Case Challenges in ACS

The Very Elderly in the Cath Lab

Sameh Salama, MD, FSCAI
Professor of Cardiology,
Cairo University
• 86 yrs old male
• IDDM (controlled on insulin and oral hypoglycemics)
• Hypertensive (controlled on valsartan/HCT 80/12.5 mg, Bisoprolol 5mg)
• Stopped smoking 6 yrs ago (smoked for > 30yrs,)
• Dyslipidemic (LDL : 142 mg/dl, on Rusovastatin 10mg)
• Positive FH for CAD and hypercholesterolemia
• Crescendo Angina since few months (nocturnal angina)
• Normal ECG / Negative Troponin
• Echocardiogram: LVEF (52%). No regional wall motion abnormalities.
• History of active peptic ulcer 10 yrs ago (on PPI, Omeprazole, for life)
• Renal impairment: Serum creatinine 1.7 mg/dl (Creatinine clearance 36)
• Antidepressant : Paroxetene {Seroxate}
• Lumbar disc prolapse (infrequent intake of NSAIDS)
• Weight : 76 Kg, BMI : 32 Kg/m2
What’s the best management strategy for this patient?

A- CABG

B- PCI

C- Medical treatment

D- Risk Stratification and Heart team decision
What’s the best management strategy for this patient?

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## EURO-SCORE II

<table>
<thead>
<tr>
<th>Patient related factors</th>
<th>Cardiac related factors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong> (years)</td>
<td>86</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>Male</td>
</tr>
<tr>
<td><strong>Renal impairment</strong></td>
<td>Severe (CC &lt;50)</td>
</tr>
<tr>
<td><strong>Extracardiac arteriopathy</strong></td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Poor mobility</strong></td>
<td>No</td>
</tr>
<tr>
<td><strong>Previous cardiac surgery</strong></td>
<td>No</td>
</tr>
<tr>
<td><strong>Chronic lung disease</strong></td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Active endocarditis</strong></td>
<td>No</td>
</tr>
<tr>
<td><strong>Critical preoperative state</strong></td>
<td>No</td>
</tr>
<tr>
<td><strong>Diabetes on insulin</strong></td>
<td>Yes</td>
</tr>
<tr>
<td><strong>NYHA</strong></td>
<td>II</td>
</tr>
<tr>
<td><strong>CCS class 4 angina</strong></td>
<td>Yes</td>
</tr>
<tr>
<td><strong>LV function</strong></td>
<td>Good (LVEF &gt; 50%)</td>
</tr>
<tr>
<td><strong>Recent MI</strong></td>
<td>No</td>
</tr>
<tr>
<td><strong>Pulmonary hypertension</strong></td>
<td>No</td>
</tr>
<tr>
<td><strong>Urgency</strong></td>
<td>elective</td>
</tr>
<tr>
<td><strong>Weight of the intervention</strong></td>
<td>isolated CABG</td>
</tr>
<tr>
<td><strong>Surgery on thoracic aorta</strong></td>
<td>No</td>
</tr>
</tbody>
</table>

### Operation related factors

<table>
<thead>
<tr>
<th><strong>EuroSCORE II</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>9.22%</td>
</tr>
</tbody>
</table>
Clinical SYNTAX SCORE (SYNTAX SCORE II)

**SYNTAX Score II**

- **PCI**
  - SYNTAX Score II: 47.1
  - PCI 4 Year Mortality: 25.7%

- **CABG**
  - SYNTAX Score II: 62.4
  - CABG 4 Year Mortality: 65.9%

Decision making -between CABG and PCI- guided by the SYNTAX Score II to be endorsed by the Heart Team.
Acute Coronary Syndromes in the Very Elderly

Is The Treatment of ACS in The Very Elderly Patient Different From The Younger Ones?

5 Decisions to make
Therapeutics in ACS Among Patients >90 Years Old

Mortality

Major Bleeding

Even among oldest old – better outcomes with better adherence to ACC/AHA Guidelines

- Skolnick et al, ACC 2006
1- Risk assessment: Thrombotic and Bleeding

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>In patients with a suspected NSTE-ACS, diagnosis and short-term ischaemic/bleeding risk stratification should be based on a combination of clinical history, symptoms, physical findings, ECG (repeated or continuous ST monitoring), and biomarkers.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>ACS patients should be admitted preferably to dedicated chest pain units or coronary care units.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>It is recommended to use established risk scores for prognosis and bleeding (e.g. GRACE, CRUSADE).</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>A 12-lead ECG should be obtained within 10 min after first medical contact and immediately read by an experienced physician. This should be repeated in the case of recurrence of symptoms, and after 6–9 and 24 h, and before hospital discharge.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Additional ECG leads (V1,R,V4R,V7–V9) are recommended when routine leads are inconclusive.</td>
<td>I</td>
<td>C</td>
</tr>
</tbody>
</table>
• Much overlap: many elderly have both high bleeding and high ischemic risk score

• GRACE score is accurate for predicting ischemic risk in elderly patients

• CRUSADE bleeding score is not predictive in elderly patients, AUC ≥75 years: 0.52

• ESC guidelines: “A high CRUSADE score should not be a reason to deny antithrombotic treatment”

• Clinical judgement e.g. when frail wait with strong antithrombotic treatment
Frailty in the elderly

- 19% frail / 47% intermediate frail / 21% not frail
- Frail pts. had more co-morbidities, LM disease and multivessel disease

<table>
<thead>
<tr>
<th></th>
<th>ODDS Ratio</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-d mortality</td>
<td>4,8</td>
<td>0.013</td>
</tr>
<tr>
<td>12-mo mortality</td>
<td>5,9</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Independent of age, gender or co-morbidities

Urali-Krishnan et al. Open Heart 2015
2- What’s the best P2Y2 inhibitor to use in this patient?

A- Clopidogrel

B- Prasugrel

C- Ticagrelor

D- Any one of them
2- What’s the best P2Y2 inhibitor to use in this patient?

A- Clopidogrel

B- Prasugrel

C- Ticagrelor

D- Any one of them
2. P2Y12

No recommendation for the elderly

A P2Y12 inhibitor is recommended, in addition to aspirin, for 12 months unless there are contraindications such as excessive risk of bleeds.

- Ticagrelor (180 mg loading dose, 90 mg twice daily) is recommended, in the absence of contraindications, for all patients at moderate-to-high risk of ischaemic events (e.g. elevated cardiac troponins), regardless of initial treatment strategy and including those pretreated with clopidogrel (which should be discontinued when ticagrelor is started).

- Prasugrel (60 mg loading dose, 10 mg daily dose) is recommended in patients who are proceeding to PCI if no contraindication.

- Clopidogrel (300–600 mg loading dose, 75 mg daily dose) is
<table>
<thead>
<tr>
<th>Study</th>
<th>compare</th>
<th>N</th>
<th>Age</th>
<th>CVD/MI/Stroke</th>
<th>Bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yusuf et al 2001 12,562</td>
<td>Clopi vs placebo</td>
<td>6354</td>
<td>≤65</td>
<td>5.4% (clopi) vs 7.6% (placebo) $P &lt; 0.001$</td>
<td>3.7% (clopi) vs 2.7% (placebo), $P = 0.001$</td>
</tr>
<tr>
<td>patients (CURE-trial)</td>
<td></td>
<td>6208</td>
<td>&gt;65</td>
<td>13.3% (clopi) vs 15.3% (placebo) $P &lt; 0.05$</td>
<td>N.A</td>
</tr>
</tbody>
</table>
TRITON-TIMI 38: Net Clinical Benefit
Bleeding Risk Subgroups
Post-hoc analysis

<table>
<thead>
<tr>
<th>Prior Stroke / TIA</th>
<th>Yes</th>
<th>No</th>
<th>Risk (%)</th>
<th>$P_{int} = \frac{.006}{.18} = .36$</th>
<th>$P_{int} = .18$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>≥ 75</td>
<td>&lt; 75</td>
<td>-1</td>
<td>-16</td>
<td>-16</td>
</tr>
<tr>
<td>Wgt</td>
<td>&lt; 60 kg</td>
<td>≥ 60 kg</td>
<td>+3</td>
<td>-14</td>
<td>-13</td>
</tr>
</tbody>
</table>

OVERALL

0.5 Prasugrel Better 1 HR Clopidogrel Better 2

PLATO: Association of age and treatment with all-cause mortality

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Hazard ratio (95% CI)</th>
<th>Total patients</th>
<th>KM % at month 12</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ti.+ Clop.+</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td></td>
<td></td>
<td></td>
<td>P value</td>
</tr>
<tr>
<td>≥75 years</td>
<td></td>
<td>293</td>
<td>9.8</td>
<td>0.81 (0.65–1.03)</td>
</tr>
<tr>
<td>&lt;75 years</td>
<td></td>
<td>608</td>
<td>3.6</td>
<td>0.78 (0.67–0.92)</td>
</tr>
</tbody>
</table>

Ticagrelor better    Clopidogrel better
Non-CABG and CABG-related major bleeding

Non-CABG TIMI major bleeding

**Tron**
- Prasugrel vs Clopidogrel: 2.4% vs 1.8%
- ARD 0.6%
- HR 1.32
- P=0.03
- NNH=167

**PLATO**
- Ticagrelor vs Clopidogrel: 2.8% vs 2.2%
- ARD 0.6%
- HR 1.25
- P=0.03
- NNH=167

K-M estimated rate (% per year)

- Non-CABG PLATO major bleeding
- Non-CABG TIMI major bleeding
- CABG PLATO major bleeding
- CABG TIMI major bleeding
3. Is pretreatment with P2Y2 inhibitor mandatory in the very elderly with UA/NSTEMI?

A- Yes

B- No
3. When to start the P2Y12 inhibitor in The elderly?

**NSTE-ACS Guidelines (2011)**

Aspirin should be given to all patients without contraindication at an initial loading dose of 150-300 mg, and at a maintenance dose of 75-100 mg daily long-term regardless of treatment strategy

A P2Y12 inhibitor should be added to aspirin as soon as possible and maintained over 12 months, unless there are contraindications such as excessive risk of bleeding


Metaanalysis
Pre-treatment with Clopidogrel

A Bellemain-Appaix et al. JAMA 2012
Timing of P2Y12

ACCOAST: pre-treatment Prasugrel

CV death, MI, stroke, UR or GPlIb/IIa Bailout

<table>
<thead>
<tr>
<th>Dagen na randomisatie</th>
<th>HR</th>
<th>95% CI</th>
<th>P value</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>7 dgn</td>
<td>1,02</td>
<td>0,84 – 1,25</td>
<td>0,81</td>
<td>4.033</td>
</tr>
<tr>
<td>30 dgn</td>
<td>0,997</td>
<td>0,83 – 1,20</td>
<td>0,98</td>
<td>4.033</td>
</tr>
</tbody>
</table>

% 15

10,0

9,8

10,8

10,8
ACCOAST
All TIMI (CABG or non-CABG Major Bleeding)
Pre-Treatment with P2Y12-inhibitors in NSTE-ACS

(95% CI 1.19, 3.02), \( P = 0.006 \). Arguments for and against pretreatment with P2Y\(_{12}\) inhibitors in NSTE-ACS patients have been discussed extensively and the topic remains controversial.\(^{165,166}\) As the optimal timing of ticagrelor or clopidogrel administration in NSTE-ACS patients scheduled for an invasive strategy has not been adequately investigated, no recommendation for or against pretreatment with these agents can be formulated. Based on the ACCOAST results, pretreatment with prasugrel is not recommended. In

Elderly:  

- More doubt on the diagnosis of UA/NSTEMI
- Higher bleeding risk
- Medical treatment is a likely option
- \textit{When in doubt, do not pre-treat.}

Roffi et al. Eur Heart J 2016
4. What is the most important goal of treatment in the very elderly?

A- Prolong life
B- Maintain mental ability
C- Maintain independence
D- All of the above
4. What is the most important goal of treatment in the very elderly?

A- Prolong life

B- Maintain mental ability

C- Maintain independence

D- All of the above
“What are the most important goals from the treatment of your heart disease?”
Invasive versus conservative strategy in patients aged 80 years or older with non-ST-elevation myocardial infarction or unstable angina pectoris (After Eighty study): an open-label randomised controlled trial

Nicolai Tegn, Michael Abildsoe, Lars Aaberge, Knut Endresen, Pål Smith, Svend Aakhus, Erik Gjersen, Ola Dahl-Hojfeldt, Anette Hylen Ranlov, Lars Guliested, Bjørn Bendz, for the After Eighty study investigators

- Consistent with RITA3, TACTICS TIMI-18
- Bleeding similar.
- Use radial (Rival elderly 3.6% vs 6.6%, p=0.03)

Figure 2: Kaplan-Meier curves of survival free from composite outcome
The primary outcome was a composite of myocardial infarction, need for urgent revascularisation, stroke, and death.
Evidence-based Guidelines & Patients with Multiple Conditions

A Balancing Act in Older Persons

Evidence-based Therapies

Personalized Care
5. The best options regarding the type of stent and duration of DAPT in this patient are:

A- BMS and DAPT for 1 month

B- DES and DAPT for 1 year

C- 2nd generation DES and DAPT for 3-6 months

D- None of the above
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A- BMS and DAPT for 1 month

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C- 2nd generation DES and DAPT for 3-6 months

D- None of the above
5. Which stent in elderly?
ZEUS and Leaders Free studies

**Zotarolimus-Eluting Versus Bare-Metal Stents in Uncertain Drug-Eluting Stent Candidates**

N=1600; >50% high bleeding risk, mean 38 days DAPT

N=2400; high bleeding risk; 1 month DAPT
Polymer-Free BIOFREEDOM DES

2466 patients with clinical indication for PCI & 1 or more inclusion criteria (high bleeding risk)

BioFreedom (n=1239)

- Age ≥ 75 years
- OAC planned after PCI
- Baseline Hb < 11g / dl or transfusion during prior 4 weeks
- Planned major surgery (within next year)
- Cancer diagnosed or treated ≤ 3 years
- Creatinine clearance < 40 ml / min
- Hospital admission for bleeding during past year
- Thrombocytopenia (< 100,000 / mm3)
- Any prior intra-cerebral bleed
- Any stroke during the past year
- Severe liver disease
- NSAID or steroids planned after PCI
- Anticipated poor DAPT compliance for other medical reason

LEADERS FREE Trial

Primary Safety Endpoint (Cardiac Death, MI, ST)

Cumulative Percentage with Event

Number at Risk

<table>
<thead>
<tr>
<th></th>
<th>DCS</th>
<th>BMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1221</td>
<td>1146</td>
<td>1105</td>
</tr>
<tr>
<td>1105</td>
<td>1081</td>
<td>1066</td>
</tr>
<tr>
<td>1081</td>
<td>1045</td>
<td>1037</td>
</tr>
<tr>
<td>1045</td>
<td>1000</td>
<td></td>
</tr>
</tbody>
</table>

390 days chosen for assessing primary EP to capture potential events driven by the 360 day FU contact

p = 0.005 for superiority

DES vs. BMS in Patients with High Bleeding Risk & DAPT for 1 Mo.

Pre-specified subgroup analysis of 828 patients (~48% ACS) with at least 1 bleeding risk criterion

**Primary EP**
- death, MI or TVR

**Bleeding Risk Criteria**
- age > 80 yrs
- indication for oral anticoagulation
- other pro-hemorrhagic medication (steroids, NSAID)
- recent bleeding episode
- known anemia (<10 mg/dl)

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**BMS**
- DES (Endeavor)

**HR 0.745; p=0.033**

**HR 0.419; p=0.016**

Ariotti et al., J Am Coll Cardiol Intv 2016
P2Y₁₂ inhibitor administration for a shorter duration of 3–6 months after DES implantation may be considered in patients deemed at high bleeding risk.
Conclusions

• The elderly (especially when > 80 yrs) as compared to younger patients have:
  – more co-morbidities
  – a higher clinical SYNTAX score
  – a higher bleeding risk
  – a less favorable clinical outcome

• Frailty is present in up to 20% in pts. >65 yrs and might influence clinical outcome independant of age and co-morbidities
What are the Recommendations in the very elderly?

- Use clopidogrel instead of stronger P2Y12-inhibitors
- Perform gastric protection
- Avoid dual antiplatelet pre-treatment if not clearly indicated
- Use DES of the latest generation
- Shorten post PCI dual antiplatelet therapy
Thank you