reasonable to administer intravenous beta blockers at the time of presentation to patients with STEMI and no contraindications to their use who are hypertensive or have ongoing ischemia (414–416). (*Level of Evidence: B*)

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http://dx.doi.org/10.1016/j.jacc.2012.11.019

European Heart Journal (2012) **33**, 2569–2619
doi:10.1093/eurheartj/ehs215

ESC GUIDELINES

# ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation

Oral treatment with beta-blockers should be considered during hospital stay and continued thereafter in all STEMI

Oral treatment with beta-blockers is indicated in patients with heart failure or LV dysfunction.

Intravenous beta-blockers must be avoided in patients with hypotension or heart failure.

Intravenous beta-blockers should be considered at the time of presentation in patients without contraindications, with high blood pressure, tachycardia and no signs of heart failure.

# CAUTION #2:
# DO NO HARM

What are clinical situations where a beta-blocker should not be given and could hurt the patient ?

# CONTRAINDICATIONS TO BETA-BLOCKER USE DURING ACUTE MYOCARDIAL INFARCTION

- Sign of Heart Failure
- Low output state
- Increased risk of cardiogenic shock
- Prolonged first-degree or high-grade AV block
- Reactive airway disease

ACCF/AHA Guideline for The Management of ST-Elevation Myocardial Infarction, 2013
ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation, 2012

# COMMIT-CCS-2 TRIAL 2005

The data of the recently completed COMMIT Trial reinforces that beta-blocker therapy should be withheld if the patient is at all unstable.

Early intravenous then oral metoprolol in 45,852 patients with acute myocardial infarction : randomized, placebo-controlled trial. Lancet 2005 Nov 5

# CAUTION #3:
# DO NOT WITHHOLD BETA-BLOCKER THERAPY FOR INAPPROPRIATE REASONS

- Elderly
- Diabetes Mellitus
- UAP/NSTEMI
- Congestive Heart Failure
- Hypertension
- COPD

The American Journal of Emergency Medicine

# Beta-blocker use in elderly ED patients with acute myocardial infarction.

Vega DD, Dolan KL, Pollack ML.

**Abstract**

**BACKGROUND:** Despite the effectiveness of early beta-blocker (BB) use in reducing mortality in acute myocardial infarction (AMI), they remain underutilized in the emergency department (ED) management of AMI. The elderly, with higher AMI mortality, and women, may be particularly vulnerable to underutilization of BB.

**OBJECTIVE:** To determine the effect of age and gender on BB use in AMI in the ED.

**METHODS:** A retrospective study of all ST-elevation AMI (STEMI) ED patients presenting to a community hospital ED from

Despite convincing evidence of effectiveness, BB remain underutilized in ED management of AMI, especially in the elderly.

group was 244 (63%). Of patients without contraindications to BB, 53% did not receive BB in the ED. By gender, 83 (54%) males and 46 (51%) females did not receive BB (P=.669). By age, 96 subjects (59%) over age 60 and 33 subjects (41%) under age 60 did not receive BB (P=.011).

**CONCLUSION:** Despite convincing evidence of effectiveness, BB remain underutilized in ED management of AMI, especially in the elderly. There does not appear to be a gender difference in BB use. Education programs should be directed towards emergency physicians regarding BB use in AMI, especially in elderly ED patients.

American Journal of Emergency Medicine
Volume 24, Issue 4 , Pages 435-439, July 2006

JACC
JOURNAL of the AMERICAN COLLEGE of CARDIOLOGY

# Effectiveness of Beta-Blocker Therapy After Acute Myocardial Infarction in Elderly Patients With Chronic Obstructive Pulmonary Disease or Asthma

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Thomas A. Marciniak, MD,§ Harlan M. Krumholz, MD, FACC*†‡‖
*New Haven and Middletown, Connecticut, and Baltimore, Maryland*

**OBJECTIVES** We evaluated the use and effectiveness of beta-blocker therapy after acute myocardial infarction (AMI) for elderly patients with chronic obstructive pulmonary disease (COPD) or asthma.

**CONCLUSIONS** Beta-blocker therapy after AMI may be beneficial for COPD or asthma patients with mild disease. A survival benefit was not found for elderly AMI patients with more severe pulmonary disease. (J Am Coll Cardiol 2001;37:1950–6) © 2001 by the American College of Cardiology

COPD or asthma.

**RESULTS** Of 54,962 patients without contraindications to beta-blockers, patients with COPD or asthma (20%) were significantly less likely to be prescribed beta-blockers at discharge after AMI. After adjusting for demographic and clinical factors, we found that beta-blockers were associated with lower one-year mortality in patients with COPD or asthma who were not on beta-agonist therapy (relative risk [RR] = 0.85, 95% confidence interval [CI] 0.73 to 1.00), similar to patients without COPD or asthma (RR = 0.86, 95% CI 0.81 to 0.92). A survival benefit for beta-blockers was not found among patients concurrently using beta-agonists or with severe COPD or asthma.

**CONCLUSIONS** Beta-blocker therapy after AMI may be beneficial for COPD or asthma patients with mild disease. A survival benefit was not found for elderly AMI patients with more severe pulmonary disease. (J Am Coll Cardiol 2001;37:1950–6) © 2001 by the American College of Cardiology

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American Diabetes Association. Diabetes Care

# The Effectiveness of β-Blockers After Myocardial Infarction in Patients With Type 2 Diabetes

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statistically significant. Similarly, use of β-blockers was not independently associated with reduced risk for recurrent MI. Importantly, however, the rate of rehospitalization within 30 days of starting a β-blocker was not increased, suggesting that the use of these agents is not associated with major adverse effects in people with type 2 diabetes.

1.40 [0.83–2.37]) between the groups.

**CONCLUSIONS** — β-Blocker therapy post-MI was not associated with reduced mortality or fewer recurrent events in people with type 2 diabetes in routine practice, although these medications were safe in this population.

*Diabetes Care* 28:2113–2117, 2005

THE AMERICAN JOURNAL of MEDICINE®

Official Journal of the Alliance for Academic Internal Medicine

# Impact of Acute Beta-Blocker Therapy for Patients with Non–ST-Segment Elevation Myocardial Infarction

Chadwick D. Miller, MD,[a] Matthew T. Roe, MD, MHS,[b] Jyotsna Mulgund, MS,[b] James W. Hoekstra, MD,[a] Renato Santos, MD,[a] Charles V. Pollack, Jr., MD, MA,[c] E. Magnus Ohman, MD,[b] W. Brian Gibler, MD,[d] Eric D. Peterson, MD, MPH[b]

## ABSTRACT

**PURPOSE:** Early use of beta-blockers is a quality indicator for the treatment of patients with non–ST-segment elevation myocardial infarction (NSTEMI), despite limited data from randomized clinical trials in this population. We sought to determine the impact of acute beta-blocker therapy on outcomes in patients

**CONCLUSIONS:** The majority of NSTEMI patients receive acute beta-blocker therapy. Certain patient subgroups remain undertreated. Because treatment with acute beta-blockers was associated with improved clinical outcomes in nearly all patient subgroups assessed, broader use in patients with NSTEMI appears warranted. © 2007 Elsevier Inc. All rights reserved.

associated with beta-blocker use and the impact of beta-blocker therapy on unadjusted, risk-adjusted, and propensity matched outcomes in the overall sample and among selected high-risk subgroups.

**RESULTS:** A total of 82.5% of patients without documented contraindications received acute beta-blocker therapy. Factors strongly associated with acute beta-blocker use included prior beta-blocker use, higher presenting systolic blood pressure, lower heart rate, lack of signs of heart failure, and cardiology care. Acute beta-blocker use was associated with lower in-hospital mortality (unadjusted 3.9% vs 6.9%, $P < .001$, adjusted odds ratio 0.66, 95% confidence interval 0.60-0.72), lower adjusted mortality among most of 6 subgroups determined by propensity to receive acute beta-blockers, and lower adjusted mortality in patients with and without signs of heart failure and in those <80 years and those ≥80 years old.

**CONCLUSIONS:** The majority of NSTEMI patients receive acute beta-blocker therapy. Certain patient subgroups remain undertreated. Because treatment with acute beta-blockers was associated with improved clinical outcomes in nearly all patient subgroups assessed, broader use in patients with NSTEMI appears warranted. © 2007 Elsevier Inc. All rights reserved.

The American Journal of Medicine (2007) 120, 685-692

European Heart Journal
Journal of the European Society of Cardiology

# Management of patients with myocardial infarction and hypertension

**G. Y. H. Lip, C. Lydakis and D. G. Beevers**

*University Department of Medicine and Department of Cardiology, City Hospital, Birmingham, U.K.*

risk of stroke if thrombolysis is unacceptable. In our evidence-based medicine era, available data from large trials show that only beta-blockers and ACE inhibitors, amongst the several antihypertensive drug classes, convincingly save lives in long-term post-myocardial infarction. Amongst the calcium antagonists, only verapamil and perhaps diltiazem may be used as an alternative if no significant left ventricular dysfunction is present.

no significant left ventricular dysfunction is present.

*European Heart Journal* (2000) **21**, 1125–1134

European Heart Journal
Journal of the European Society of Cardiology

# Are beta-blockers effective in patients who develop heart failure soon after myocardial infarction? A meta-regression analysis of randomised trials

Timothy Houghton[a], Nick Freemantle[b], John G.F. Cleland[a,*]

**Abstract**

greater in this group. *Conclusions:* This analysis suggests that the relative benefit of beta-blockers on mortality after a myocardial infarction is similar in the presence or absence of heart failure but that the absolute benefit may be greater in the former. However, as current clinical practice has changed radically from the time when the majority of these trials were conducted, further trial evidence would be desirable.© 2000 Society of Cardiology. All rights reserved

after myocardial infarction. The primary analysis was to assess the extent to which the proportion of patients included in each trial with heart failure influenced the relative odds of all-cause mortality in the trials. All randomised trials without crossover with treatment lasting more than one month and with 50 or more patients were considered. All those that provided information on the proportion of patients with heart failure or major cardiac dysfunction in the original or subsequent articles were included in the analysis. *Results:* Overall treatment with a beta-blocker was associated with a 22.6% reduction in the odds of death (95% C1 11–32.3%). There were very few data on the effects of beta-blockers after myocardial infarction in patients with documented left ventricular systolic dysfuntion. In the analysis that included heart failure as a factor, treatment with a beta-blocker was associated with a non-significant interaction with the presence of heart failure. However, because the group including heart failure patients were at higher risk, the absolute benefit of treatment with beta-blockers appeared greater in this group. *Conclusions:* This analysis suggests that the relative benefit of beta-blockers on mortality after a myocardial infarction is similar in the presence or absence of heart failure but that the absolute benefit may be greater in the former. However, as current clinical practice has changed radically from the time when the majority of these trials were conducted, further trial evidence would be desirable.© 2000 Society of Cardiology. All rights reserved

European Journal of Heart Failure 2 (2000) 333–340

The statistical mortality benefits for the elderly, diabetic, COPD, UAP/NSTEMI, hypertension, and congestive heart failure subgroups are all quite similar

# DOSAGES OF BETA-BLOCKERS AFTER MYOCARDIAL INFARCTION

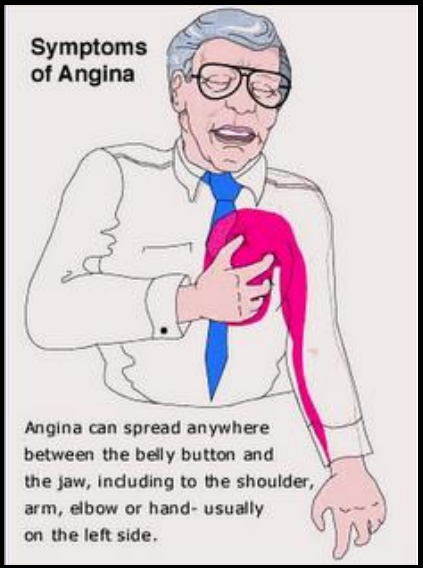
- Metoprolol tartrate 25 to 50 mg every 6 to 12 h orally, then transition over next 2 to 3 d to twice-daily dosing of metoprolol tartrate or to daily metoprolol succinate; titrate to daily dose of 200 mg as tolerated
- Carvedilol 6.25 mg twice daily, titrate to 25 mg twice daily as tolerated
- Metoprolol tartrate IV 5 mg every 5 min as tolerated up to 3 doses; titrate to heart rate and BP
- Bisoprolol 1.25 mg once daily, titrate to 10 mgonce daily as tolerated

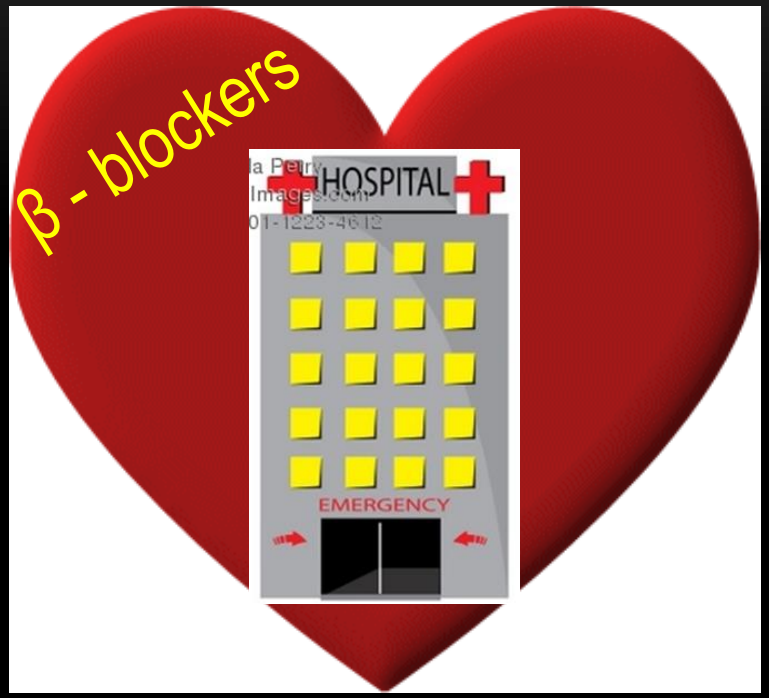
ACCF/AHA Guideline for The Management of ST-Elevation Myocardial Infarction, 2013
ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation, 2012

# SUMMARY

- NOT all of β – blockers are the same
- On the day of admission, all patients should receive beta-blocker therapy unless there are absolute contraindications or if the patient is unstable.
- If therapy was withheld because the patient was unstable, it should be given once the patient is stable.
- By the day of discharge, all patients should be on a beta-blocker unless there is an absolute contraindication.
- Before and After Reperfusion era, β – blockers are beneficial for patients post myocardial infarction

# Take Home Message




# THANK YOU