Care of the Post-Cardiac Surgery Patient

Lundy J. Campbell, M.D.
Associate Professor
University of California
Post-Operative Issues

- Post-op atrial fibrillation
- Acute kidney injury
- Acute respiratory failure
- Post-operative glycemic control
- Deep sternal wound infection
- Blood transfusion
- Stroke
Post-Operative Issues

- Post-op atrial fibrillation
- Acute kidney injury
- Acute respiratory failure
- Post-operative glycemic control
- Deep sternal wound infection
- Blood transfusion
- Stroke
Atrial Fibrillation

• Post-op incidence
  – Historically
    • CABG 11-40%
    • All CT 10-65%

• Increasing incidence with increasing age
  – 24% increasing frequency with each add’l 5 yr

• Initially thought to be more of a “nuisance”

• Long-term morbidity/mortality?
Atrial Fibrillation After Isolated Coronary Surgery Affects Late Survival

- 1832 patient prospective observational study
- No history of permanent afib prior to surgery
- Patient management and anesthesia technique standardized
- 31% patients developed afib post op
  - Longer hospital LOS
  - Increased hospital and long-term mortality
- Adjusted hazard ratio for afib 2.13 based on propensity scoring

Mariscalco, et al. Circulation 2008;118;1612-1618
Kaplan-Meier survival estimates according to the occurrence of postoperative AF

New Onset A-Fib After Isolated CABG and Long-Term Survival

- Single-center, retrospective observational study of 6899 consecutive patients without pre-op a-fib
- 26% developed a-fib post-op
- 10 year unadjusted survival:
  - 52.3% with post-op a-fib
  - 69.4% no post-op a-fib
- Risk adjusted to STS mortality risk factors
  - HTN, CHF, PVD, DM, EF, IABP, resp failure, etc
- Afib increased risk of adjusted mortality by 29%

Effect of new-onset postoperative AFIB on survival in CABG surgery patients

New Onset A-fib and Long-Term Mortality After CABG

- Single center, retrospective observational study of 16,169 consecutive CABG patients
- OPCABG in 41.5% of patients
- Propensity adjusted to STS risk factors
- Post-operative a-fib occurred in 18.5% of patients

Chami, et al. JACC Vol 55, no 13, 2010:1370-6
New Onset A-fib and Long-Term Mortality After CABG

• Adjusted HR 1.21
  – At 1 yr: 96.3% vs 90.1% survival
  – At 10 yrs: 70.2% vs 55.2% survival
• Only 20.5% of patients in a-fib discharged with warfarin
• Patients in a-fib less likely to get beta-blocker, statin or anti-platelet therapy
• Adjusting for warfarin: HR 0.78
  – 22% relative reduction in mortality

Chami, et al. JACC Vol 55, no 13, 2010:1370-6
Adjusted Kaplan-Meier Survival Curves

Chami, et al. JACC Vol 55, no 13, 2010:1370-6
Post-Operative Atrial Fibrillation

- Increased short and long term mortality
- Increased with age and severity of illness
- Warfarin, beta-blockade, amiodarone, atrial pacing shown to be protective
- Likely no difference in CABG or OPCABG
Acute Renal Failure

- Studies of renal failure post-CT surgery limited by lack of uniform ARF (AKI) definition.
- Historical risk of ARF post CT-surgery 5-31% depending on criteria.
- Up to 30% of CT surgery patients develop clinically important renal failure.
- 1-2% require dialysis – Conveys approx 8-fold increase risk of death.
ARF Incidence

• Large prospective, cohort study (>43,000) VA patients undergoing CT surgery
• ARF defined as >50% increase in serum Cr from baseline
• Risk of ARF req dialysis 1.1%
  – 0.9% CABG and 2.0% valve
• 63.7% mortality in pts with ARF requiring dialysis vs 4.3% in pts without

Risk of acute renal failure with increasing age

ARF Post-CABG Mortality

- Canadian multicenter 3500 pt retrospective study. All on pump
- Patients divided into quartiles
  - ≤ 25% decrease in GFR
  - > 25% decrease in GFR (24%)
    - 4 fold increased risk of death
  - > 50% decrease in GFR (7%)
    - 5.9 fold increased risk of death
  - > 75% decrease in GFR (3%)
    - 9.5 fold increased risk of death

Risk Factors of Post-Op ARF

- Duration of CPB
- Pre-operative use of IABP
- Pre-operative anemia
- Pre-operative RBC transfusions
- Post-operative re-operation

Probability of AKI (>50% decrease in eGFR or dialysis)

A

B

C

Pathogenesis of Post-Op Renal Failure

• Normal autoregulation
  – Normal GFR maintained until MAP<80
  – Typically MAP<80 on CPB

• Impaired autoregulation
  – Age, HTN, CRI, atherosclerosis

• Drugs
  – ACE-I, NSAID, ARB, contrast agents

• Pro-inflammatory state
  – Operative trauma, reperfusion injury, blood contact with CPB circuit
Recent Trends in ARF Mortality

- Nationwide database CABG patients 1988-2003
- Estimated 7,339,520 CABG procedures
- 0.4% patients developed ARF-D
- ARF-D incidence increased over time
  - 0.22% in 1988 to 0.57% in 2003
- Decline in ARF-D mortality over same period
  - 47.4% in 1988 to 29.7% in 2003

AKI and OPCABG

• Meta analysis of 6 RCTs and 16 observational studies
• Comparing On-Pump CABG with OPCABG
• Overall found decreased risk in OPCABG (OR 0.57)
• No difference in AKI requiring dialysis
• No uniform definition of AKI between studies

Am J Kidney Dis 2009;54:413-423
Overall Acute Kidney Injury

### Review:
Off pump bypass and acute kidney injury (Version 04)

### Comparison:
01 Off pump vs on pump

### Outcome:
04 Overall acute kidney injury

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Off pump bypass</th>
<th>On pump bypass</th>
<th>OR (random)</th>
<th>Weight</th>
<th>OR (random)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>95% CI</td>
<td></td>
<td>95% CI</td>
</tr>
<tr>
<td>01 Observational</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aiscione 2001</td>
<td>5/31</td>
<td>32/202</td>
<td>3.51</td>
<td>0.39</td>
<td>[0.10, 1.13]</td>
</tr>
<tr>
<td>Beauford 2004</td>
<td>16/188</td>
<td>18/103</td>
<td>6.32</td>
<td>0.44</td>
<td>[0.21, 0.90]</td>
</tr>
<tr>
<td>Buczkowski 2004</td>
<td>14/761</td>
<td>381/8970</td>
<td>7.79</td>
<td>0.42</td>
<td>[0.24, 0.72]</td>
</tr>
<tr>
<td>Chukwuemeka 2005</td>
<td>16/146</td>
<td>66/438</td>
<td>7.43</td>
<td>0.69</td>
<td>[0.35, 1.24]</td>
</tr>
<tr>
<td>Di Mauro 2007 A</td>
<td>23/862</td>
<td>69/962</td>
<td>8.27</td>
<td>0.32</td>
<td>[0.20, 0.52]</td>
</tr>
<tr>
<td>Di Mauro 2007 B</td>
<td>10/80</td>
<td>13/90</td>
<td>5.18</td>
<td>0.74</td>
<td>[0.30, 1.79]</td>
</tr>
<tr>
<td>Giancoso 2000</td>
<td>5/65</td>
<td>49/626</td>
<td>4.74</td>
<td>1.40</td>
<td>[0.46, 3.14]</td>
</tr>
<tr>
<td>Hayashi 2002</td>
<td>2/52</td>
<td>5/53</td>
<td>2.18</td>
<td>0.38</td>
<td>[0.07, 0.70]</td>
</tr>
<tr>
<td>Hix 2006</td>
<td>34/1348</td>
<td>671/1330</td>
<td>8.80</td>
<td>0.49</td>
<td>[0.32, 0.74]</td>
</tr>
<tr>
<td>Landolfi 2007</td>
<td>23/848</td>
<td>45/228§</td>
<td>8.06</td>
<td>1.37</td>
<td>[0.82, 2.28]</td>
</tr>
<tr>
<td>Loet 2002</td>
<td>0/12</td>
<td>29/101</td>
<td>2.59</td>
<td>1.10</td>
<td>[0.32, 2.84]</td>
</tr>
<tr>
<td>Massoudy 2008</td>
<td>14/100</td>
<td>28/101</td>
<td>5.39</td>
<td>3.05</td>
<td>[0.84, 2.37]</td>
</tr>
<tr>
<td>Schwann 2004</td>
<td>19/220</td>
<td>119/119</td>
<td>5.58</td>
<td>0.47</td>
<td>[0.21, 0.97]</td>
</tr>
<tr>
<td>Stahlwood 2004</td>
<td>10/716</td>
<td>43/1483</td>
<td>6.53</td>
<td>0.47</td>
<td>[0.24, 1.18]</td>
</tr>
<tr>
<td>Weerasinghe 2005</td>
<td>290/617</td>
<td>459/1224</td>
<td>10.51</td>
<td>0.92</td>
<td>[0.77, 1.11]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>4284</td>
<td>17767</td>
<td>91.29</td>
<td>0.61</td>
<td>[0.46, 0.81]</td>
</tr>
</tbody>
</table>

Total events: 476 (Off pump bypass), 1282 (On pump bypass)
Test for heterogeneity: Chi² = 40.96, df = 13 (P < 0.0001), I² = 68.3%
Test for overall effect: Z = 3.43 (P = 0.0006)

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Off pump bypass</th>
<th>On pump bypass</th>
<th>OR (random)</th>
<th>Weight</th>
<th>OR (random)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>95% CI</td>
<td></td>
<td>95% CI</td>
</tr>
<tr>
<td>02 Randomized controlled studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aiscione 1999</td>
<td>5/25</td>
<td>5/25</td>
<td>0.59</td>
<td>0.39</td>
<td>[0.10, 1.16]</td>
</tr>
<tr>
<td>Carrier 2003</td>
<td>2/28</td>
<td>5/37</td>
<td>2.11</td>
<td>0.49</td>
<td>[0.20, 0.83]</td>
</tr>
<tr>
<td>Kobayashi 2005</td>
<td>0/61</td>
<td>1/66</td>
<td>0.07</td>
<td>0.35</td>
<td>[0.09, 0.82]</td>
</tr>
<tr>
<td>Saji 2007</td>
<td>17/56</td>
<td>39/60</td>
<td>5.91</td>
<td>0.23</td>
<td>[0.11, 0.51]</td>
</tr>
<tr>
<td>Tang 2002</td>
<td>0/20</td>
<td>0/20</td>
<td>0.00</td>
<td>0.27</td>
<td>[0.01, 0.54]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>210</td>
<td>228</td>
<td>8.72</td>
<td>0.27</td>
<td>[0.13, 0.54]</td>
</tr>
</tbody>
</table>

Total events: 19 (Off pump bypass), 45 (On pump bypass)
Test for heterogeneity: Chi² = 0.62, df = 1 (P = 0.73), I² = 0%
Test for overall effect: Z = 3.71 (P = 0.0002)

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Off pump bypass</th>
<th>On pump bypass</th>
<th>OR (random)</th>
<th>Weight</th>
<th>OR (random)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>95% CI</td>
<td></td>
<td>95% CI</td>
</tr>
<tr>
<td>02 Randomized controlled studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aiscione 1999</td>
<td>5/25</td>
<td>5/25</td>
<td>0.59</td>
<td>0.39</td>
<td>[0.10, 1.16]</td>
</tr>
<tr>
<td>Carrier 2003</td>
<td>2/28</td>
<td>5/37</td>
<td>2.11</td>
<td>0.49</td>
<td>[0.20, 0.83]</td>
</tr>
<tr>
<td>Kobayashi 2005</td>
<td>0/61</td>
<td>1/66</td>
<td>0.07</td>
<td>0.35</td>
<td>[0.09, 0.82]</td>
</tr>
<tr>
<td>Saji 2007</td>
<td>17/56</td>
<td>39/60</td>
<td>5.91</td>
<td>0.23</td>
<td>[0.11, 0.51]</td>
</tr>
<tr>
<td>Tang 2002</td>
<td>0/20</td>
<td>0/20</td>
<td>0.00</td>
<td>0.27</td>
<td>[0.01, 0.54]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>210</td>
<td>228</td>
<td>8.72</td>
<td>0.27</td>
<td>[0.13, 0.54]</td>
</tr>
</tbody>
</table>

Total events: 19 (Off pump bypass), 45 (On pump bypass)
Test for heterogeneity: Chi² = 0.62, df = 1 (P = 0.73), I² = 0%
Test for overall effect: Z = 3.71 (P = 0.0002)

Total (95% CI) 4464 17995 100.00 0.57 [0.43, 0.76]
Acute Kidney Requiring Dialysis

Review: Off pump bypass and acute kidney injury (Version 04)
Comparison: 01 Off pump vs on pump
Outcome: 01 Acute kidney injury requiring renal replacement therapy

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Off pump bypass n/N</th>
<th>On pump bypass n/N</th>
<th>OR (random) 95% CI</th>
<th>Weight %</th>
<th>OR (random) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Observational studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ascone 2001</td>
<td>3/51</td>
<td>32/202</td>
<td>4.20</td>
<td>0.33 [0.10, 1.13]</td>
<td></td>
</tr>
<tr>
<td>Beaufort 2004</td>
<td>6/149</td>
<td>10/103</td>
<td>5.81</td>
<td>0.31 [0.11, 0.87]</td>
<td></td>
</tr>
<tr>
<td>Bucur 2004</td>
<td>14/761</td>
<td>381/8870</td>
<td>21.76</td>
<td>0.42 [0.24, 0.72]</td>
<td></td>
</tr>
<tr>
<td>Chukwunemeka 2005</td>
<td>3/146</td>
<td>11/438</td>
<td>3.79</td>
<td>0.81 [0.22, 2.96]</td>
<td></td>
</tr>
<tr>
<td>Fisher 2006</td>
<td>0/313</td>
<td>19/2963</td>
<td>0.80</td>
<td>0.25 [0.01, 4.08]</td>
<td></td>
</tr>
<tr>
<td>Gamoso 2000</td>
<td>1/55</td>
<td>2/635</td>
<td>1.08</td>
<td>5.86 [0.52, 65.60]</td>
<td></td>
</tr>
<tr>
<td>Hayashi 2002</td>
<td>2/52</td>
<td>4/53</td>
<td>2.08</td>
<td>0.49 [0.09, 2.80]</td>
<td></td>
</tr>
<tr>
<td>Hirose 2001</td>
<td>2/16</td>
<td>6/43</td>
<td>2.15</td>
<td>0.80 [0.16, 4.09]</td>
<td></td>
</tr>
<tr>
<td>Hix 2005</td>
<td>17/1365</td>
<td>35/1365</td>
<td>18.48</td>
<td>0.49 [0.27, 0.86]</td>
<td></td>
</tr>
<tr>
<td>Loef 2002</td>
<td>0/10</td>
<td>0/12</td>
<td>Not estimable</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Massoudy 2008</td>
<td>4/100</td>
<td>12/101</td>
<td>4.63</td>
<td>0.31 [0.10, 0.99]</td>
<td></td>
</tr>
<tr>
<td>Schwanw 2004</td>
<td>1/220</td>
<td>0/119</td>
<td>0.61</td>
<td>1.63 [0.07, 40.40]</td>
<td></td>
</tr>
<tr>
<td>Weerasinha 2005</td>
<td>32/817</td>
<td>577/1224</td>
<td>32.26</td>
<td>0.85 [0.54, 1.30]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>16028</td>
<td>4094</td>
<td>97.64</td>
<td>0.54 [0.40, 0.73]</td>
<td></td>
</tr>
<tr>
<td>Total events: 85 (Off pump bypass), 568 (On pump bypass)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: Ch² = 12.63, df = 11 (P = 0.32), I² = 12.9%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 3.69 (P &lt; 0.0001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| 02 Randomized controlled trials |
| Ascone 1999 | 0/25 | 0/25 | 1.05 | Not estimable |
| Celik 2005 | 1/30 | 2/30 | 0.48 [0.04, 5.63] |
| Kobayashi 2005 | 0/61 | 1/86 | 0.35 [0.01, 8.71] |
| Saja 2007 | 0/6 | 3/60 | 0.15 [0.01, 2.98] |
| Tang 2002 | 0/20 | 0/20 | Not estimable |
| Subtotal (95% CI) | 212 | 211 | 2.36 | 0.31 [0.06, 1.59] |
| Total events: 1 (Off pump bypass), 6 (On pump bypass) |
| Test for heterogeneity: Ch² = 0.39, df = 2 (P = 0.82), I² = 0% |
| Test for overall effect: Z = 1.40 (P = 0.16) |

| Total (95% CI) | 4306 | 16249 | 100.00 | 0.55 [0.43, 0.71] |
| Total events: 86 (Off pump bypass), 574 (On pump bypass) |
| Test for heterogeneity: Ch² = 13.51, df = 14 (P = 0.49), I² = 0% |
| Test for overall effect: Z = 4.65 (P < 0.00001) |

Am J Kidney Dis 2009;54:413-423
Deep Sternal Wound Infection

- Historical incidence between 1-3%
- Reported mortality up to 20%
- Retrospective study of 3760 consecutive CABG patients from 1992-2002
- 1.1% developed DSWI
- Predictors
  - DM (OR 5.5)
  - Pre-op hemodynamic instability (OR 3.4)
  - Pre-op renal failure (OR 2.6)
  - Sepsis and/or endocarditis (OR 29.9)

Deep Sternal Wound Infection

- No difference in early mortality
- Large difference in long-term mortality
  - 1 yr: 93.6 vs 66.2%
  - 5 yrs: 82.3 vs 50.8%
  - 10 yrs 67.3 vs 40.6%

Blood Transfusions

- Association with ARF
- Association with respiratory failure
- Association with infections
  - Deep sternal wound infection
- STS reportable data

- Are there specific factors important in the CT surgical patient?
Age of RBC’s Important

- Decreased deformability
- Decreased ATP
- Decreased 2,3 DPG
- Decreased NO generation
- Increased adhesion to vascular endothelium
Duration of RBC Storage

- Hypothesis: Older blood worse
- By FDA: Can transfuse up to 42 days
- Single-center randomized prospective study
  - 2872 pts got new (<14 days old) blood
  - 3130 pts got old (>14 days old) blood
- Median storage
  - 11 days in newer arm
  - 20 days in older arm

Duration of RBC Storage

• Standard surgical / anesthesia practice
• All patients done on CPB
• Increased mortality with older blood
  – In hospital: 2.8 vs 1.4%
  – 1 yr: 11 vs 7.4% (NNT 28)
• Increased morbidity with older blood
  – Intubation > 72 hours: 9.7 vs 5.6%
  – Renal Failure: 2.7 vs 1.6%
  – Sepsis: 4 vs 2.8%

Kaplan-Meier Estimates of Survival and Death

Number of Red-Cell Units Transfused in Relation to the Percentage of Patients Receiving Transfusion

Stroke

Incidence approximately 1-2%
Multiple associated risk factors

- Carotid stenosis
- Prior stroke history
- Valve surgery
- Re-do heart surgery
- Duration of pump time
- Diabetes
- Aortic atherosclerosis
- Recent MI
- Age > 75 years
- Low CO
- Mod/severe LV dysfx
- HTN
- CRI

Independent predictors of postoperative stroke after CABG

- CRI
- Recent MI
- Previous CVA
- Carotid artery disease
- Diabetes
- Hypertension
- Moderate/severe LV dysfunction
- Age > 75 years
- Low cardiac output syndrome
- Post-op atrial fibrillation

OP-CABG and Stroke

• Meta-analysis of 41 RCTs comparing off-pump and on-pump CABG with stroke risk
• No difference in mortality on vs off pump
• Off-pump technique:
  – 50% relative risk reduction in stroke
  – 30% relative risk reduction in risk of afib
  – 48% relative risk reduction in wound infection
  – Significant increased risk of reintervention (RR1.9)

Stroke reported in the trials of off-pump surgery

Clinical outcomes in the trials of off-pump surgery


- Mortality
- Stroke
- Atrial fibrillation
- Wound infection
- Renal Failure
- Myocardial infarction
- Angina recurrence
- Re-intervention
- Cross-over

Relative risk

OP-CABG vs On-Pump CABG

• 2203 VA patients at 18 med centers randomly assigned to on or off-pump CABG

• Primary short-term endpoint: composite of death or complications
  – Reoperation, new mechanical support, cardiac arrest, coma, stroke, renal failure

• Primary long-term endpoint: composite of death or:
  – Repeat revascularization procedure, non-fatal MI

Results

• No significant difference in 30 day composite outcome
• No difference in overall survival between 2 groups
• Worse long-term composite outcome for off-pump than on-pump patients (9.9 vs 7.4%)
• Higher proportion of patients with fewer grafts than originally planned with off-pump technique
  • 17.8 vs 11.1%

Kaplan-Meier Estimates of Survival after Surgery

Summary

• CT surgery patients at high risk for post-op morbidity and mortality

• Atrial fibrillation
  – Long term mortality risks
  – Treat aggressively to restore SR and anticoagulation

• Acute kidney injury
  – Incidence increasing due to increasing patient age and severity of illness
  – Overall mortality decreasing due to improved dialysis
  – ? OP-CABG benefit
Summary

• Deep sternal wound infection
  – Associated with increased transfusions
  – High mortality
  – Associated with patient severity of illness

• Blood transfusions
  – Minimize transfusions if possible
  – Evidence to use newer RBCs

• Stroke
  – Severe morbidity and mortality
  – Occurs during perioperative period
  – ? Benefit with OP-CABG