'Coronary artery bypass grafting in patients with acute coronary syndromes: perioperative strategies to improve outcome'

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No Disclosures
CABG in ACS: Strategies to Improve Outcome

**Acute Coronary Syndromes**

*What Are We Talking About?*

- **Wide Spectrum**: Continuum from Prinzmetal Angina to STEMI

- **NSTEMI**
  - Unstable Angina: recent change severity, character, trigger threshold, new onset *(Braunwald Classification Class A, B, C; I, II or III)*
  - Non Q Wave MI
  - Post Infarction Angina

- **STEMI**
  - Killip I – IV Cardiogenic Shock
  - Mechanical Complications: VSD, Acute Mitral Regurgitation, Rupture
CABG in Patients with Acute Coronary Syndromes: Perioperative Strategies to Improve Outcome

• Medical Strategies
  – Double Antiplatelet Therapy
    • Preoperatively
    • Postoperatively
  – New Antiplatelet Agents

• Surgical Strategies
  – Indications for Surgery
  – Timing of Surgery
  – Type of Surgery
Medical Strategies

Antiplatelet Therapy in ACS

- ESC NSTEMI Guidelines 2007

- Aspirin is recommended for all patients presenting with NSTE-ACS without contraindication at an initial loading dose of 160–325 mg (non-enteric) (I-A), and at a maintenance dose of 75–100 mg long-term (I-A).
- For all patients, an immediate 300 mg loading dose of clopidogrel is recommended, followed by 75 mg clopidogrel daily (I-A). Clopidogrel should be maintained for 12 months unless there is an excessive risk of bleeding (I-A).
- In patients pretreated with clopidogrel who need to undergo CABG, surgery should be postponed for 5 days for clopidogrel withdrawal if clinically feasible (IIa-C).
- Temporary interruption of dual antiplatelet therapy (aspirin and clopidogrel) within the first 12 months after the initial episode is discouraged (I-C).
CABG in ACS: Strategies to Improve Outcome

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Cardiac/Noncardiac Surgery

- Emergency: Proceed to surgery
- Semi-elective and urgent: “Case-by-case” decision
- Elective: Wait until completion of the mandatory dual antiplatelet regime

Risk of thrombosis:
- Continue aspirin + clopidogrel

Risk of bleeding:
- Continue aspirin
- Stop clopidogrel
- Stop aspirin
- Stop clopidogrel
CABG in ACS: Strategies to Improve Outcome

Medical Strategies
Antiplatelet Therapy in ACS
CURE: CV Death/MI/Stroke in Various Intervention Groups

CURE overall

Medical therapy (no CABG/PCI any time)
Medical therapy (no CABG/PCI in index hospitalization)
Revasc (PCI or CABG) (any time)
Revasc (PCI or CABG) (index hospitalization)

CABG (any time)
CABG (index hospitalization)

PCI (any time)
PCI (index hospitalization)

CI = confidence interval, CURE = Clopidogrel in Unstable angina to prevent Recurrent ischemic Events trial, PCI = percutaneous coronary intervention, Revasc = revascularization, RR = relative risk.
CABG in ACS: Strategies to Improve Outcome

Medical Strategies

Antiplatelet Therapy in ACS

CURE Major Bleeding

CURE overall: N=12,562

Medical therapy (no CABG/PCI at any time)

CURE (overall)

Revasc (PCI or CABG) (any time)

Medical therapy (no CABG/PCI in index hospitalization)

CABG (any time)

Revasc (PCI or CABG) (index hospitalization)

PCI (any time)

PCI (index hospitalization)

RR (95% CI)

Clopidogrel withdrawn >5 days prior to CABG
Reoperation 12/454 (plac) vs 7/456 (clop) RR 0.58 95% CI 0.23–1.46
Life-threatening bleed 2 fewer (clop) deaths

Clopidogrel withdrawn ≤5 days prior to CABG
Reoperation 11/476 (plac) vs 18/436 (clop) RR 1.79 95% CI 0.85–3.74
Life-threatening bleed excess death (clop) 10 (2.8%)

CABG in ACS: Strategies to Improve Outcome

Medical Strategies

New Antiplatelet Agents

• Thienopyridines are prodrugs requiring activation (i.e., metabolism) to an active metabolite: Ticlopidine, clopidogrel

• Limitations with current standard of care: Delayed onset of action, modest inhibition of platelet activity, and interpatient variability in response to therapy

• Prasugrel 3rd generation thienopyridine:
  – Increased Inhibition Platelet Activity
  – Rapid onset of IPA activity
  – More consistent IPA response

• Ticagrelor:
  – No Hepatic Metabolism
  – Reversible
CABG in ACS: Strategies to Improve Outcome

**Prasugrel**

PCI in Acute Coronary Syndromes

**Dual Platelet Inhibition: Evidence from TRITON-TIMI 38**

*Wiviott SD et al. NEJM 2007; 357: 2001*

**CV Death / MI / Stroke**

- **Prasugrel**
  - 12.1 events
  - RR 0.81 (0.73-0.90)
  - P < 0.001
  - NNT = 46

- **Clopidogrel**
  - 9.9 events

**Major non-CABG TIMI**

- **Prasugrel**
  - 2.4 events
  - RR 1.32 (1.03-1.68)
  - P = 0.003
  - NNH = 167

- **Clopidogrel**
  - 1.8 events

**Bleeding**

Net clinical benefit

- Prior Stroke or TIA
  - HR 1.54 (P=0.04)

- Age ≥75 years
  - HR 0.99 (P=0.92)

- Weight <60 Kg
  - HR 1.03 (P=0.89)
CABG in ACS: Strategies to Improve Outcome

TRITON-TIMI 38: Other TIMI Bleeds at 15 Months (All ACS)

- **Clopidogrel** (n=6,716)
- **Prasugrel** (n=6,741)

**End Point (%)**

- **TIMI Major or Minor**
  - Clopidogrel: 3.8% (n=231)
  - Prasugrel: 5.0% (n=303)

- **Requiring Transfusion**
  - Clopidogrel: 3.0% (n=182)
  - Prasugrel: 4.0% (n=244)

- **CABG-related TIMI Major Bleeding**
  - At risk: 3.2% (6/189)

**Odds Ratio 4.73**

- **P<0.001**
- **P=0.002**

ACS=Acute Coronary Syndrome; CABG=Coronary Artery Bypass Graft surgery; HR=Hazard Ratio; TIMI=Thrombolysis In Myocardial Infarction

CABG in ACS: Strategies to Improve Outcome

**Ticagrelor**

Inhibition of Platelet Aggregation

*Ticagrelor versus Clopidogrel*

- **Ticagrelor is a cyclo-pentyl-triazolo-pyrimidine**
- **Direct acting (not a prodrug)**
  - Faster offset of effect than clopidogrel
  - Greater inhibition of platelet aggregation than clopidogrel
- **Reversibly bound**
Primary Efficacy Endpoint: CV Death, MI or Stroke

<table>
<thead>
<tr>
<th>Event</th>
<th>Ticagrelor</th>
<th>Clopidogrel</th>
<th>HR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>5.8</td>
<td>6.9</td>
<td>0.84</td>
<td>0.005</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.5</td>
<td>1.3</td>
<td>1.17</td>
<td>0.220</td>
</tr>
<tr>
<td>CV Death</td>
<td>4.0</td>
<td>5.1</td>
<td>0.79</td>
<td>0.001</td>
</tr>
<tr>
<td>Definite ST</td>
<td>1.3</td>
<td>1.9</td>
<td>0.67</td>
<td>0.009</td>
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<tr>
<td>Death</td>
<td>4.5</td>
<td>5.9</td>
<td>0.78</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

HR 0.84 (0.77–0.92) P=0.0003

CABG in ACS: Strategies to Improve Outcome

**Ticagrelor**

Acute Coronary Syndromes

*Ticagrelor versus Clopidogrel*

Non-CABG and CABG-Related Major Bleeding

![Graph showing Non-CABG and CABG-Related Major Bleeding](image)

Non-CABG Major Bleed

- Ticagrelor: 4.5%
- Clopidogrel: 3.8%

CABG Major Bleed

- Ticagrelor: 7.4%
- Clopidogrel: 7.9%

K-M estimated rate (% per year)

- PLATO: 4.5, 7.4, 5.3
- TIMI: 3.8, 7.9, 5.8

P-values:

- Non-CABG Major Bleed: P=0.026
- CABG Major Bleed: P=0.025
- P=NS

CABG in ACS: Strategies to Improve Outcome

**Time From CABG to Any Death (CABG Population)**

- **Clopidogrel**: 9.7 months
- **Ticagrelor**: 4.7 months

**HR:** 0.49 (95% CI 0.32–0.77), p<0.01
CABG in ACS: Strategies to Improve Outcome

**Ticagrelor**

Reversible, more intense P2Y$_{12}$ receptor inhibition in comparison with clopidogrel in a broad population with ST- and non-ST-elevation ACS:

- Reduction in myocardial infarction and stent thrombosis
- Reduction in cardiovascular and total mortality
- No change in the overall risk of major bleeding
Surgical Strategies in ACS
Timing of Surgery

• NSTEMI
  – Risk Stratification
  – High Risk = Urgent Angio
  – Wait 48/72h Same Hospital Stay

ESC Guidelines Myocardial Revascularisation Stockholm 2010
Impact of Early Coronary Artery Bypass Graft in an Unselected Acute Coronary Syndrome Patient Population

Pedro Monteiro, MD; on behalf of the Portuguese Registry on Acute Coronary Syndromes

Background—Performance of coronary artery bypass graft (CABG) during an acute coronary syndrome (ACS) is mainly used in high-risk patients. Although potentially life-saving, patients undergoing early CABG are traditionally associated with a worse outcome than those not requiring CABG. Is this really true in an unselected ACS population? The aim of this study was to evaluate, in an ACS population, if the performance of CABG during the index hospitalization influences in-hospital outcome.

Methods and Results—Retrospective analysis of a nationwide database of 12,988 ACS patients admitted since 2002. Of those, 267 patients underwent CABG during the index hospitalization (group A) and 12,721 did not (group B). Group B patients were further divided in 2 subgroups: those submitted to percutaneous coronary interventions (PCI) (group B₁; n=3948) during the index hospitalization and those not submitted to mechanical revascularization (group B₂; n = 8773). Patients from group A more frequently had diabetes, hypercholesterolemia, hypertension, and previous angina; they were also more often on cardiovascular medication before admission. Patients that underwent CABG were more often in Killip class IV at admission (4.8% versus 1.4% versus 2.0%); they also received more nitrates and catecholamines. Left ventricular function was better in group B₁. Group A patients were more often on mechanical ventilation and intra-aortic pump and they had more in-hospital complications (31.1% versus 18.7% versus 17.3%), namely recurrent angina, re-infarction, and mechanical complications. They had a more severe coronary anatomy and the culprit lesion was more frequently on the left main (7.7% versus 0.5% versus 2.2%). However, their in-hospital mortality was significantly lower (1.1% versus 2.2% versus 6.8%; P<0.001). Multivariate analysis showed that performance of early CABG was an independent predictor of lower mortality (odds ratio of 0.12), as were the use of low-molecular-weight heparins, beta-blockers, and angiotensin-converting enzyme inhibitors.

Conclusions—in unselected patients admitted for ACS, performance of early CABG, despite being performed in higher-risk patients, is associated with very low in-hospital mortality, even when compared with the mortality of lower-risk population not submitted to early CABG. Therefore, early performance of this procedure should be considered more often in eligible patients. (Circulation. 2006;114[suppl I]:I-467–I-472.)
Surgical Strategies in ACS
Timing of Surgery

• STEMI
  – Emergent
    • Mechanical Complications
    • PCI Failure
    • Unfavourable Anatomy + Large Area at Risk < 4 h
  – Urgent
    • Inverse Relationship Between Mortality and Time
    • Waiting Period 3-7 Days
  – Elective
    • MVD + Culprit PCI After Risk Statification

ESC Guidelines Myocardial Revascularisation Stockholm 2010
Appropriate timing of surgical intervention after transmural acute myocardial infarction

Daniel C. Lee, MD
Mehmet C. Oz, MD
Alan D. Weinberg, MS
Windsor Ting, MD

J Thorac Cardiovasc Surg 2003;125:115-20

Figure 1. Hospital mortality versus timing of CABG. The horizontal bar represents the baseline mortality rate (2.7%) from the entire patient population.

Conclusions: Coronary revascularization within 3 days of a transmural acute myocardial infarction might be an added risk for mortality. In the absence of absolute indications for emergency surgical intervention, such as structural complications and ongoing ischemia, a 3-day waiting period before surgical revascularization should be considered.
Optimal timing of coronary artery bypass after acute myocardial infarction: A review of California discharge data


Doubling Mortality
CABG<3 Days

High Acuity:
Benefit From Deferring
CABG 2-3 Days

Figure 1. CABG volume and mortality over time. Distribution of CABG volume (left Y-axis, number of cases per day) and percent mortality (right Y-axis) per day of hospitalization. Dashed horizontal line represents total mortality over the study period (4.8%). Black arrow points to nadir of mortality occurring on day 3. CABG, Coronary artery bypass graft.

Figure 2. Mortality in patients undergoing acute CABG. Percent mortality for those patients with transmural AMI (defined as acute infarctions not coded as "subendocardial") and shock (light grey bars) or IABP placement preoperatively (dark grey bars). Note that for both patient sets, the nadir of mortality occurs on hospital day 3. Total patient numbers for each day (n) are given below each bar. IABP, Intra-aortic balloon pump; CABG, coronary artery bypass graft.
CABG in ACS: Strategies to Improve Outcome

**Surgical Strategies in ACS**

**Type of Surgery**

- Off-Pump vs On-Pump vs Assisted Beating Heart
- Left Internal Mammary Artery in All Patient
- Avoid Additional Ischemia
- Nitrates+++ 
- Prevent Arrhythmias and End Organ Damage
- IABP Rather Than High Dose Cathecolamines
Surgical Strategies
Type of Surgery

Off-pump versus on-pump myocardial revascularization in patients with ST-segment elevation myocardial infarction: A randomized trial

Khalil Fattouch, MD, PhD, Francesco Guccione, MD, Pietro Dioguardi, MD, Roberta Sampognaro, MD, Egile Corrado, MD, Marco Canuso, MD, and Giovanni Ruvolo, MD

Objective: Conventional cardioplegic arrest coronary artery bypass grafting after ST-segment elevation myocardial infarction is associated with high mortality and morbidity. The benefits of off-pump surgery have been suggested. This study randomly evaluated the impact of the off-pump technique on clinical results.

Methods: Between February 2002 and October 2007, 128 patients with ST-segment elevation myocardial infarction who underwent myocardial revascularization within 48 hours from the onset of symptoms were randomly assigned to 2 groups: on-pump group (66 patients/51.5%) and off-pump group (63 patients/48.5%). The primary end point was the incidence of in-hospital death and outcomes (low cardiac output syndrome, prolonged mechanical and pharmacologic cardiac support, prolonged mechanical ventilation support, and postoperative length of stay in intensive care unit and hospital). The secondary end point was the evaluation of myocardial infarct size measured by the perioperative serum release of cardiac troponin I and the improvement of contractile cardiac function evaluated by the wall motion score index.

Results: Overall in-hospital mortality was 4.6%. In-hospital mortality was 7.7% (5 patients) in the on-pump group and 1.6% (1 patient) in the off-pump group (P = .04). Statistically significant differences were found between the 2 groups concerning the incidence of low cardiac output syndrome (P = .001), time of inotrope drugs support (P = .001), time of mechanical ventilation (P = .006), reoperation for bleeding (P = .04), intensive care unit stay (P = .01), and in-hospital stay (P = .02). Statistically significant differences also were found between the 2 groups concerning the incidence of in-hospital death in patients who were admitted to surgery in cardiac shock (P = .0018) and patients who underwent surgery within 6 hours from the onset of symptoms (P = .0026). The procedure in 1 patient (1.6%) in the off-pump group was converted to the on-pump beating heart technique. The serum levels of cardiac troponin I were high in the on-pump group during the first 48 hours after surgery. Myocardial function was better in the off-pump group. There were no cardiac-related late deaths, and patients had no recurrent cardiac events.

Conclusion: Off-pump surgery reduced early mortality and morbidity in patients with ST-segment elevation myocardial infarction in respect to the conventional procedure. Off-pump surgery showed better results than on-pump surgery in patients who underwent surgery within 6 hours from the onset of symptoms and in patients with cardiogenic shock.
Emergency Coronary Artery Bypass Graft Surgery for Acute Coronary Syndrome

Beating Heart Versus Conventional Cardioplegic Cardiac Arrest Strategies

Ardawan Julian Rastan, MD; Judith Isabell Eckenstein, MD; Bettina Hentschel, PhD; Anne Kathrin Funkat, PhD; Jan Fritz Gummert, MD, PhD; Nicolas Doll, MD, PhD; Thomas Walther, MD, PhD; Volkmar Falk, MD, PhD; Friedrich Wilhelm Mohr, MD, PhD

Background—Aim of this study was to compare the outcome of beating heart versus conventional coronary artery bypass graft (CABG) strategies in acute coronary syndromes for emergency indications.

Methods and Results—638 patients received emergency CABG surgery via midline sternotomy. Cardioplegia (n=398) was used to predict the probability of emergency CABG using the EuroSCORE. Shock (n=107). Patients on the beating heart group had lower inotropes, stroke, MI, renal failure, AF, and reduced hospital mortality. The results are shown in the table.

<table>
<thead>
<tr>
<th></th>
<th>N= 638</th>
<th>Cardioplegia N=398</th>
<th>Beating Heart N=240</th>
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</thead>
<tbody>
<tr>
<td>Shock</td>
<td>N=107</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Beating Heart:
Less Inotropes, Stroke, MI, Renal Failure, AF
Reduced Hospital Mortality

Conclusions—Beating heart strategies are associated with an improved hospital outcome and comparable long-term results for high-risk patients presenting acute coronary syndrome with or without CS. (Circulation. 2006;114[suppl I]:I-477–I-485.)
CABG in ACS: Strategies to Improve Outcome

**Surgical Strategies in ACS**

**Management at Cruz Vermelha Hospital**

- **Indications and Timing for CABG in ACS**
  - *Emergent*: Persistent Ischemia or Pump Failure And PCI Not Possible or Failed
  - *Urgent* (During Same Hospital Stay): Severe Anatomy And/Or Re Angina

- **Preoperative Management**
  - Nitrates, Antiplatelets, +/- Adrenaline
  - IABP+++, Swan-Ganz

- **Surgical Technique**
  - OPCAB: First Line (+ IABP)
  - Beating Heart with Cardiopulmonary Support: If Pump Failure, Arrythmias

- **Postoperative Management**
  - Blood Sparing: Cell Saver, Antifibrinolytics, Platelets
  - IABP, Inotropic, Ventilatory, Renal Support, ECMO?
Cardiogenic Shock/Acute Heart Failure

Medical therapy
Inotropic support
Ventilatory support
IABP
Reperfusion
Revascularization

Assess neurologic / end organ function

Weaning
Irreversible neurological deficit

ECMO support
Cardiac function recovers

Weaning

Weaning

Pat. unstable

Weaning

Echocardiogram

Weaning

Pat. stable

Cardiac function recovers

Weaning

Standard therapy

Normal neurological function

Consider LVAD/BVAD therapy (BTT/DT)

2010 ESC Guidelines Myocardial Revascularisation
### Postoperative Medical Strategies

**Resume Aspirin 6 Hours After Surgery**
**Clopidogrel As Soon As No Bleeding till 12 Months**
**Statins +++**

#### Syntax Trial: Stroke 1 Year

<table>
<thead>
<tr>
<th>Stroke</th>
<th>CABG</th>
<th>PCI</th>
<th>p</th>
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<tbody>
<tr>
<td>Total</td>
<td>2.2% (19)</td>
<td>0.6% (5)</td>
<td>0.003</td>
</tr>
<tr>
<td>Pre-Procedure</td>
<td>3 (0.3%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Intra-Procedure</td>
<td>3 (0.3%)</td>
<td>1 (0.1%)</td>
<td></td>
</tr>
<tr>
<td>Post &lt; 30 days</td>
<td>6 (0.7%)</td>
<td>2 (0.2%)</td>
<td></td>
</tr>
<tr>
<td>Post 30-365 d</td>
<td>7 (0.8%)</td>
<td>3 (0.3%)</td>
<td></td>
</tr>
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</table>

#### Double Antiplatelet Therapy

<table>
<thead>
<tr>
<th></th>
<th>16%</th>
<th>80%</th>
</tr>
</thead>
</table>

Kappetein P. personal communication
Conclusion

• STEMI: PCI for Culprit Lesion First Line
• CABG and PCI are Complementary in NSTEMI ACS: Heart Team Approach Applies: Discussion On Individual Patient

• There Is a Low But Not Negligible Need For Urgent/Emergent CABG in ACS (10-15%)

• Should Clopidogrel Be Stopped Prior to CABG?
  • Guidelines Recommend Stopping 5 Days Prior to Surgery
  • Debate Not Closed: Selection Bias; No Randomized Trial
  • Heart Team Approach: Weighing Risks vs Benefits
  • Double Antiplatelet Therapy Should Be Continued for 12 Months
Conclusion

• **Timing**
  
  • **If Feasible Delaying Surgery for 3-7 Days After Acute STEMI Reduces Mortality; 24-48h for NSTEMI (?)**
  
  • **If Refractory Symptoms or Hemodynamic Unstability: Emergent CABG**

  • **Two Mistakes To Avoid:**
    – Operate Too Early: stable patients
    – Operate Too Late: end organ failure

• **How?** **Off-Pump** CABG in Experienced Hands or **Assisted Beating Heart** May Improve Results of Urgent Surgery for ACS

• **Management of Cardiogenic Shock After AMI**
  
  • **Require Special Dedicated Units with Assist Device Capabilities**
Thank you.